CASE REPORT

Five-Site Disseminated Rifampicin-Resistant Tuberculosis with Marasmic Severe Acute Malnutrition in a 14-Year-Old Girl: An Eighteen-Month Longitudinal Observation in Which the Nutritional and Psychosocial Instruments Did Not Agree

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ABSTRACT

Background: Adolescent rifampicin-resistant tuberculosis is usually reported through microbiological and treatment-outcome endpoints, while nutritional and psychosocial recovery is described mainly in narrative terms.

Objective: To describe the 18-month course of five-site disseminated rifampicin-resistant tuberculosis with marasmic severe acute malnutrition and assess agreement among nutritional and psychosocial recovery instruments.

Methods: This CARE-guided longitudinal case report followed a 14-year-old Indonesian girl using serial clinical, laboratory, anthropometric, imaging, and psychosocial assessments during an all-oral bedaquiline-based regimen with nutritional support.

Results: Tuberculosis involved the lung, ovary, peritoneum, sacrum, and temporal bone. Weight increased from 31 to 45 kg, body-mass-index-for-age z score from −3.27 to −0.68, haemoglobin from 10.1 to 13.5 g/dL after a nadir of 8.7 g/dL, and quality of life from 61.25 to 85.75. Nutritional indices were irreconcilable at the same visit, and two behavioural screens remained normal despite a psychiatric diagnosis and impaired quality of life.

Conclusion: Microbiological, nutritional, and psychosocial recovery did not proceed synchronously, and instruments within the same domain could disagree. The absent mid-point height prevented temporal ordering of recovery; a ten-item minimum longitudinal data set is proposed.

1. Introduction

Tuberculosis caused by strains of *Mycobacterium tuberculosis* resistant to rifampicin remains one of the least well characterised infectious diseases of childhood and adolescence. Adolescents aged 10 to 19 years account for close to a tenth of annual global tuberculosis incidence, yet they are systematically under-represented in both paediatric and adult research programmes, falling between the two.[1] Approximately 30,000 children under 15 years develop multidrug-resistant tuberculosis each year, and only a small fraction are diagnosed, notified and treated.[2] Where programmatic cohorts do exist, the picture they give is sobering. In an eight-year retrospective cohort from Bandung, Indonesia, 84 children and adolescents with multidrug- or rifampicin-resistant disease included 69 (82%) adolescents aged 10 to 17 years and 54 (64%) who were malnourished; among the 69 with known outcomes, 48 (70%) were successfully treated, 14 (20%) died and 7 (10%) were lost to follow-up.[3] National registry data from Namibia cover 205 treatment episodes in children aged 0 to 14 years, with an unfavourable outcome in 46 individuals (24.1%) and 18 deaths (9.4%); the report expresses those proportions against the number of individuals treated, which is smaller than the number of episodes and is not stated,[4] and a programmatic cohort of 262 treatment episodes in Karachi, whose median age was 16 years, reported a favourable outcome in 194 (74.1%) with 26 (9.9%) deaths on treatment.[5]

The advent of all-oral bedaquiline-containing regimens has changed what is achievable. A multicentre matched cohort of 79 children found favourable outcomes in 100% of the bedaquiline group against 83.3% of injectable-treated controls, with fewer adverse events (48.6% against 71.4%).[6] A cohort of 105 Indian children over five years of age treated with longer oral bedaquiline-based regimens achieved treatment completion in 75 (71.43%) over a mean of 22.50 months, but adverse drug reactions occurred in 51 (48.6%), of which corrected QT interval prolongation in 25 (23.8%) was the commonest.[7] Ten Chinese adolescents on bedaquiline-containing regimens achieved 100% culture conversion by week 4, but five of the ten (50.0%) had an adverse event and leucopenia accounted for three of the six events recorded.[8] The oral regimens are more effective and more tolerable, but they are not without cost, and the determinants of that cost are measurable: bedaquiline exposure in older children and adolescents reaches the adult reference in a minority of patients,[9] and the odds of severe linezolid-associated anaemia rise 2.64-fold for every 1 g/dL by which the baseline haemoglobin is lower.[10]

Undernutrition and tuberculosis reinforce one another, and in children the relationship is quantitatively strong. In a cohort of 640 Ethiopian children, baseline undernutrition carried an adjusted risk ratio of 2.68 for an unfavourable treatment outcome, and among the subset who had been on treatment for two months or more, sustained undernutrition carried a ratio of 3.76.[11] Among 1658 Ugandan children with

tuberculosis, moderate malnutrition carried an adjusted hazard ratio for death of 2.22 and severe malnutrition 2.92.[12] Disease at multiple sites is the phenotype most strongly associated with poor nutritional status: in 368 Chinese children the prevalence of malnutrition was highest in those with tuberculosis at multiple sites (82 of 118, 69.5%) and in the 10 to 16 year age band (63 of 87, 72.4%); anaemia followed the same pattern by site, being commonest in the multiple-site group (67 of 95, 70.5%), but the opposite pattern by age, peaking at 48 of 68 (70.6%) in children aged 6 months to 2 years. Every child in that cohort had tuberculous meningitis, which our patient did not.[13] Among 339 adolescents receiving tuberculosis treatment in Dhaka, 14.2% were severely and 21.2% moderately malnourished by z score, and 59.3% were underweight.[14]

Adolescence adds a third dimension that neither the microbiological nor the nutritional literature captures well. Of 249 adolescents on treatment for rifampicin-susceptible tuberculosis in Lima, 98 (39%) had mild, 62 (25%) moderate and 33 (13%) severe depression.[15] Of 158 children and adolescents with tuberculosis who completed the Children's Depression Inventory, 146 (92.4%) had clinically significant depressive symptoms, and the highest risk band was 15 to 18 years.[16] Stigma in this age group is measurable and correlates with depression and suicidal ideation.[17] Qualitative work with adolescents and with children and their caregivers shows that the burden is not confined to the treatment period.[2,18] Yet health-related quality of life is rarely instrumented serially in this population, and when it has been measured in children with presumptive tuberculosis it did not distinguish them from symptomatic controls.[19]

What is largely absent from the literature is a single patient in whom all three domains — the mycobacterial, the nutritional and the psychosocial — were measured repeatedly with named instruments over the same period, so that the question of whether they recover together can actually be asked. The assumption embedded in routine practice is that they do: that as the organism is controlled the child eats, gains weight, returns to school and feels better, more or less in step. That assumption has never, to our knowledge, been tested against serial instrumented data in an adolescent with disseminated rifampicin-resistant disease.

Novelty and aim of the study. We report an adolescent girl with bacteriologically confirmed rifampicin-resistant tuberculosis involving five anatomical sites — lung, ovary, peritoneum, sacrum and temporal bone — coexisting with marasmic severe acute malnutrition, followed for 18 calendar months from July 2023 to December 2024 inclusive — 520 days from the first to the last recorded measurement — with 18 sets of laboratory measurements, serial anthropometry and three psychosocial instruments administered on three occasions, and reviewed again in mid-2026. To our knowledge this is the first report of paediatric rifampicin-resistant tuberculosis in which the nutritional and psychosocial trajectories are reported against published thresholds rather than described, and the first in which whether the record can order those threshold crossings at all is itself put to the test. Our aims were threefold: to describe the presentation and 18-month course of five-site rifampicin-resistant tuberculosis with marasmus in an adolescent treated with an all-oral bedaquiline-based long regimen; to determine, by computing every index from the raw measurements, when each domain crossed its own published threshold and whether the instruments used within each domain agreed with one another at the same visit; and to audit the record itself against the determinants of outcome that the recent primary literature quantifies, and to close with a numbered minimum data set that any programme following such a patient could adopt.

2. Methods

Case design and reporting framework

This CARE-guided, single-patient longitudinal case report was prepared from routine clinical records at a tertiary referral hospital in West Sumatera, Indonesia. The observation covered 18 calendar months from July 2023 to December 2024, with the most recent clinical contact reviewed in mid-2026.

Patient information and consent

Relevant history, examination findings, laboratory results, imaging, treatment records, anthropometric measurements, and psychosocial instrument scores were abstracted from the de-identified clinical record. Written informed consent for publication, including the clinical photographs, was obtained from the patient and her parent, and the patient provided written assent.

Clinical assessment, intervention, and follow-up

Diagnostic reasoning was based on bacteriological, histopathological, radiological, and clinical evidence. Treatment exposure, laboratory monitoring, anthropometry, and psychosocial outcomes were arranged chronologically and evaluated against the published thresholds stated in the Results and Discussion.

Ethical considerations

The report describes routine clinical care. All directly identifying information was removed, and facial and institutional identifiers were masked before reproduction.

3. Results

Presentation and referral pathway

A 14-year-old girl (age 14 years 3 months) was referred to the paediatric ward of a tertiary referral hospital in West Sumatera, Indonesia, in July 2023. Her presenting complaint was that she had not menstruated for three months. Menarche had occurred at the expected age and cycles had previously been regular at 28 days, lasting four to five days with three to four pad changes daily and no dysmenorrhoea. For the same three months she had had intermittent low-grade fever, worst at night and never measured, accompanied by night sweats but without rigors or seizures; an intermittent productive cough with sputum that was difficult to expectorate, without dyspnoea or haemoptysis; progressive anorexia, eating two to three times a day and finishing only a quarter to a half of a medium portion; and fatigue on minimal exertion. She had lost 7 kg in three months, from 38 kg to 31 kg. A painless swelling on the right side of the head, initially the size of a marble, had grown to the size of a table-tennis ball over the same three months; it is the lesion shown, after shaving of the overlying scalp, in Figure 1A. Low back pain had begun one month before referral, worse on walking and relieved by lying down.

Her grandfather, who lived in the same house, had been treated for pulmonary tuberculosis for six months and had completed treatment five years earlier; whether his isolate was drug-susceptible or drug-resistant was never established. Six other household members had been screened at the primary health centre by sputum smear alone, all negative, and none received preventive therapy at that time. She had received a complete primary immunisation schedule including bacille Calmette-Guerin, with a visible scar, and had no previous serious illness, surgery, chronic disease or

allergy. She was the second of four children and had a twin sister. Developmental milestones had been normal. Her mother was 162 cm and her father 172 cm tall, giving a mid-parental target height range of 152 to 169 cm.

The referral pathway is itself instructive. She had first been taken to a private hospital gynaecologist because of amenorrhoea and weight loss, and a suspected ovarian mass was diagnosed. A chest radiograph performed on 5 June 2023 was reported as showing a heart and lungs within normal limits with a scoliosis. Contrast-enhanced abdominal computed tomography on the same day showed destruction of the right side of the sacrum with a paravertebral abscess and was reported as peritonitis with suggestive tuberculous spondylitis of the sacrum, together with a suspected ovarian malignancy. She therefore underwent laparotomy and biopsy of the peritoneum and ovary on 26 June 2023. Histopathology showed adipose tissue infiltrated by lymphocytes, plasma cells, histiocytes and epithelioid cells in the peritoneum, and caseous necrosis with Langhans giant cell tubercles in the ovary, reported as chronic specific inflammation consistent with tuberculosis at both sites. Sputum Xpert MTB/RIF then detected *M. tuberculosis* at a very low level with rifampicin resistance detected, and a second consecutive assay detected it at a low level, again with rifampicin resistance. She was referred for definitive management. The clinical appearance at presentation, and the appearance of the right temporal swelling, are shown in Figure 1.

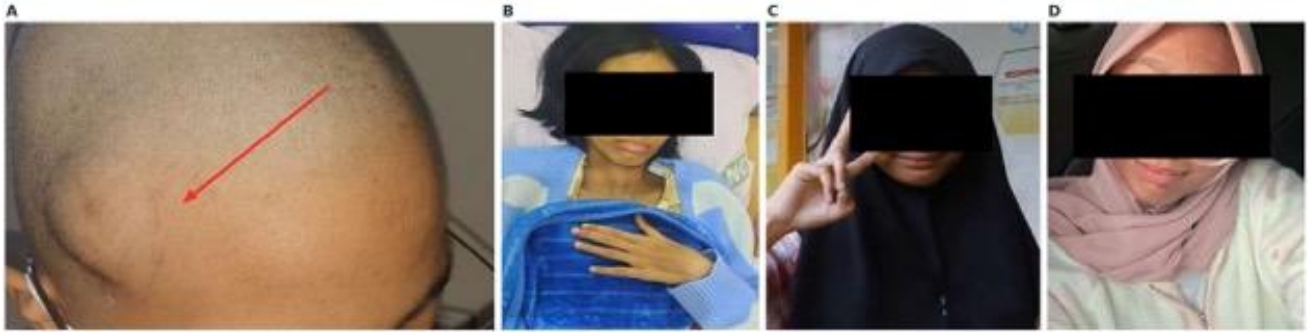

Figure 1. *Clinical photographs across the treatment course.* ***(A)*** *The shaved right temporal scalp at presentation; the arrow marks the site of the swelling, which is subtle in this projection and is demonstrated more convincingly on computed tomography (Figure 2C and 2D). The eyes are outside the frame.* ***(B)*** *General appearance on the day of admission in July 2023, showing generalised wasting with temporal hollowing and loss of subcutaneous fat, at a weight of 31 kg and a body-mass-index-for-age z score of -3.27.* ***(C)*** *28 June 2024, at month 12 of a clofazimine-containing regimen, showing the diffuse hyperpigmentation of the face and hand that is characteristic of clofazimine.* ***(D)*** *2026, approximately 19 months after the end of the formal observation period, showing progressive fading of the hyperpigmentation. The periocular region is masked in panels B, C and D. No photograph of any other person is reproduced. The panels were taken on different devices under different lighting, so the apparent change in skin tone is illustrative and not quantitative.*

Examination and anthropometry at presentation

She appeared moderately unwell but fully alert. The pulse was 86 beats per minute, the respiratory rate 21 per minute, the axillary temperature 37.0 °C and the oxygen saturation 99% in air. She weighed 31 kg and measured 150 cm, with a mid-upper arm circumference of 12 cm. The skin was thin and dry with markedly reduced subcutaneous fat and the ribs were prominent. A round, firm, well-circumscribed, non-tender mass measuring 3 × 3 × 1 cm was palpable in the right temporal region, without overlying erythema or warmth, as illustrated in Figure 1A. Multiple non-tender cervical lymph nodes about 1 cm in diameter were palpable on both sides. The conjunctivae were pale. Cardiovascular and respiratory examination was normal apart from the wasting; there was no retraction, wheeze or crackle. The abdomen was soft, with a 10 cm suprapubic laparotomy scar that was tender to palpation, no organomegaly and normal bowel sounds. There was no gibbus. Neurological examination was normal, with power 5 of 5 in all four limbs, normal reflexes and no pathological reflexes, although the lumbosacral region was tender. Pubertal staging was A2 M2 P2.

Computed from these measurements and the 2007 World Health Organization growth reference for 5 to 19 years,[20] her body mass index was 13.78 kg/m^2, giving a body-mass-index-for-age z score of -3.27 and a height-for-age z score of -1.50. A body-mass-index-for-age z score below -3 SD defines severe undernutrition in this age band, so the diagnosis of severe acute malnutrition is supported; the height-for-age z score places her within the normal range for stature. The margin on which the severity classification rests is small and we state it explicitly: at 150 cm and 171 months of age, a weight of 31.77 kg would have given a z score of exactly -3, so the classification of severe rather than moderate undernutrition rests on 0.77 kg, or, equivalently, on 1.8 cm of measured height, since at 31 kg a z score of exactly -3 corresponds to a height of 148.2 cm. The mid-upper arm circumference of 12 cm is not marginal in the same way: it lies far below any threshold that has been proposed for this age group, an issue we return to below.[21]

Investigations at presentation

Laboratory investigations performed on 5 July 2023 are set out in Table 1, together with their reference intervals. They showed an anaemia with a haemoglobin of 10.1 g/dL that the record labels microcytic and hypochromic, although the mean corpuscular volume of 79 fL, mean corpuscular haemoglobin of 26 pg and mean corpuscular haemoglobin concentration of 33% all lie at the lower limit of, but within, the reference interval, a leucocytosis of 15.09 × 10^3/mm^3 with 84% segmented neutrophils and only 7% lymphocytes, a reactive thrombocytosis of 568 × 10^3/mm^3, mild transaminitis, hyponatraemia at 129 mmol/L with hypokalaemia at 3.4 mmol/L and hypochloraemia at 92 mmol/L, and hypoalbuminaemia at 3.3 g/dL. Renal function and thyroid function were normal and a rapid test for human immunodeficiency virus was non-reactive. Three results deserve attention because they were not commented on in the source record: a fasting blood glucose of 63 mg/dL (3.50 mmol/L), a serum uric acid of 1.3 mg/dL and a high-density-lipoprotein cholesterol of 21 mg/dL. All three are the expected biochemical signature of prolonged energy and protein deficit, and the first of them proved to be the first of a series. All three are marked in Table 1, in which every value outside the reference interval is highlighted.

Table 1. Laboratory investigations at presentation.

Investigation	Result	Reference interval
Haemoglobin	**10.1 g/dL**	12.0-15.0
Haematocrit	**31%**	36-46
Erythrocytes	**3.94 × 10^6/µL**	4.0-5.2
Mean corpuscular volume	79 fL	78-95
Mean corpuscular haemoglobin	26 pg	26-32
Mean corpuscular haemoglobin concentration	33%	32-36
Reticulocytes	1.16%	0.5-2.5
Leucocytes	**15.09 × 10^3/mm^3**	4.5-13.5
Segmented neutrophils	**84%**	40-70
Band forms	1%	0-5
Lymphocytes	**7%**	20-45
Monocytes	8%	2-10
Eosinophils	**0%**	1-5
Basophils	0%	0-1
Platelets	**568 × 10^3/mm^3**	150-450
Aspartate aminotransferase	**61 U/L**	<40
Alanine aminotransferase	**64 U/L**	<41
Total bilirubin	*sample insufficient*	0.2-1.0
Urea	30 mg/dL	10-50
Creatinine	0.8 mg/dL	0.5-1.0
Albumin	**3.3 g/dL**	3.5-5.0
Sodium	**129 mmol/L**	135-145
Potassium	**3.4 mmol/L**	3.5-5.1
Chloride	**92 mmol/L**	98-107
Calcium	10.0 mg/dL	8.8-10.8
Magnesium	2.1 mg/dL	1.7-2.4
Fasting blood glucose	**63 mg/dL (3.50 mmol/L)**	70-100
Uric acid	**1.3 mg/dL**	2.5-6.0
Total cholesterol	99 mg/dL	<200
High-density-lipoprotein cholesterol	**21 mg/dL**	40 or above
Low-density-lipoprotein cholesterol	56 mg/dL	<130
Triglycerides	111 mg/dL	<150
Free thyroxine	14.02 pmol/L	12.0-22.0
Thyroid-stimulating hormone	1.54 µIU/mL	0.5-4.3
Anti-HIV rapid test	non-reactive	non-reactive
Sputum Xpert MTB/RIF, two consecutive assays (June 2023)	**MTB detected (very low, then low); rifampicin resistance detected**	MTB not detected

All results are those of 5 July 2023 except the sputum Xpert MTB/RIF assays, which were performed before referral in June 2023. Values outside the reference interval are shown in bold red; a grey cell indicates a result that was not obtained. AST, aspartate aminotransferase; ALT, alanine aminotransferase; HIV, human immunodeficiency virus; MTB, Mycobacterium tuberculosis; RIF, rifampicin. The leucocyte differential sums to 100%. Reference intervals are those of the reporting laboratory for an adolescent girl.

Imaging and bacteriological findings are shown in Figure 2. The chest radiograph shown in Figure 2A was reported as normal, and we concur on review: there is no consolidation, cavitation, effusion or convincing lymphadenopathy, in a girl whose sputum was Xpert MTB/RIF positive on two consecutive occasions. Sagittal reformatting of the abdominal computed tomogram, reproduced as Figure 2B, shows the lumbosacral spine with destruction of the right sacrum and an adjacent paravertebral collection. Cranial computed tomography without contrast on 18 August 2023, shown in Figure 2C, shows a rounded, well-defined hypodense soft-tissue mass of 8 to 14 Hounsfield units in the right temporal region measuring 1.2 × 4 × 5.7 cm, with destruction of the right temporal bone; the three-dimensional volume rendering of the affected side, shown in Figure 2D, shows the corresponding moth-eaten calvarial defect. The Xpert MTB/RIF report reproduced as Figure 2E records *M. tuberculosis* detected at a very low level with rifampicin resistance detected. The twelve-lead electrocardiogram recorded on 11 July 2023 is reproduced as Figure 2F and is discussed separately below.

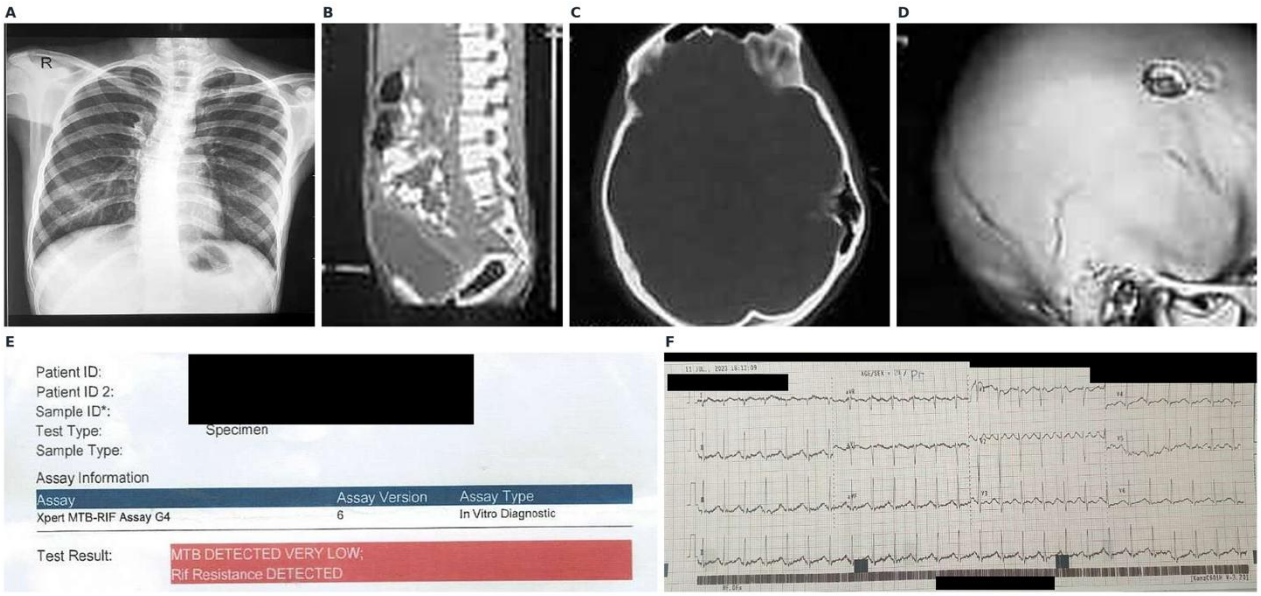

Figure 2. Imaging, bacteriological and electrocardiographic findings at presentation. ***(A)*** *Chest radiograph, 5 June 2023, reported as normal; no consolidation, cavitation, effusion or convincing lymphadenopathy is present, three to four weeks before two consecutive sputum Xpert MTB/RIF assays detected Mycobacterium tuberculosis with rifampicin resistance. Native resolution 409 × 399 pixels.* ***(B)*** *Sagittal reformat of the contrast-enhanced abdominal computed tomogram, 5 June 2023, showing the lumbosacral spine with destruction of the right sacrum and an adjacent paravertebral collection; native resolution 70 × 88 pixels.* ***(C)*** *Axial cranial computed tomogram, bone window, 18 August 2023, showing an expansile soft-tissue mass with adjacent cortical destruction; the slice is displayed in radiological convention, so the lesion, which lies on the viewer's left, is on the patient's right, concordant with the clinical and reported laterality. Native resolution 186 × 176 pixels.* ***(D)*** *Three-dimensional volume rendering of the calvarium from the same study, viewed from the side bearing the lesion, showing the moth-eaten lytic defect; native resolution 126 × 106 pixels.* ***(E)*** *Xpert MTB/RIF report of the first sputum specimen; patient identifiers have been masked.* ***(F)*** *Twelve-lead electrocardiogram recorded at 16:12 on 11 July 2023, the day before the first dose, reported as sinus rhythm at 150 beats per minute; re-measurement of the archived tracing at the standard paper speed of 25 mm/s gives a median R-R interval of 0.379 to 0.391 s, that is 153 to 158 beats per minute. No QT interval was measured or reported at this or any later date. Handwritten identifiers and the institutional footer have been masked. Every panel is a reproduction of a photograph of hard-copy film or paper and is below the resolution at which it could be independently re-reported.*

The five anatomical sites

Five anatomical sites were involved, each supported by a different kind of evidence and each therefore carrying a different level of diagnostic certainty. Because conflating them would overstate the case, the evidence for each is tabulated separately in Table 2. Two sites — the peritoneum and the ovary — are histologically proven. One — the lung — is bacteriologically proven by two consecutive molecular assays, with rifampicin resistance detected on both. Two — the sacrum and the right temporal bone — rest on characteristic cross-sectional imaging in a patient with proven tuberculosis elsewhere, without tissue from either site. Magnetic resonance imaging of the lumbar spine was recommended by the orthopaedic service and was never performed. This distribution is unusual but not unprecedented: in a series of 115 patients with bone tuberculosis, about 30% were first diagnosed in another organ, most often the lung, before dissemination to bone was recognised, and the spine was involved in 66%.[22] Calvarial tuberculosis is rarer; a series of 15 patients aged 12 to 45 years reported a mean symptom duration of 2.9 months and found that 11 of 15 could be managed conservatively.[23] Abdominal tuberculosis accounts for approximately 1 to 3% of all paediatric tuberculosis and no more than 10% of extrapulmonary presentations,[24] and in a cohort of 75 children with abdominal tuberculosis the mean age was 10.1 years with mesenteric nodes involved in 67% and the small intestine in 33%.[25] Osteoarticular disease at an unusual site is likewise recognised in children and is characteristically indolent: in five children with biopsy-proven tuberculosis of the talus the symptom duration ranged from three to 12 months and four of the five lesions were purely osseous, which matches the three-month history of a painless, slowly enlarging temporal swelling in our patient.[26] Female genital tuberculosis has a reported incidence above 1% in high-burden settings and its diagnosis rests on histopathology or microbiology because bacteriological testing is frequently omitted.[27] In a Syrian cohort of 129 children, microbiological confirmation was obtained in 76.5% of pulmonary but only 25.3% of extrapulmonary cases, and mortality was 16.8% among the extrapulmonary group.[28]

The Indonesian paediatric tuberculosis scoring system was applied and totalled 11 of a possible 13, comprising three points for a household contact with a positive sputum smear, three for a positive tuberculin test, two for clinical severe malnutrition, and one each for fever of more than two weeks, chronic cough of more than two weeks and cervical lymphadenopathy; the joint-swelling and chest-radiograph items scored zero. Two observations follow. First, two of the eleven points cannot be verified from the record. Three were awarded for a positive tuberculin test, but no tuberculin result appears anywhere else; and three were awarded for a household contact with a positive sputum smear, although the record states that the six household members who were screened were all smear-negative and that the grandfather's smear and resistance status five years earlier are unknown. Six of the eleven points therefore rest on items the record does not substantiate. Second, and more importantly, a clinical scoring system designed to support the diagnosis of drug-susceptible tuberculosis in resource-limited settings adds nothing to a case that is already bacteriologically confirmed with a molecular resistance result, and it cannot detect rifampicin resistance at all. The evidence that did establish the diagnosis is set out in Table 2 and illustrated in Figure 2. We record the score for completeness and note that the diagnosis rested entirely on the Xpert MTB/RIF result and the histopathology.

Table 2. The five anatomical sites of tuberculous involvement, with the evidence supporting each and the level of diagnostic certainty it confers.

Anatomical site	Modality and date	Finding	Level of diagnostic certainty
Lung	Sputum Xpert MTB/RIF, two consecutive assays, June 2023	*M. tuberculosis* detected (very low, then low) with rifampicin resistance detected on both; chest radiograph reported as normal	Bacteriologically confirmed, with molecular resistance result
Peritoneum	Laparotomy biopsy, 26 June 2023	Adipose tissue infiltrated by lymphocytes, plasma cells, histiocytes and epithelioid cells; chronic specific inflammation	Histologically proven
Ovary	Laparotomy biopsy, 26 June 2023	Caseous necrosis with Langhans giant cell tubercles	Histologically proven
Sacrum	Contrast abdominal computed tomography, 5 June 2023	Destruction of the right sacrum with an adjacent paravertebral abscess; reported as suggestive of tuberculous spondylitis	**Imaging only; no tissue obtained. Magnetic resonance imaging was recommended and never performed**
Right temporal bone	Cranial computed tomography without contrast, 18 August 2023	Rounded, well-defined hypodense soft-tissue mass of 8-14 Hounsfield units measuring 1.2 × 4 × 5.7 cm with destruction of the right temporal bone	**Imaging only; no tissue obtained**
Cervical lymph nodes	Clinical examination, July 2023	Multiple non-tender nodes of about 1 cm bilaterally; not sampled and not counted as one of the five sites	*Clinical only*

Red text marks a site for which no tissue diagnosis was obtained; the grey row records a clinical finding that was not sampled and is not counted among the five sites. M. tuberculosis, Mycobacterium tuberculosis. Cervical lymphadenopathy is listed for completeness but is not counted among the five sites because no node was aspirated or excised.

Treatment and monitoring

Before treatment began the patient and her family received structured education about the disease, the purpose and duration of treatment, the importance of adherence, the possible adverse effects and the prevention of transmission. Baseline evaluation included a full blood count, liver and renal function, electrolytes, albumin, blood glucose, thyroid function, human immunodeficiency virus testing, chest radiography, ophthalmological assessment and electrocardiography. She was reviewed jointly by the obstetric and gynaecological service, which agreed to co-manage her because of the ovarian involvement and the secondary amenorrhoea; by ophthalmology, which recorded a corrected visual acuity of 20/20 in each eye, normal anterior and posterior segments, normal intraocular pressure on palpation and normal colour vision; by child and adolescent psychiatry, which diagnosed an adjustment disorder with mixed emotional features and instituted supportive psychotherapy and family counselling without psychotropic medication; by neuropaediatrics, which advised surveillance for neurological deficit given the spinal and calvarial involvement; and by orthopaedics, which recommended magnetic resonance imaging of the lumbar spine. That recommendation, and the two sites for which no tissue was ever obtained, are recorded in the last column of Table 2.

She began an all-oral long regimen: bedaquiline 200 mg once daily for two weeks followed by 100 mg on Mondays, Wednesdays and Fridays for 22 weeks, together with levofloxacin 750 mg, linezolid 300 mg, clofazimine 100 mg and cycloserine 500 mg once daily and pyridoxine. Nutritional treatment consisted of an ordinary high-energy high-protein diet providing 1800 kcal per day with zinc 20 mg and folic acid 1 mg daily. The energy target was internally consistent with the dietetic assessment: an ideal body weight of 40 kg at a height age of 11 years 9 months multiplied by 60 kcal/kg gives a recommended daily allowance of 2400 kcal, of which 1800 kcal is 75%, while the Schofield-type estimate of basal metabolic rate from the actual weight (12.2 × 31 + 746 = 1124 kcal) multiplied by stress and activity factors of 1.3 and 1.2 gives a total energy expenditure of 1753 kcal, of which 1800 kcal is 103%. Planned monitoring comprised symptom review and adherence assessment at every visit, monthly blood counts, liver and renal function and electrolytes, serial electrocardiography, periodic ophthalmological assessment including visual fields, colour vision and contrast sensitivity, and serial anthropometry. The date on which the regimen began is the fifth event of the timeline in Figure 3; the results of the monitoring that was actually performed are tabulated date by date in Table 3; and the milligram doses stated here are the numerators of the weight-normalised exposures plotted in Figure 4F.

The twelve-lead electrocardiogram

A twelve-lead electrocardiogram was recorded at 16:12 on 11 July 2023, the day after admission and immediately before the regimen was started; the tracing is reproduced as Figure 2F. It was reported as sinus rhythm at 150 beats per minute with a non-prolonged PR interval, no ST-segment shift, normal T-wave amplitude, no QRS widening and no abnormal rhythm. We re-measured the archived tracing. The small-square period on the record is 3.386 pixels and the large-square period 16.86 pixels, giving 3.379 pixels per millimetre and, at the standard paper speed of 25 mm/s, 84.5 pixels per second. Automated R-wave detection across the rhythm strip and across lead I gave a median R-R interval of 0.379 to 0.391 s, corresponding to a rate of 153 to 158 beats per minute, in agreement with the rate printed in the record. Two things follow. First, a resting rate of about 155 beats per minute in a 14-year-old is a marked sinus tachycardia, and it cannot be reconciled with the pulse of 86 beats per minute documented at the physical examination the previous day; a pulse of 120 beats per minute was recorded at the semester I review, and 99 beats per minute at the home visit in November 2024. Second, and more consequentially, no QT interval and no corrected QT interval appear anywhere in the record, at this or any later date, and no further electrocardiogram is documented, in a patient who received bedaquiline, clofazimine and levofloxacin concurrently. At an R-R interval of 0.38 s the T wave and the following P wave overlap, so the end of the T wave cannot be identified with confidence on the archived paper tracing, and we have not attempted a retrospective measurement. That difficulty is itself part of the argument: the interval had to be measured at the time, on the machine, and it was not.

Course of treatment: semesters I to III

The course is summarised in Table 3, which lists all 18 sets of laboratory results obtained between 5 July 2023 and 6 December 2024, and in Figure 3, which places the clinical, radiological, laboratory and psychosocial events on a single timeline.

Table 3. Serial laboratory results, 5 July 2023 to 6 December 2024.

Date	Hb g/dL	WBC 10^3/mm^3	Plt 10^3/mm^3	MCV fL	Alb g/dL	AST U/L	ALT U/L	Na mmol/L	K mmol/L	Glucose mg/dL
5 Jul 2023	**10.1**	**15.09**	**568**	79	**3.3**	**61**	**64**	**129**	**3.4**	**63**
31 Jul 2023	**8.7**	13.05	305	85	**2.8**	25	17	138	**3.2**	*nr*
14 Aug 2023	**8.9**	**13.91**	320	89	3.6	21	6	139	3.6	*nr*
6 Sep 2023	12.9	11.27	364	85	3.8	28	10	137	4.1	**60**
27 Sep 2023	12.2	7.81	308	88	4.0	*nr*	*nr*	139	**3.4**	**61**
10 Nov 2023	**10.4**	5.47	240	87	3.8	*nr*	*nr*	138	3.5	*nr*
7 Dec 2023	**11.8**	4.76	213	82	4.0	34	19	137	3.9	75
9 Jan 2024	12.0	6.28	240	80	4.0	24	8	136	3.8	**69**
6 Feb 2024	12.8	5.94	265	83	4.1	37	14	136	4.2	*nr*
1 Mar 2024	12.6	6.22	260	84	*nr*	36	14	139	4.2	*nr*
2 Apr 2024	13.4	6.17	289	82	*nr*	28	11	138	4.0	*nr*
7 May 2024	13.3	**4.23**	**138**	83	*nr*	**42**	9	139	4.0	*nr*
3 Jun 2024	13.0	8.84	354	81	4.3	*nr*	*nr*	137	4.2	*nr*
9 Jul 2024	12.8	8.83	321	80	4.7	20	6	138	*nr*	*nr*
6 Aug 2024	12.4	9.84	298	80	4.6	19	7	139	4.1	80
6 Sep 2024	12.3	12.07	357	79	4.1	23	7	138	4.0	*nr*
5 Nov 2024	13.0	8.43	313	80	*nr*	35	12	140	4.1	*nr*
6 Dec 2024	13.5	8.22	344	80	*nr*	28	10	138	4.2	*nr*

Values outside the reference interval are shown in bold red; grey cells marked nr indicate that the test was not requested on that date. Hb, haemoglobin; WBC, leucocytes; Plt, platelets; MCV, mean corpuscular volume; Alb, albumin; AST, aspartate aminotransferase; ALT, alanine aminotransferase; Na, sodium; K, potassium; nr, not requested. The glucose value of 5 July 2023 was a fasting sample; the remainder were random samples. Reference intervals are given in Table 1.

Figure 3. *Clinical course from the onset of symptoms in April 2023 to the most recent contact in mid-2026. Colour groups the events by domain: navy for imaging, red for bacteriological and cardiac events, amber for anthropometry, green for treatment and recovery milestones and purple for psychosocial assessments.*

During the first semester (July to December 2023) she was admitted for one week to prepare for long-term treatment. Cough persisted with white sputum, without haemoptysis or dyspnoea; there was no fever and no jaundice; the scalp swelling did not enlarge; back pain persisted; appetite and oral intake were good. Menstruation resumed in the second month of treatment and cycles were regular at 28 to 30 days thereafter. The haematological response was not monotonic. Haemoglobin fell from 10.1 to 8.7 g/dL by day 26, and serum albumin fell from 3.3 to 2.8 g/dL over the same interval, before both rose steadily, as plotted in Figure 4C and Figure 4D; haemoglobin reached 12.9 g/dL by 6 September 2023 and 13.5 g/dL by the end of the observation. The leucocytosis resolved, falling from 15.09 to 4.76 × 10^3/mm^3 by December 2023, and the reactive thrombocytosis fell from 568 to 213 × 10^3/mm^3. Sodium normalised within the first month. Potassium was 3.4 mmol/L at baseline before the first dose, and three further values at or below 3.5 mmol/L were recorded on 31 July, 27 September and 10 November 2023 — 3.2, 3.4 and 3.5 mmol/L — all of them within the 24-week bedaquiline phase. Assessment of visual fields, Ishihara colour vision and contrast sensitivity during this semester was normal. That is the last documented ophthalmological assessment in the record.

During the second semester (January to June 2024) systemic symptoms continued to settle: fever and night sweats ceased, cough resolved, appetite improved and activity increased. Back pain diminished and she reported no limb weakness, paraesthesia or sphincter disturbance. The scalp mass did not enlarge and there were no features of raised intracranial pressure. Weight had reached 38 kg by June 2024. Neither height nor mid-upper arm circumference was measured at that visit. One laboratory finding in this period was not remarked on in the record and is, in our view, the single most important safety signal it contains: on 7 May 2024 the platelet count was 138 × 10^3/mm^3 and the leucocyte count 4.23 × 10^3/mm^3 on the same sample. These are the only platelet value below the reference interval and the lowest leucocyte value in the entire series, and they occurred together, at month 10 of continuous linezolid, in a patient whose haemoglobin had already fallen once; both values are marked in Figure 4C and Figure 4D. Both had recovered by 3 June 2024, when, as the thirteenth row of Table 3 records, the platelet count was 354 and the leucocyte count 8.84 × 10^3/mm^3. The record states that no acute complication requiring interruption of treatment was found.

During the third semester (July to December 2024) the clinical picture was of consolidation. At a home visit in November 2024 she appeared well, with no cough, fever, dyspnoea or night sweats, no nausea, vomiting or diarrhoea, and a good appetite. Menstruation was regular. The back pain had gone, with no gait disturbance, weakness, numbness or sphincter disturbance. The scalp swelling was no longer palpable. The pulse was 99 beats per minute, the respiratory rate 20 per minute and the temperature 36.8 °C. She weighed 45 kg and measured 155 cm with a mid-upper arm circumference of 16 cm. There was no lymphadenopathy, pallor, jaundice, respiratory abnormality or oedema. Treatment continued to completion. No follow-up sputum culture or molecular test, and no repeat imaging of the sacrum or the temporal bone, is documented at any point after the start of treatment; the assessment of cure rests on clinical grounds. The anthropometry of this visit is the November 2024 row of Table 4, and the laboratory results of this semester occupy the last four columns of Table 3.

Anthropometric trajectory

The anthropometric data, and the nutritional classification each index yields, are set out in Table 4 and plotted in panels A and B of Figure 4. Weight rose from 31 to 45 kg, a gain of 14 kg or 45.2%; height from 150 to 155 cm; and mid-upper arm circumference from 12 to 16 cm. The body-mass-index-for-age z score rose from -3.27 to -0.68, crossing the -2 SD boundary somewhere between July 2023 and November 2024. It cannot be located more precisely than that, because height was not measured in June 2024; using the two heights that bracket that visit, the z score at 38 kg lies somewhere between -2.07 and -1.47, an interval that straddles the boundary between moderate and normal, so the crossing may have occurred either before or after that visit. Only three weights, two heights and two arm circumferences were recorded in 18 months, which is why three of the four assessment columns of Table 4 contain grey cells and why the second point in Figure 4B is an interval rather than a point.

Table 4. Anthropometric trajectory and the nutritional classification produced by each of three indices at each assessment.

Index	Jul 2023	Jun 2024	Nov 2024	Jun-Jul 2026
Age (years:months)	14:03	15:02	15:07	17:02
Weight (kg)	31	38	45	45-47
Height (cm)	150	*not recorded*	155	155
Mid-upper arm circumference (cm)	**12**	*not recorded*	**16**	*not recorded*
Body mass index (kg/m^2)	**13.78**	*not recorded*	18.73	18.73-19.56
Body-mass-index-for-age z score	**-3.27**	**-2.07 to -1.47**	-0.68	-0.88 to -0.54
Height-for-age z score	-1.50	*not recorded*	-1.06	-1.18
Weight as% of the WHO median for height and age	**69.8%**	*not recorded*	91.3%	*not recorded*
Weight as% of the ideal body weight stated in the record	77.5%	*not recorded*	*not recorded*	*not recorded*
Classification by body-mass-index-for-age	**severe undernutrition**	**moderate or normal (indeterminate)**	normal	normal
Classification by% of median weight-for-height	**severe (69.8%) or moderate (77.5%), depending on the denominator used**	*not recorded*	normal	*not recorded*
Mid-upper arm circumference against the thresholds proposed for this age band	**far below**	*not recorded*	**below**	*not recorded*

Red marks a value or classification indicating undernutrition; grey cells indicate measurements that were never made. MUAC, mid-upper arm circumference; WHO, World Health Organization. z scores are computed from the raw measurements using the L, M and S coefficients of the WHO 2007 growth reference for girls: $z = [(BMI/M)^L - 1]/(L \times S)$ for body-mass-index-for-age, and $z = (height - M)/SD$ for height-for-age, height-for-age being normally distributed at these ages. The June 2024 body-mass-index-for-age entry is an interval rather than a point because height was not measured at that visit; the two bounds are obtained by substituting the heights recorded immediately before and immediately after it. The percentage-of-median row uses the WHO median body mass index for the patient's age applied to her measured height; the row below it uses the ideal body weight of 40 kg stated in the dietetic assessment. A third value of 67% appears in the source record and cannot be reconstructed from any stated denominator.

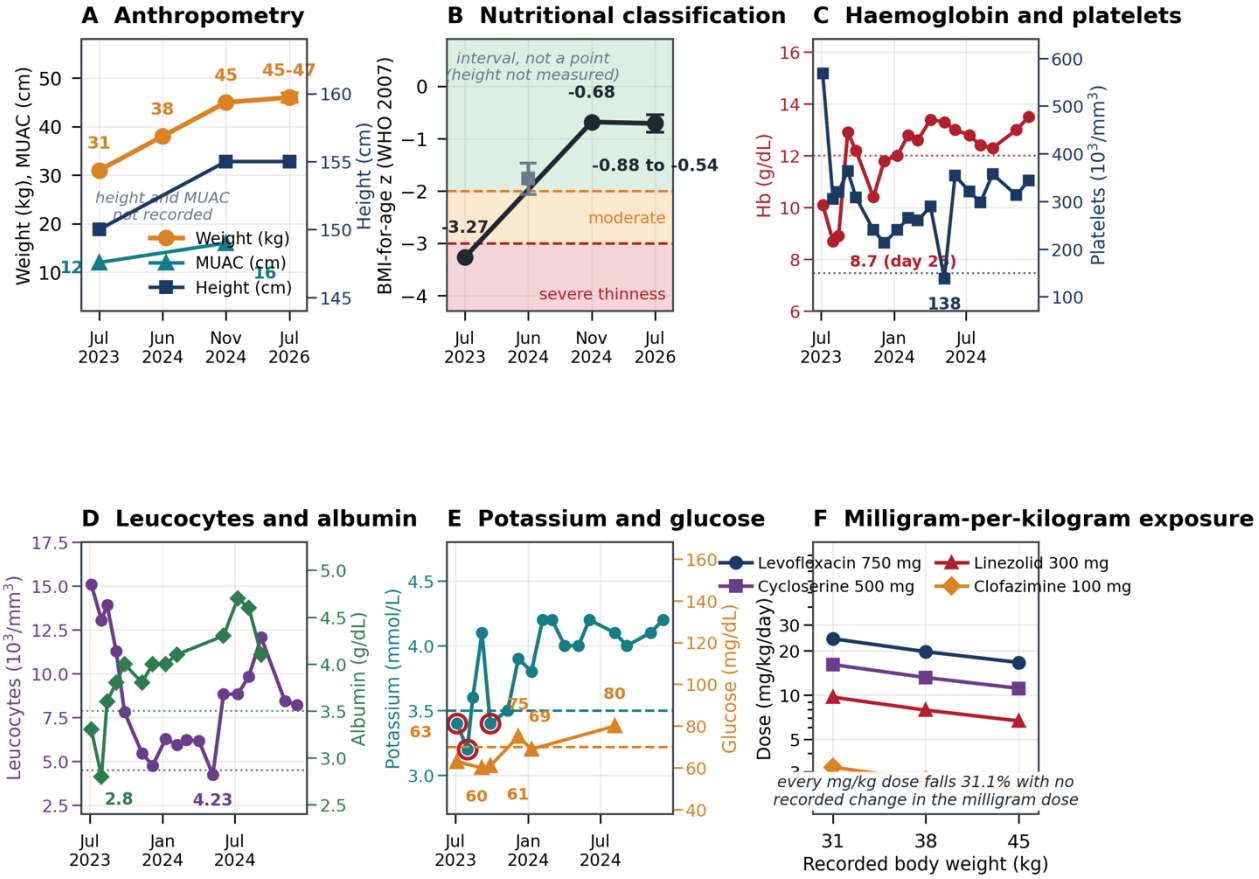

Figure 4. *Anthropometric, haematological, biochemical and pharmacological trajectories.* ***(A)*** *Weight at the four assessments at which it was recorded, height at three and mid-upper arm circumference at two; neither was measured in June 2024, and arm circumference was not measured at the final contact either. The final weight is drawn as the 45 to 47 kg range the record gives, not as a point.* ***(B)*** *Body-mass-index-for-age z score against the World Health Organization 2007 reference bands; the June 2024 point is drawn as an interval rather than a point because height was not measured, and the interval straddles the -2 SD boundary.* ***(C)*** *Haemoglobin and platelets across all 18 sampling dates; the dotted lines mark the lower reference limits of 12.0 g/dL and 150 × 10³/mm³.* ***(D)*** *Leucocytes and albumin, with lower reference limits of 4.5 × 10³/mm³ and 3.5 g/dL.* ***(E)*** *Potassium and blood glucose; the dashed lines mark 3.5 mmol/L and 70 mg/dL. The three values strictly below 3.5 mmol/L — 5 July, 31 July and 27 September 2023 — are ringed in red; a fourth value of exactly 3.5 mmol/L on 10 November 2023 is not ringed.* ***(F)*** *The weight-normalised dose of each of the four daily drugs at each of the three recorded weights, on a logarithmic scale.*

Three separate percentages of median weight-for-height appear in the source record for the same July 2023 assessment: 67%, approximately 68.9% and 77%. Two of them can be reconstructed. The dietetic assessment recorded an ideal body weight of 40 kg, derived from the median weight at her height age of 11 years 9 months, and 31/40 gives 77.5%. A denominator of 45 kg gives 68.9%, and the WHO median weight for a girl of her height and age, computed from the median body mass index of the reference at 171 months, is 44.4 kg, which gives 69.8%. The figure of 67% cannot be reconstructed from any denominator that appears in the record. This matters because the two reconstructible values fall on opposite sides of the classical 70% boundary between moderate and severe wasting. The index that the record printed to support the diagnosis of severe marasmic malnutrition does not, on its own arithmetic, support it; the index the record did not compute — body-mass-index-for-age z — does. Both reconstructible percentage-of-median values occupy their own rows of Table 4, and the note beneath that table states the denominator used for each.

Psychosocial trajectory

Three instruments were administered at the end of each semester: the 17-item Paediatric Symptom Checklist, the Strengths and Difficulties Questionnaire and the Paediatric Quality of Life Inventory version 4.0 Generic Core Scales. Their subscale scores, totals and published cut-offs are set out in Table 5, and they are plotted against those cut-offs in Figure 5. The Paediatric Symptom Checklist total fell from 3 to 2 to 1 against a positive-screen threshold of 15; the whole of the two-point fall is attributable to the internalising subscale, which fell from 2 to 1 to 0, while the attention subscale was 0 and the externalising subscale 1 at all three assessments.[29] The Strengths and Difficulties Questionnaire total difficulties score fell from 7 to 5 to 3 against a self-report abnormal band beginning at 20 and a borderline band beginning at 16; the emotional subscale contributed the largest part of that fall, from 3 to 2 to 1, and the prosocial score, which is not part of the total, rose from 8 to 9 to 10.[30,31] The instrument's structure — 25 items in five scales of five, with the total difficulties score the sum of all scales except the prosocial scale — is that of the original derivation paper;[30] the banding we have applied is the United Kingdom three-band solution as printed in a recent primary study.[31] Population-specific norms differ substantially: independently derived Dutch self-report cut-offs place the abnormal band at 16 rather than 20.[32] Our patient's highest total difficulties score of 7 lies below the abnormal band of every published norm set we could find, so the conclusion does not depend on which is chosen, as Figure 5B shows. Neither instrument was ever abnormal, or even borderline, on either the self-report or the parent-report bands; both lines stay well below the shaded bands of Figure 5A and Figure 5B throughout.

Table 5. The three psychosocial instruments: subscale and total scores at each of three assessments, the published thresholds, and the assessment at which each threshold was crossed.

Instrument and subscale	Range	Threshold	Sem I Dec 2023	Sem II Jun 2024	Sem III Dec 2024	Visit at which the threshold was crossed
PSC-17 internalising	0-10	5 or more	2	1	0	*never abnormal*
PSC-17 attention	0-10	7 or more	0	0	0	*never abnormal*
PSC-17 externalising	0-14	7 or more	1	1	1	*never abnormal*
PSC-17 total	0-34	15 or more	3	2	1	*never abnormal*
SDQ emotional symptoms	0-10	7 or more (self)	3	2	1	*never abnormal*
SDQ conduct problems	0-10	5 or more (self)	1	1	0	*never abnormal*
SDQ hyperactivity/inattention	0-10	7 or more (self)	1	1	1	*never abnormal*
SDQ peer problems	0-10	6 or more (self)	2	1	1	*never abnormal*
SDQ prosocial behaviour[a]	0-10	4 or less (self)	8	9	10	*never abnormal*
SDQ total difficulties	0-40	20 or more (self); 17 or more (parent)	7	5	3	*never abnormal*
PedsQL 4.0 physical functioning	0-100	72.98 (self); 63.28 (parent)	**60**	75	90	semester II, by 2.02 points
PedsQL 4.0 emotional functioning	0-100	59.57 (self); 63.29 (parent)	65	72	85	*never below either threshold*
PedsQL 4.0 social functioning	0-100	66.61 (self); 62.07 (parent)	75	80	88	*never below either threshold*
PedsQL 4.0 school functioning	0-100	62.99 (self); 56.75 (parent)	**45**	65	80	semester II, by 2.01 points
PedsQL 4.0 psychosocial summary	0-100	66.03 (self); 64.38 (parent)	**61.67**	72.33	84.33	semester II
PedsQL 4.0 total, as reported	0-100	69.71 (self); 65.42 (parent)	**61.25**	73.00	85.75	semester II, by 3.29 points
PedsQL 4.0 total, item-weighted[b]	0-100	69.71 (self); 65.42 (parent)	**61.09**	73.26	86.30	semester II, by 3.55 points

Red marks a score beyond its threshold in the impaired direction; grey marks a scale that never crossed its threshold. PSC-17, 17-item Paediatric Symptom Checklist; SDQ, Strengths and Difficulties Questionnaire; PedsQL, Paediatric Quality of Life Inventory. [a]The prosocial scale is scored in the opposite direction to the other four and is excluded from the total difficulties score. [b]The Paediatric Quality of Life Inventory Total Scale Score is properly the mean of all 23 items; because the physical domain contains 8 items and the other three contain 5 each, the item-weighted total differs slightly from the unweighted mean of the four domain scores that the source record reports. Both are given so that the reader can see that no threshold comparison changes. The SDQ thresholds shown are those of the original three-band solution for the self-completed version; the total difficulties score did not reach the borderline band of either the self-report or the parent-report banding at any assessment.

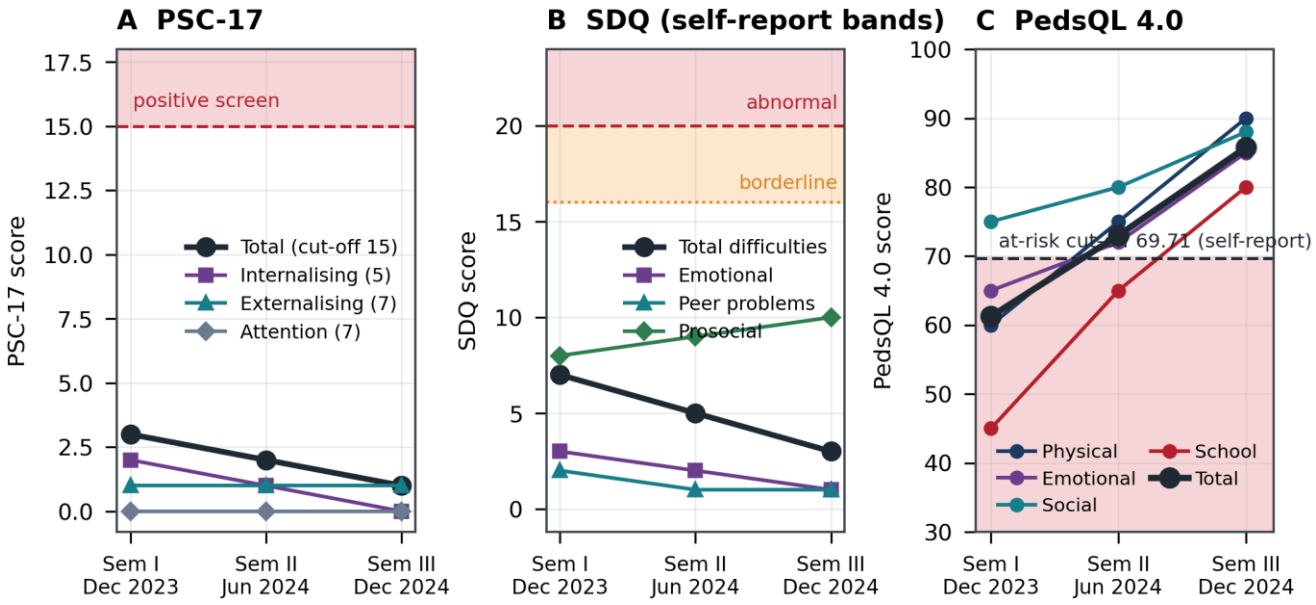

Figure 5. *The three psychosocial instruments plotted against their published thresholds. **(A)** The 17-item Paediatric Symptom Checklist; the shaded band marks a positive screen at a total of 15 or more. **(B)** The Strengths and Difficulties Questionnaire, with the original three-band solution for the self-completed version; the borderline band begins at 16 and the abnormal band at 20. **(C)** The Paediatric Quality of Life Inventory 4.0 by domain and in total; the shaded band marks scores below the at-risk cut-off of 69.71 for child self-report. Neither behavioural instrument entered its abnormal band at any assessment; the quality-of-life total began below its cut-off and crossed it between the first and second assessments.*

The Paediatric Quality of Life Inventory behaved differently. Reported as the unweighted mean of the four domain scores, the total was 61.25 at semester I, 73.00 at semester II and 85.75 at semester III. The published at-risk cut-off for impaired health-related quality of life is 69.71 for child self-report and 65.42 for parent proxy-report, both derived as one standard deviation below the mean of a population sample.[33] The semester I total lies below both, by 8.46 and 4.17 points respectively, so the conclusion does not depend on which report was used — a point worth making, because the source record contains both parent-report and self-report scoring sheets for all three semesters and does not state which set the tabulated totals came from. By semester II the total had crossed both cut-offs. We also note, because it changes nothing but ought to be stated, that the correct Paediatric Quality of Life Inventory Total Scale Score is the mean of all 23 items rather than of the four domain scores, and that because the physical domain contains 8 items and the others 5 each the item-weighted totals are 61.09, 73.26 and 86.30 — differing from the reported values by 0.16, 0.26 and 0.55 points and leaving every threshold comparison unchanged. Both totals are printed in the Paediatric Quality of Life Inventory block of Table 5, and the unweighted series is the heavy line of Figure 5C.[33]

Domain by domain the pattern is sharper still. At semester I only two of the four domains lay below their own at-risk cut-offs: school functioning at 45 against a self-report cut-off of 62.99 and a parent cut-off of 56.75, and physical functioning at 60 against cut-offs of 72.98 and 63.28. Emotional functioning at 65 and social functioning at 75 were above their cut-offs on both conventions. School functioning was the lowest domain at all three assessments and also the one that improved most, rising 35 points to 80, followed by physical functioning, which rose 30 points to 90; emotional and social functioning, which were never impaired, rose 20 and 13 points respectively. The claim that every domain had cleared its cut-off by semester II rests on narrow margins in exactly the two domains that had been impaired: physical functioning cleared its cut-off by 2.02 points and school functioning by 2.01 points, so a fall of just over two points in either would have reversed it. The four domain series and the two cut-off conventions against which they are judged are drawn together in Figure 5C, and the numbers behind them are the four domain rows of Table 5.

Outcome and current status

She completed the full course of treatment. The record does not state the date on which treatment was completed, so every interval after December 2024 is anchored to the end of the observation rather than to the end of treatment. When last reviewed in June and July 2026, at 17 years of age and approximately 19 months after the end of the formal observation period, her weight was stable at 45 to 47 kg with a height of 155 cm, giving a body-mass-index-for-age z score between -0.88 and -0.54 and a height-for-age z score of -1.18. She reported a weight difference of about 2 kg from her twin sister. She was in the final year of secondary school, attending normally and taking a full part in extracurricular activities. The clofazimine-associated hyperpigmentation that had appeared during treatment was still visible but had faded progressively, as the comparison between Figure 1C and Figure 1D shows. During 2024, while still on treatment, she accepted an invitation to speak at a national conference session on tuberculosis and undernutrition about her own experience — an outcome that none of the three instruments we administered is designed to capture, and which we mention because it is the clearest single indication that her social recovery outran the numbers. This event and the two follow-up reviews of 2026 are the closing entries of Figure 3.

Inconsistencies within the source record

We have handled the source record as data and report its internal disagreements and its material omissions rather than silently resolving them. Ten are relevant to the interpretation of this case. (i) The percentage of median weight-for-height at presentation is given as 67% in the clinical examination, as approximately 68.9% in the monitoring plan and as 77% in the dietetic assessment; only the last two can be reconstructed from a stated denominator, and they straddle the moderate-severe boundary. (ii) The right temporal mass is recorded as 3 × 3 × 1 cm on palpation in July 2023 and as 1.2 × 4 × 5.7 cm on computed tomography on 18 August 2023; the studies are five and a half weeks apart and the record elsewhere describes the mass as non-progressive, so the two descriptions cannot both be right unless it grew. (iii) The abdominal computed tomogram is dated 5 June 2023 in the narrative and 5 June 2024 in a figure legend; the earlier date is the only one compatible with the sequence of events. (iv) The heart rate is 86 beats per minute at the physical examination and 150 beats per minute on the electrocardiogram recorded the following day. (v) The patient's age is given as 16 years at the November 2024 home visit, but she was 14 years 3 months in July 2023, which makes her 15 years 7 months in November 2024. (vi) The tuberculin test is scored as positive, contributing 3 of the 11 scoring points, but no tuberculin result is reported anywhere. (vii) A figure legend describes the weight gain from 31 to 38 kg as averaging about 1 kg per month; over the six months of the second semester this is arithmetically defensible, but over the 11 months from the first recorded weight it is 0.64 kg per month, and over the whole 16-month interval from 31 to 45 kg it is 0.88 kg per month. (viii) The tabulated psychosocial scores do not state whether the Paediatric Quality of Life Inventory values are the adolescent self-report or the parent proxy-report, although scoring sheets for both appear in the record. (ix) The date on which treatment was completed is not stated anywhere, so no interval can be anchored to the end of treatment. (x) The anaemia is labelled microcytic and hypochromic, but the red-cell indices reported alongside it — a mean corpuscular volume of 79 fL, a mean corpuscular haemoglobin of 26 pg and a mean corpuscular haemoglobin concentration of 33% — all lie within the reference intervals of the reporting laboratory, at their lower limits; the mean corpuscular volume then rose to 89 fL within six weeks, which is against a fixed microcytic process. None of these alters the diagnosis or the outcome, and we report them because the reader is entitled to know the precision of the data on which the rest of this report rests.

4. Discussion

The three domains did not recover in step

The organising observation of this case is negative and, we think, useful. Over 18 months this girl recovered in three domains that are usually described together, and the record does not show that they recovered together. Two things can be said with confidence and one cannot, and separating them is the point. **First, a dated, same-record dissociation between the mycobacterial-inflammatory and the psychosocial domain.** By the sample of 7 December 2023 the leucocyte count had fallen from 15.09 to 4.76 and the platelet count from 568 to 213 × 10^3/mm^3, both within the reference interval; fever and night sweats had ceased during the same semester and menstruation had resumed in September 2023. At that same assessment the health-related

quality-of-life total was 61.25, below the at-risk cut-off on both scoring conventions. On one date, therefore, the systemic markers of infection were normal and the patient's own account of her functioning was not. **Second, disagreement between instruments within a single domain at a single visit** — illustrated in Figure 5 for the psychosocial instruments and in Table 4 for the nutritional indices — which we set out in the following nutritional and psychosocial subsections.

What cannot be said is the order in which the nutritional and psychosocial thresholds were crossed, and the reason is a single missing measurement. The quality-of-life total crossed its at-risk cut-off between the assessments of December 2023 and June 2024. The body-mass-index-for-age z score crossed the -2 SD boundary of moderate undernutrition somewhere between July 2023 and November 2024, and the record cannot narrow that window, because height was not measured at the June 2024 visit. The arithmetic is unforgiving: at 38 kg and 182 months of age the z score would be exactly -2.00 at a height of 154.5 cm, so the crossing had already occurred by June 2024 if she was shorter than that and had not if she was taller. She measured 150 cm eleven months earlier and 155 cm five months later. Linear interpolation between those two heights gives 153.4 cm in June 2024 and a z score of about -1.88, which would place the crossing before that visit and therefore possibly before, or at the same time as, the psychosocial crossing; but interpolation is an assumption and not a measurement, and the recorded data alone, set out in Figure 3 and in Table 4, bracket the nutritional crossing across a 16-month window that entirely contains the six-month window within which the psychosocial crossing occurred. No ordering follows. We state this rather than asserting the sequence that the interpolation suggests, because the whole argument of this report is that a recovery you have not measured is a recovery you cannot date.

That is not a null result. It is the finding, and it has a concrete consequence: the one measurement that would have ordered the two recoveries — a stadiometer reading at a routine outpatient visit — costs nothing, takes seconds, and was the only thing missing. It is item (4) of the minimum data set in the minimum-data-set subsection, and it is the gap that the grey cell in the June 2024 column of Table 4 and the error bar in Figure 4B both record. The practical importance is that weight and quality of life are commonly used as proxies for one another. In a cross-sectional study of 72 patients with drug-resistant tuberculosis in Botswana, physical and mental component summary scores were highest in the 13 to 24 month band and lower both earlier and later, a pattern that a simple monotonic recovery would not predict.[34] Serial interviews with 15 children and adolescents an average of 41 months after treatment completion found that physical, psychological and social effects persisted well beyond the end of treatment.[18] Neither observation is compatible with treating the domains as interchangeable, and neither can be checked against a record that measures one of them three times in 18 months, as the timeline in Figure 3 makes plain.

Which nutritional index? The percentage-of-median problem

The 2007 World Health Organization growth reference for school-aged children and adolescents was constructed for height-for-age, weight-for-age and body-mass-index-for-age.[20] Weight-for-height is not among its indicators, and weight-for-age is not published beyond the age of 10 years because it cannot distinguish height from mass during the pubertal growth spurt. For children and adolescents aged 5 to 19 years, severe undernutrition is defined by a body-mass-index-for-age z score below -3 SD and moderate undernutrition by a z score between -3 and -2 SD. Percentage of median weight-for-height, the index the source record used throughout, has no standing above the age of five, and this case shows concretely why that matters: it produced three mutually irreconcilable values for the same measurements, two of which fall on opposite sides of the classification boundary. The classification that each of the three indices yields at each assessment is set out side by side in Table 4.

The evidence that these systems are not interchangeable above five years of age is now substantial, although most of it comes from the paediatric eating-disorder literature rather than from global health. Percentage of median body mass index and body-mass-index z score are not interconvertible, and across ages 10 to 18 years the divergence between them is greatest at the lowest and highest z scores — precisely where a severely wasted patient sits.[35] In a study of 12,047 adolescents aged 12 to 19 years, expected body weight computed by the weight-for-stature method was on average 3.52% higher in girls than by the body-mass-index method, and the sensitivity of the body-mass-index method to detect adolescents whom the weight-for-stature method classified as below 75% of expected body weight was only 0.329.[36] In 97 young people with eating disorders the correlation between percentage of median body mass index and an individualised expected body mass index was only 0.29, with a mean difference of 7.3.[37] The direction of disagreement is not constant, which is why a single conversion factor cannot rescue the older index.

Mid-upper arm circumference tells a third story again, and in this case it is the most informative of the three. There is no World Health Organization or International Union Against Tuberculosis and Lung Disease cut-off defining severe acute malnutrition by mid-upper arm circumference in the 10 to 19 year age band; the only mortality-validated threshold is a mid-upper arm circumference-for-age z score, against which a value below -3 carried a hazard ratio for death within one year of 5.15 in a Kenyan cohort, and for which the area under the curve for one-year mortality was 0.73 against 0.58 for body-mass-index-for-age z score, with sensitivities at a -2 z score cut-off of 72% and 39% respectively.[21] In a retrospective study of 473 children, the correlation between mid-upper arm circumference severity and body-mass-index-for-age classification in those aged 5 years and over was strong (rho 0.649), yet agreement between the two categorical classifications across the whole cohort was only moderate, with a kappa of 0.55.[38] Our patient's arm circumference of 12 cm at presentation was far below any proposed adolescent threshold, and at 16 cm in November 2024 it was still below the values that have been proposed for a girl of 15 to 16 years, at a visit when her body-mass-index-for-age z score of -0.68 was comfortably normal and her percentage of the median weight for her height and age was 91.3%. Three indices, one visit, two incompatible answers. The record's own label at that visit was undernutrition, which agrees with the arm circumference and with neither of the other two — and, on the evidence above, the arm circumference is the index with the best claim to predict what actually matters. The disagreement is visible in the last three rows of Table 4.

What the psychosocial instruments did and did not detect

At every one of three assessments the Paediatric Symptom Checklist and the Strengths and Difficulties Questionnaire were normal, and not marginally so: the highest Paediatric Symptom Checklist total was 3 against a threshold of 15, and the highest total difficulties score was 7 against a self-report abnormal band beginning at 20 and a

parent-report band beginning at 17. Over the same period the same girl carried a diagnosis of adjustment disorder with mixed emotional features made by a child and adolescent psychiatrist, and a health-related quality-of-life score below the at-risk cut-off on both scoring conventions. The three instruments are set against one another, assessment by assessment and threshold by threshold, in Table 5, and the same comparison is drawn in the three panels of Figure 5. On the face of it the instruments disagree.

They do not, in fact, disagree; they measure different things, and the domain-level data show exactly where the difference lies. The Paediatric Symptom Checklist and the Strengths and Difficulties Questionnaire sample emotional and behavioural symptoms. The two Paediatric Quality of Life Inventory domains that were below their cut-offs at semester I were school functioning and physical functioning; emotional functioning and social functioning were above their cut-offs on both conventions. In other words the burden this girl was carrying at the end of her first semester of treatment was functional — she could not do what a 14-year-old does, and above all she could not be at school, which is the domain drawn lowest in Figure 5C and marked red in Table 5 — and it was not, at that point, symptomatic. A screening instrument designed to detect psychiatric disorder correctly reported that she did not have one. It was never designed to report that she was missing school, and it did not.

The practical implication is that using a behavioural screening instrument as the psychosocial monitoring tool for an adolescent on an 18-month regimen will systematically miss the commonest and most consequential burden. Of 249 adolescents on treatment for tuberculosis in Lima, 193 (78%) had at least mild depression, and symptoms and treatment side-effects correlated with depression severity, so behavioural instruments are certainly not useless in this population.[15] But when 158 children and adolescents with tuberculosis completed the Children's Depression Inventory, 146 (92.4%) had clinically significant depressive symptoms, a prevalence so high that it cannot be reconciled with our patient's uniformly normal behavioural screens unless the instruments are measuring different constructs or the thresholds behave very differently in different settings.[16] Health-related quality of life measured with a generic instrument in 201 children with presumptive tuberculosis did not distinguish those who turned out to have the disease from symptomatic controls,[19] which is a reminder that a functional instrument is not a diagnostic one. The domain-level divergence is drawn in Figure 5C, where the school functioning line begins 20 points below the emotional functioning line, closes 13 of those 20 points by the second assessment, and is still 5 points below it at the third. The conclusion we draw is narrow: report the domain scores, not only the totals, and pick the instrument whose construct matches the question being asked.

Two further features of these data deserve comment because they are easy to miss when only totals are reported. First, the entire two-point improvement in the Paediatric Symptom Checklist total is attributable to the internalising subscale; attention was 0 throughout and externalising was 1 throughout. A composite that changes only through one of its components is not the same as a composite that changes through all of them, and reporting only the total conceals which of them changed; every subscale is therefore given separately in Table 5. Second, the prosocial score of the Strengths and Difficulties Questionnaire, which is deliberately excluded from the total difficulties score, rose from 8 to 10, the top of its range; it is the only subscale of the two behavioural instruments on which a higher score is the better score, and it reached that maximum. Her social capacity was never the problem. That is consistent with what the qualitative literature describes in adolescents with tuberculosis, in whom anticipated stigma and disrupted schooling dominate over frank behavioural disturbance;[1] caregiver-reported anticipated stigma is documented in younger children too.[39] The contrast with another chronic infection is instructive: among children and adolescents with perinatally acquired human immunodeficiency virus infection assessed with the same self-report instrument, 72.9% had raised total difficulties scores, against a maximum of 7 of a possible 40 in our patient.[40]

The monitoring that was planned and the monitoring that happened

The regimen this girl received contained three drugs with recognised effects on ventricular repolarisation: bedaquiline, clofazimine and levofloxacin. The paediatric evidence is specific. In a pooled analysis of 88 children, a corrected QT interval by Fridericia's formula above 450 ms occurred at seven patient-visits, and two of those seven were on the exact combination of clofazimine, bedaquiline and levofloxacin that this patient received; the addition of clofazimine to moxifloxacin was associated with a 13.0 ms increase in the change in corrected QT interval.[41] In 54 children receiving clofazimine, a linear concentration-effect relationship on the corrected QT interval was demonstrated, with a slope of 0.05 ms per µg per litre.[42] In children given moxifloxacin, clofazimine use increased the maximum drug effect on the corrected QT interval 3.3-fold.[43] In adults the combination is more clearly dangerous: among 321 patients monitored prospectively in Taiwan, 59 (18.4%) had a corrected QT interval of 501 ms or more, clofazimine carried an adjusted hazard ratio of 4.35 for that endpoint; among the subgroup who received neither bedaquiline nor delamanid, clofazimine with high-dose moxifloxacin carried a ratio of 6.54 against a fluoroquinolone alone, a stratum that does not include patients such as ours; and four patients had documented ventricular tachycardia.[44] Among 202 patients on bedaquiline, concomitant clofazimine was associated with grade 3 or higher cardiac adverse events with an odds ratio of 3.66.[45] Among 410 participants in two trials, significant corrected QT prolongation occurred in 29 of 85 (34.1%) receiving bedaquiline with clofazimine, and nearly half of all such events occurred within four months of starting treatment.[46] In a retrospective comparison, 18 of 52 (34.6%) patients on bedaquiline combined with a fluoroquinolone or clofazimine had a change in corrected QT interval exceeding 60 ms, against 3 of 33 (9.1%) on bedaquiline alone, an adjusted risk 4.82 times higher.[47]

Against that background the record contains one electrocardiogram, taken before the first dose, on which no QT interval was measured, and no subsequent electrocardiogram at all. It also contains three potassium values at or below 3.5 mmol/L during the bedaquiline phase, and hypokalaemia is among the commonest adverse events of special interest in large drug-resistant tuberculosis cohorts — electrolyte depletion occurred in 26.0% of 2296 patients in the endTB cohort — and it lowers the threshold for torsadogenicity.[48] Nothing adverse happened, and the potassium values that would have mattered had it done so are plotted in Figure 4E and listed in Table 3. The point is not that harm occurred but that it could not have been detected: the one parameter that the choice of regimen itself made mandatory is among the several parameters the record never reports — the others being a tuberculin result, any follow-up bacteriology, any repeat imaging of the sacrum or the temporal bone, the recommended magnetic resonance image

of the lumbar spine, and the June 2024 height. It is worth stating plainly that the reassuring paediatric data are reassuring partly because those studies measured the interval. Two children in a bedaquiline pharmacokinetic study of 15 older children and adolescents had mild corrected QT prolongation that would not have been apparent clinically;[9] in a phase 2 trial of 30 paediatric patients no corrected QT interval above 460 ms was observed, which is only meaningful because it was looked for.[49]

A second cardiac observation follows from the same tracing and points in the opposite direction from what starvation physiology predicts. Sustained undernutrition in adolescents characteristically produces sinus bradycardia rather than tachycardia: in a cohort of 99 adolescents hospitalised for anorexia nervosa, severe bradycardia was the reason for 48% of admissions, recent weight loss was its independent predictor, and it normalised after a mean weight gain of 0.25 ± 0.18 kg per day for three to ten days.[50] A resting rate of about 155 beats per minute in a severely marasmic 14-year-old is therefore discordant with uncomplicated starvation physiology and should prompt a search for a superimposed process — active inflammation, hypovolaemia, anaemia, thyrotoxicosis or drug effect. The tracing on which this rate was measured is Figure 2F. In this patient the plausible contributors are all present at once: a haemoglobin of 10.1 g/dL falling to 8.7 g/dL, a leucocytosis of 15.09 × 10^3/mm^3, a platelet count of 568 × 10^3/mm^3 and active disease at five sites. Thyroid function was normal. The relevant comparison from the global-health literature is instructive rather than reassuring: among 88 Kenyan children with severe acute malnutrition — a much younger cohort, median age 19 months — the median admission heart rate was 132 beats per minute, which was *lower* than the 141 beats per minute of clinically matched non-malnourished controls, and over 6831 hours of continuous electrocardiographic monitoring only three malnourished children had any bradycardic episode; the authors concluded that there is little evidence that such children are at greater risk of cardiac dysfunction, although they did record significant ventricular arrhythmias in 33 of 55 malnourished children (60%) against 6 of 18 controls (33%) (p = 0.049). We note, against our own reading, that the direction of the heart-rate finding in that study depends on how it was measured: the admission twelve-lead rate was lower in the malnourished children, but on continuous monitoring their median hourly minimum and maximum rates were both higher than those of the controls, and by day 7 and day 28 the twelve-lead rates were non-significantly higher as well.[51] In other words tachycardia in acute severe malnutrition usually reflects the comorbid illness rather than the malnutrition, which is precisely how it should be read here. Sinus tachycardia is not itself dangerous. It matters because it shortens the R-R interval, and Bazett's correction, the one most commonly applied at the bedside, is least reliable at high rates — so the single electrocardiogram this patient had was recorded at the rate at which a corrected QT interval is hardest to interpret, and none was calculated. In the TB-PRACTECAL trial, 397 of 3744 recorded QTcF values exceeded 450 ms and only one exceeded 500 ms across 328 participants, the highest mean peak being 446.5 ms in the clofazimine-containing arm.[52]

The same argument applies to ophthalmological monitoring, though less sharply. Visual fields, colour vision and contrast sensitivity were assessed at baseline and once during the first semester, both normal, and not thereafter. The dates on which each blood count was taken, and the two dates on which the counts fell, can be read off Table 3 and Figure 4C. In a cohort of 132 patients on linezolid, the median time to optic neuritis was 8.3 months (interquartile range 6.2 to 10.7) and the median time to peripheral neuropathy 3.6 months (2.1 to 5.9).[53] The optic-neuritis window opens well after the last documented eye examination in this record; the peripheral-neuropathy window closes before the optic-neuritis window opens, and peripheral neuropathy was in any case assessed only by symptom enquiry and never by examination. In 81 patients with linezolid-related adverse events, 2 of 11 (18%) with optic neuropathy and 20 of 44 (45%) with peripheral neuropathy had not recovered one year after the drug was stopped, so these are not self-limiting problems.[54]

The haematological signal that was not acted on

Linezolid is the drug in this regimen most likely to have caused the haematological changes we observed, and the paediatric data allow the risk to be quantified for this particular patient. In 112 children with rifampicin-resistant tuberculosis, every 1 g/dL lower baseline haemoglobin raised the odds of grade 3 or 4 anaemia by 2.64, and every 1 mg/L.h higher linezolid area under the curve raised them by 1.012.[10] Our patient started with a haemoglobin of 10.1 g/dL, roughly 2 g/dL below the lower reference limit given in Table 1, and weighed 31 kg. In 132 patients, a linezolid dose of 12 mg/kg/day or more carried a hazard ratio of 6.62 for anaemia and 5.23 for leucopenia relative to lower doses.[53] At 31 kg, 300 mg daily is 9.68 mg/kg/day, below that threshold but not far below it. In 412 patients on linezolid-containing regimens in Uganda, first-detected anaemia, thrombocytopenia and leucopenia occurred in 88 (21.4%), 61 (14.8%) and 57 (13.8%) respectively, and patients with any haematological adverse event had lower treatment success (83.0% against 93.5%).[55] In 151 adults, linezolid was permanently stopped for toxicity in 32 (21%).[56] A brief report on South African children with rifampicin-resistant tuberculosis states that anaemia, thrombocytopenia and peripheral neuropathy were common, sometimes severe and often required active management, and that grade 3 or 4 events typically occurred after three or more months of treatment; no denominators are given in the published abstract, so we cite it for the pattern and not for a rate.[57]

Two events in this record fit that pattern. The first is the fall in haemoglobin from the 10.1 g/dL recorded in Table 1 to 8.7 g/dL over the first 26 days, concurrent with a fall in albumin from 3.3 to 2.8 g/dL. Both are equally consistent with the catabolic phase of severe tuberculosis and with early linezolid effect, and we cannot distinguish them; both recovered. The second is less ambiguous. On 7 May 2024, at month 10 of continuous linezolid, the platelet count was 138 × 10^3/mm^3 — the only value below the reference interval in 18 measurements — and the leucocyte count was 4.23 × 10^3/mm^3, the lowest in the series, on the same sample. Two cell lines fell together at one visit, at a time when the paediatric and adult literature predicts that grade 3 to 4 linezolid events occur, and the record does not mention it. Both had recovered a month later without a dose change, which is the most likely explanation — a transient, self-limited marrow effect. But the alternative reading, that this was the first appearance of a dose-related toxicity that would have progressed had exposure continued to rise, cannot be excluded from a single unrepeated sample, and it is the reading that would have mandated action. In 10 Chinese adolescents on bedaquiline-containing regimens, five (50.0%) had at least one adverse event and leucopenia was three of the six events reported.[8]

A falling milligram-per-kilogram exposure

Between the first and last recorded weights this girl gained 14 kg, an increase of 45.2%. The milligram doses of

levofloxacin, linezolid, clofazimine and cycloserine recorded in the first and second semesters are identical. It follows arithmetically that every weight-normalised dose fell by 31.1%: levofloxacin from 24.2 to 16.7 mg/kg/day, cycloserine from 16.1 to 11.1, linezolid from 9.68 to 6.67 and clofazimine from 3.23 to 2.22. All four are plotted on the logarithmic axis of Figure 4F. Whether that fall was clinically important cannot be determined from this record, and we do not assert that it was. What can be said is that it was not documented as a decision, that only three weights were recorded in 18 months in a patient whose principal comorbidity was undernutrition and whose drug doses are weight-banded, and that the direction of the change matters in both directions at once. Falling exposure reduces the risk of the dose-dependent linezolid toxicity described above,[53] and it simultaneously moves a patient away from the exposures at which efficacy has been demonstrated. Bedaquiline bioavailability in older children and adolescents is 57% of the adult value and the adult area-under-the-curve reference was attained in only 3 of 15 such patients,[9] so the margin for under-exposure in this age group is not generous. Modelling work has since proposed a simpler once-daily bedaquiline schedule, on the grounds that the complexity of the registered schedule is a barrier to uptake, and found that in children the cumulative exposure distributions of the two schedules differ by less than 5%.[58] In 23 children under five treated with bedaquiline and delamanid, weight gain was observed in 19 (82.6%), so weight change during treatment is the rule rather than the exception, although that series does not report its magnitude.[59] The practical point is small and cheap: weigh at every visit and record whether the dose band changed.

The glucose values nobody commented on

Six blood glucose measurements appear in this record across 13 months: 63 mg/dL fasting at baseline, then 60, 61, 75, 69 and 80 mg/dL as random samples. In millimoles per litre these are 3.50, 3.33, 3.39, 4.17, 3.83 and 4.44. Four of the six, tabulated in the last column of Table 3, lie below the 70 mg/dL (3.9 mmol/L) value conventionally used to define hypoglycaemia, and none reaches the 45 mg/dL threshold used to define dysglycaemia in a paediatric critical-care series in which dysglycaemia was present at admission in 139 of 481 (28.9%) children, hypoglycaemia in 24 (5.0%), and severe acute malnutrition was independently associated with it (adjusted odds ratio 3.09).[60] Symptomatic hypoglycaemia was an independent predictor of in-hospital death among 843 children with severe acute malnutrition.[61] The record contains no comment on any of the six values, no repeat within a single admission, and no glucose measurement at all after August 2024. All six are plotted against the 70 mg/dL line in Figure 4E, where the pattern that the individual results conceal becomes visible. We do not claim that this girl had clinically significant hypoglycaemia; she was ambulant, alert and asymptomatic, and the samples were not standardised for fasting state. We note, against our own reading, that the two lowest values (60 and 61 mg/dL, in September 2023) were recorded when the albumin had already returned to 3.8 and 4.0 g/dL, so they do not coincide with the period of greatest measured protein deficit, which the albumin column of Table 3 places in July 2023. We claim only that a persistently low-normal glucose in a severely marasmic adolescent is a finding, not a set of unrelated numbers, and that a pattern visible only when the values are tabulated is exactly the kind of pattern that serial single results conceal. Persistent dysglycaemia in the other direction is also relevant: among 125 adults with pulmonary tuberculosis it was present in 29.6% and was independently associated with unfavourable treatment outcomes (adjusted odds ratio 6.1).[62] Two further results listed in Table 1 belong to the same picture: a serum uric acid of 1.3 mg/dL and a high-density-lipoprotein cholesterol of 21 mg/dL, both of which are the biochemistry of prolonged energy and protein deficit rather than of any separate disorder. Longer-term, pooled data from 2251 participants across six cohorts found no overall association between prior malnutrition and diabetes risk, but did find that children of about 12 years who had been hospitalised with wasting before the age of two had a higher 120-minute glucose (difference 0.50 mmol/L, 95% CI 0.10 to 0.91), so the metabolic consequences of wasting may not be confined to the acute illness.[63]

A normal chest radiograph in bacteriologically confirmed disease

Her chest radiograph was reported as normal on 5 June 2023, three to four weeks before two consecutive sputum Xpert MTB/RIF assays detected *M. tuberculosis* with rifampicin resistance. This is not an error of reporting; it is the expected performance of the test. In a two-cohort study spanning high- and low-burden settings, the sensitivity of chest radiography for bacteriologically confirmed paediatric tuberculosis was 31.0% in Mozambique and 46.1% in Spain, with specificities of 94.7% and 96.5%, and interobserver agreement for tuberculosis-related findings was only fair, with intraclass correlations of 0.29 to 0.31.[64] In 181 children the specificity of chest radiography exceeded 75% while its sensitivity remained below 50%.[65] The features that do carry weight when present — enlarged perihilar or paratracheal nodes, bronchial compression, cavitation, pleural effusion — were absent here, and alveolar opacification, the finding most likely to be over-called, is not itself associated with confirmed disease.[66] The molecular tests behave in the mirror image: Xpert MTB/RIF Ultra had a sensitivity against culture of 55.0% and a specificity of 95.0% in 193 West African children,[67] and 45.0% sensitivity with 96.7% specificity in 391 Chinese children.[68] Both tests are specific and neither is sensitive. A normal chest radiograph in an adolescent with three months of cough, fever, night sweats and 7 kg of weight loss should not have reduced the index of suspicion. The radiograph itself is reproduced as Figure 2A so that the reader can see that there is nothing to find on it. In this case a normal film did not prevent the diagnosis only because an abdominal computed tomogram was performed for an unrelated reason.

Clofazimine hyperpigmentation and its psychosocial weight

Skin hyperpigmentation is among the most consistently reported adverse effects of clofazimine. In a pharmacovigilance analysis of 1287 clofazimine-related reports, skin hyperpigmentation was among the strongest disproportionality signals with a reporting odds ratio of about 13.07, the third strongest signal after QT prolongation at about 37.61 and drug resistance at about 17.31.[69] In 12 children given a novel clofazimine formulation, one of the two grade 3 adverse events possibly related to the drug was skin hyperpigmentation.[70] The Indonesian retrospective cohort of children and adolescents cited above recorded rash or hyperpigmentation among the grade 3 to 4 adverse events of 4 of its 74 treated patients.[3] The quantitative work on its social consequences comes from leprosy rather than tuberculosis: in 51 patients whose skin colour was measured objectively by spectrophotometric individual typology angle, hyperpigmentation was present in 100%, the mean stigma score on the Explanatory Model Interview Catalogue was 18.8, and the impact fell most heavily on the social domain.[71] Even so, when 23 participants in a therapeutic trial were

interviewed, most preferred a shorter clofazimine-containing regimen despite the pigmentation, and the authors suggest that preference for a longer regimen may have been influenced by anticipated concerns about inadvertent disclosure and by a belief that longer regimens were more potent, rather than by appearance itself.[72] That distinction is important and matches what we observed: the family's concern was not the colour but what the colour would reveal, and for most of the observation period they chose not to disclose the diagnosis to neighbours or classmates. The change in skin tone over the course of treatment is illustrated in Figure 1C and Figure 1D, taken 24 months apart.

In an adolescent girl this adverse effect sits directly on the developmental task of the age. Our patient's emotional and social quality-of-life domains were nevertheless above their at-risk cut-offs at every assessment, and her prosocial score rose to its ceiling, as the prosocial row of Table 5 and the green line of Figure 5B both show. By the third semester she had chosen to speak publicly about her illness. We would not generalise from one adolescent, and the counterfactual is unknowable; but the sequence recorded in Figure 3 — hyperpigmentation appearing, non-disclosure maintained, then voluntary public disclosure in a controlled and educational setting — is a plausible model of what supported adaptation to a visible drug effect looks like, and it is worth reporting because the qualitative literature on this population documents the opposite outcome much more often.[2,73]

The household, and the preventive therapy that was not given

The index contact for this girl was almost certainly her grandfather, who lived in the same house and had completed six months of treatment for pulmonary tuberculosis five years earlier with an unknown resistance pattern. Six household members, including her twin sister, were screened by sputum smear microscopy alone and none received preventive therapy. Smear microscopy is the least sensitive screening modality available and is not an appropriate instrument for household contact investigation: among 276 children living with patients with drug-resistant tuberculosis, 22 (8.0%) were started on treatment, of whom 5 of the 7 bacteriologically confirmed cases were asymptomatic, so symptom or smear screening alone would have missed them.[74] Among 850 household contacts of patients with rifampicin- or multidrug-resistant tuberculosis followed for a median of 51.4 weeks, the one-year cumulative incidence of infection was 21.6% in the 242 contacts in whom it could be assessed and the one-year cumulative incidence of disease was 2.3% in 742 contacts.[75] Among 785 young children exposed to multidrug-resistant tuberculosis in a randomised trial, 160 (20.4%) had a positive interferon-gamma release assay.[76]

Preventive treatment for such contacts now has trial evidence. In the TB-CHAMP cluster-randomised trial, 922 children from 497 households received levofloxacin or placebo; by week 48 tuberculosis had developed in 5 (1.1%) of the levofloxacin group and 12 (2.6%) of the placebo group, a hazard ratio of 0.44 with a confidence interval from 0.15 to 1.25 that crosses unity.[77] In VQUIN, 2041 contacts were randomised and confirmed tuberculosis occurred in 6 (0.6%) on levofloxacin against 11 (1.1%) on placebo, an incidence rate ratio of 0.55 with a confidence interval from 0.19 to 1.62.[78] Neither trial reached conventional significance individually, and we state that rather than describing the results as positive; both point in the same direction and both showed the regimen to be deliverable, with grade 3 or higher adverse events in 4 against 8 participants in TB-CHAMP. Programmatic experience confirms feasibility: of 112 child and adolescent household contacts of rifampicin-resistant index cases, 95 of 101 (94%) started preventive therapy, 79 of them levofloxacin, and 76 (80%) completed it.[79] Adherence is the practical limitation: among 911 children in TB-CHAMP, 135 (15%) discontinued early.[80] In this case preventive therapy was eventually given to a younger sibling in cooperation with the primary health centre, but not at the time of the index diagnosis and not, as far as the record shows, to the co-twin.

How this case compares with the published cohorts

Placed against the paediatric literature, this patient's outcome is at the favourable end and her presentation at the severe end. Her presenting body-mass-index-for-age z score of -3.27 places her in the 14.2% of 339 adolescents on tuberculosis treatment in Dhaka classified as severely malnourished by z score,[14] and in the same category as the 51 of 168 (30%) hospitalised Ugandan children with a weight-for-age z score below -3 SD in a series in which the whole-cohort in-hospital mortality was 34 of 199 (17.1%); in that series malnutrition was not itself an independent predictor of death, only tuberculous meningitis was.[81] Disease at five sites, detailed in Table 2, corresponds to the multiple-site group in which anaemia and malnutrition were commonest in that cohort, although every child in it also had tuberculous meningitis.[13] Her serial anthropometry is detailed in Table 4 and her serial laboratory results in Table 3. Her survival and functional recovery therefore sit against a background in which severe malnutrition carried an adjusted hazard ratio for death of 2.92,[12] and in which undernourished patients had twice the risk of an unsuccessful outcome.[82] Comparable treatment-success figures are 70% in the Indonesian adolescent-predominant cohort,[3] 72.8% in a Pakistani tertiary series,[83] 71.43% in the Indian bedaquiline cohort,[7] 83.4% among 1028 Ghanaian children with tuberculosis of all susceptibilities,[84] and 91.5% — 118 of the 129 children with a known outcome, from 136 enrolled — in a well-resourced prospective South African cohort.[85] A nationwide Belarusian cohort of 40 children and adolescents on bedaquiline- or delamanid-containing regimens achieved culture conversion in all 34 who were culture-positive at baseline, at a median of 1.1 months.[86] Weight gain during treatment is the norm and its velocity is measurable: in 152 children living with human immunodeficiency virus, those co-treated for tuberculosis had lower weight-for-age and height-for-age z scores over six months but a greater rate of increase in weight-for-age z score, that is, faster catch-up from a lower starting point.[87] Our patient's gain of 14 kg in 16 months is tabulated in Table 4; none of the series cited here reports a distribution of absolute weight gain against which it could be ranked, and we therefore make no comparative claim about it.

A minimum data set for the longitudinal follow-up of an adolescent on a long all-oral regimen

Auditing this record against the determinants of outcome that the recent primary literature quantifies produces a short list of measurements that were either never made or made too rarely to be interpretable. We set it out as a minimum data set, giving for each item the measurement, the moment at which it should be made, and the reason. The list has ten items. (1) **Corrected QT interval**, before the first dose and at weeks 2, 4, 8, 12 and 24 and thereafter as indicated, because bedaquiline, clofazimine and a fluoroquinolone were given together and nearly half of significant events occur within four months.[41,46] (2) **Serum potassium and magnesium** alongside every electrocardiogram, because electrolyte depletion occurred in 26.0% of 2296 patients on such

regimens and lowers the threshold for arrhythmia.[48] (3) **Weight at every visit, with the weight band and any dose change recorded explicitly**, because a 45% weight gain over 16 months changes every milligram-per-kilogram exposure by nearly a third. (4) **Height and mid-upper arm circumference at least three-monthly**, because body-mass-index-for-age cannot be computed without height, and the absence of a June 2024 height is the sole reason the nutritional threshold crossing in this case cannot be dated. (5) **Nutritional status expressed as body-mass-index-for-age z score, with mid-upper arm circumference reported alongside it**, and percentage of median weight-for-height abandoned above five years of age.[20,21] (6) **Full blood count monthly for the first six months and at least two-monthly thereafter, with any two-lineage change repeated within two weeks**, because grade 3 to 4 linezolid events cluster after three months and a single unrepeated bicytopenia cannot be interpreted.[10,53] (7) **Visual acuity, colour vision and contrast sensitivity at least six-monthly for as long as linezolid continues**, because the median time to optic neuritis is 8.3 months and recovery is incomplete in a fifth of those affected.[53,54] (8) **Follow-up bacteriology and, where a bone or joint lesion was the indication for a longer regimen, follow-up imaging of that site**, because the decision to stop rests on them. (9) **A function-based health-related quality-of-life instrument reported by domain, not a behavioural screening instrument alone**, because in this patient the two behavioural screens were normal at every assessment while the school and physical domains were below their at-risk cut-offs. (10) **Documented screening and preventive therapy status for every household contact by name**, because smear microscopy alone missed the opportunity here and levofloxacin preventive therapy has been tested in two randomised trials, both of which point to benefit without reaching conventional statistical significance individually.[77,78] None of these ten requires technology that was unavailable to this programme, and each of the ten corresponds to a point on the course set out in Figure 3 at which the measurement could have been made; three of them — items (5), (9) and (10) — require nothing beyond a decision to record or re-express a number the programme already generates, and the remaining seven require a test, a measurement or a repeat that this record shows was either not performed at all or not performed at the stated frequency.

Limitations

This is a single case and no causal inference is available from it. Several specific limitations qualify what we have reported. The observation was not designed prospectively as a research study, so the assessment intervals, which are set out in Figure 3 and in Table 5, were driven by clinical convenience: the psychosocial instruments were administered only three times, six months apart, which brackets the psychosocial crossing within a six-month window but fixes neither the order of the two crossings nor the interval between them. Height was not measured at the June 2024 visit, so the nutritional threshold crossing can be bracketed but not dated. The record does not state whether the tabulated quality-of-life scores are the adolescent self-report or the parent proxy-report; we have therefore evaluated every comparison against both sets of cut-offs and report that the conclusions are unchanged, but this is a workaround and not a substitute for knowing. Two of the five anatomical sites — the sacrum and the temporal bone — were never sampled histologically and rest on imaging in a patient with proven disease elsewhere; the alternative diagnoses at those two sites are unlikely but were not formally excluded, and the evidence that was obtained for each is set out in Table 2, and magnetic resonance imaging of the spine was recommended and never obtained. No follow-up bacteriology is documented, so bacteriological cure is inferred rather than demonstrated. All archived imaging exists only as photographs of hard-copy film, and the native pixel dimensions of each radiological panel in Figure 2 are stated in its legend; the panels are reproduced to document the findings, not to permit independent re-reading, and the abdominal computed tomogram in particular is well below the resolution at which a radiologist could re-report it. The photographs in Figure 1 were taken on different devices under different lighting, so the apparent change in skin tone is illustrative and not quantitative; clofazimine pigmentation was assessed clinically. The heart rate we report from the archived electrocardiogram is a re-measurement from a photograph of the paper tracing, corroborated by the rate the machine itself printed, and the QT interval could not be recovered from it. Finally, the patient has a twin sister living in the same household, who would have been an informative internal control for growth, exposure and outcome; her anthropometry was never systematically recorded and no measurement of any kind for her appears in the record, so the only comparison the record permits is a reported weight difference of about 2 kg some 19 months after the observation ended.

5. Conclusion

A 14-year-old Indonesian girl presented with rifampicin-resistant tuberculosis involving the lung, ovary, peritoneum, sacrum and right temporal bone together with marasmic severe acute malnutrition, and recovered on an all-oral bedaquiline-based long regimen with structured nutritional and psychosocial support. Eighteen months of serial measurement show two things. The first is that on a single dated occasion, 7 December 2023, the systemic markers of infection had normalised — leucocytes 4.76 and platelets 213 × 10^3/mm^3 — while the same girl's health-related quality of life remained below its at-risk cut-off on both scoring conventions, at 61.25. The second is that within each domain the instruments disagreed with one another at the same visit. At presentation, percentage of median weight-for-height appeared in the record in three mutually irreconcilable forms that straddle the moderate-severe boundary, while a body-mass-index-for-age z score of -3.27 and a mid-upper arm circumference of 12 cm both indicated severe disease; at the November 2024 visit the same three indices gave two incompatible answers. In the psychosocial domain, as set out in Table 5, two behavioural screening instruments were normal at every one of three assessments in a girl who simultaneously carried a psychiatric diagnosis and a quality-of-life score below its at-risk cut-off, because the burden she was carrying was functional rather than symptomatic.

What the record cannot show is the order in which the nutritional and psychosocial thresholds were crossed. The two windows overlap, and they overlap because height was not measured at the June 2024 visit — the single cheapest measurement in paediatrics, and the only one that would have separated them. That is the sharpest lesson of this case and it generalises: a recovery that has not been measured is a recovery that cannot be dated, and a domain measured three times in 18 months cannot be compared with one measured eighteen times.

Three practical conclusions follow. Nutritional status in a patient over five years of age should be expressed as body-mass-index-for-age z score, with mid-upper arm circumference reported alongside it, and percentage of median weight-for-height should not be used. Psychosocial monitoring during a long regimen should use a function-

based instrument reported by domain, because a behavioural screen will report correctly that an adolescent has no psychiatric disorder while missing the fact that she is not at school. And the parameters that a regimen is chosen to require monitoring of — here the corrected QT interval on three concurrent QT-prolonging drugs, and the weight that determines every milligram-per-kilogram exposure — must actually be measured and written down; in this record the corrected QT interval never was, and the weight was recorded three times in 18 months while every weight-normalised dose fell by 31.1%. We offer a ten-item minimum data set that would close each of these gaps; three of its ten items require nothing beyond a decision to record or re-express a number the programme already generates, and the remaining seven require a test, a measurement or a repeat that this record shows was either not performed at all or not performed at the stated frequency.

Declarations

Ethics approval

This report describes routine clinical care. Written informed consent for publication of this case report and of the accompanying clinical images was obtained from the patient's parent, and written assent was obtained from the patient herself. All directly identifying information has been removed: names, medical record numbers, addresses, telephone numbers and dates of birth do not appear in the manuscript or in any image, the periocular region has been masked in every photograph in which the face appears, and the institutional and patient identifiers burned into the radiological, molecular and electrocardiographic printouts have been removed before reproduction.

Consent for publication

Written informed consent for publication was obtained from the patient's parent and written assent from the patient. A copy is available to the Editor on request.

Data availability

All data supporting the findings are contained within the article. The anthropometric z scores were computed from the raw measurements using the published L, M and S coefficients of the 2007 World Health Organization growth reference for girls; the computation is stated in the text so that any reader can reproduce it.

Conflict of interest

The authors declare that they have no financial or non-financial conflicts of interest relevant to this work.

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Author contributions

All authors contributed to the clinical care of the patient, to the conception and drafting of the manuscript and to the critical revision of its intellectual content, and all have read and approved the final version. All authors agree to be accountable for all aspects of the work.

CARE guideline statement

This case report was prepared in accordance with the CARE guideline; the reporting framework is described in the Methods section.

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Use of artificial intelligence

No artificial intelligence (AI) tools were used in the preparation of this manuscript.

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