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Multifocal SAPHO-like osteomyelitis caused by Mycobacterium intracellulare as the presenting manifestation of de novo autosomal dominant partial IFN-γ receptor 1 deficiency: a case report

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Case Report

Keywords: Mendelian susceptibility to mycobacterial disease, IFNGR1, interferon-γ receptor 1 deficiency, Mycobacterium intracellulare, multifocal osteomyelitis, SAPHO syndrome, case report

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Multifocal SAPHO-like osteomyelitis caused by *Mycobacterium intracellulare* as the presenting manifestation of de novo autosomal dominant partial IFN-γ receptor 1 deficiency: a case report

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Abstract

Background: Multifocal bone lesions with repeatedly negative microbiological investigations are often attributed to chronic non-bacterial osteomyelitis (CNO), including SAPHO syndrome. Invasive infection, particularly due to non-tuberculous mycobacteria (NTM), can produce an almost identical clinical and radiological picture and may be the first manifestation of an inborn error of immunity.

Case presentation: An 18-year-old woman with clinically diagnosed mycobacterial bone and joint disease since infancy presented with six months of progressive low back pain. Imaging showed multifocal destructive lesions of the L2–L3 vertebral bodies, multiple ribs, the thoracic vertebrae and their appendages, the sacrum, both iliac bones and the scapula, together with acneiform skin lesions, suggesting SAPHO syndrome. Acid-fast staining, mycobacterial DNA and RNA, an *rpoB*-based assay, Xpert MTB/RIF, routine cultures and a 42-day mycobacterial liquid culture of the first vertebral biopsy were negative. A second vertebral biopsy became culture-positive after nine days of incubation, and the isolate was identified as *Mycobacterium intracellulare*. Genetic testing identified a de novo heterozygous pathogenic *IFNGR1* variant, NM_000416:c.819_822del (p.Asn274HisfsTer2), establishing autosomal dominant partial IFN-γ receptor 1 deficiency (immunodeficiency 27B; OMIM 615978). Multidrug antimycobacterial therapy was complicated by pruritus, fatigue and cytopenia and

required sequential drug withdrawal guided by therapeutic drug monitoring. After approximately 13 months of treatment, inflammatory markers had normalised and imaging showed partial improvement with residual bone lesions.

Conclusions: Invasive NTM disease should be excluded before multifocal bone lesions are attributed to SAPHO syndrome or CNO, particularly when a single biopsy is non-diagnostic or when there is a history of recurrent mycobacterial infection. Repeat biopsy with prolonged culture and genetic testing for Mendelian susceptibility to mycobacterial disease can establish the correct diagnosis and prevent inappropriate immunosuppressive treatment.

Keywords: Mendelian susceptibility to mycobacterial disease; *IFNGR1*; interferon-γ receptor 1 deficiency; *Mycobacterium intracellulare*; multifocal osteomyelitis; SAPHO syndrome; case report

Background

Multifocal bone lesions are a non-specific radiological pattern that may be produced by infectious osteomyelitis, chronic non-bacterial osteomyelitis (CNO), malignancy, metabolic disorders and rare inherited conditions [1]. Distinguishing infectious osteomyelitis from CNO is both the most important and the most difficult step, because the two entities overlap clinically and radiologically while their treatment is fundamentally different. CNO comprises autoinflammatory disorders of bone, including chronic recurrent multifocal osteomyelitis (CRMO) and SAPHO syndrome (synovitis, acne, pustulosis, hyperostosis and osteitis), which are managed with anti-

inflammatory and immunomodulatory therapy [1,2]; their imaging features overlap with those of infection and other condensing bone diseases [3]. Infectious osteomyelitis, in contrast, requires identification of the causative organism and prolonged antimicrobial treatment [4,5].

The diagnosis of SAPHO syndrome rests on characteristic osteoarticular involvement (most often the anterior chest wall, but also the sacroiliac joints, the spine and peripheral joints), skin manifestations such as palmoplantar pustulosis and severe acne, and — critically — the exclusion of infection, because no laboratory test or histological finding is diagnostic [2,3]. When a bone biopsy shows non-specific inflammation and cultures are negative, a sterile autoinflammatory process may be assumed. However, mycobacterial cultures require prolonged incubation, and the sensitivity of acid-fast staining, culture and *M. tuberculosis*-directed molecular assays is limited for non-tuberculous mycobacteria (NTM) [5,6]. Culture-independent methods such as metagenomic next-generation sequencing can improve pathogen detection in bone and joint infection [7,8], but they do not replace culture and remain dependent on the amount of organism present in the sampled tissue. A single negative biopsy therefore cannot exclude infection.

A small but important subset of patients with multifocal or recurrent mycobacterial bone disease has an inborn error of immunity affecting interferon-γ (IFN-γ) immunity, grouped under the term Mendelian susceptibility to mycobacterial disease (MSMD) [9,10]. MSMD is caused by pathogenic variants in more than 20 genes and results in impaired IFN-γ production or impaired cellular responses to IFN-γ, with a phenotype that ranges from localised, late-onset and relatively mild disease to life-threatening

disseminated infection after BCG vaccination [9–11]. Patients with autosomal dominant (AD) partial IFN-γ receptor 1 (IFN-γR1) deficiency present later than those with complete receptor deficiency, and osteomyelitis caused by *Mycobacterium avium* complex (MAC), single or multifocal, is characteristic [12–15]. Because impaired IFN-γ immunity is now recognised as a determinant of mycobacterial susceptibility in otherwise healthy individuals [16], and because disseminated *M. intracellulare* infection has been described in a child with *IFNGR1* deficiency [17], MSMD is increasingly recognised in adolescence and adulthood.

We report a young woman with recurrent mycobacterial bone and joint disease since infancy who presented at 18 years of age with multifocal bone lesions that were initially attributed to SAPHO syndrome. A second vertebral biopsy with prolonged culture identified *M. intracellulare*, and genetic testing revealed a de novo pathogenic *IFNGR1* variant.

Case presentation

The case is reported in accordance with the CARE guidelines [18]; the completed checklist is provided as Additional file 1. The timeline of the clinical course, from the first manifestations in infancy to the last follow-up, is shown in Figure 1.

History of recurrent mycobacterial disease

The patient was born to non-consanguineous parents with no family history of immunodeficiency or mycobacterial disease. At two months of age she developed right axillary lymphadenitis after BCG vaccination; the episode was treated surgically and

recorded as tuberculous lymphadenitis, without microbiological confirmation. Between the ages of 2 and 14 years she received oral antituberculous drugs for clinically diagnosed tuberculosis of the hip (2 years), the right ring finger (8 years), the left index finger (12 years, with surgical debridement) and the left elbow (14 years, with a regimen that included prothionamide, para-aminosalicylic acid and ethambutol and was continued until the age of 16). None of these episodes was supported by culture, molecular testing or histopathology, and no immunological evaluation was performed.

Initial presentation and evaluation

In July 2025, at the age of 18 years, the patient was admitted with low back pain that had progressed over approximately six months and had become disabling during the previous month, with bilateral pain radiating to the buttocks and lower limbs; she was unable to stand or walk for prolonged periods. Physical examination revealed tenderness and percussion pain of the paraspinal region from L1 to the sacrum and bilateral lumbar and gluteal pain; lower-limb muscle strength and tendon reflexes were normal, and the straight-leg-raising and femoral nerve stretch tests were negative. Acneiform skin lesions were present on the trunk and face. Her height was 165 cm and weight 85 kg (body mass index 31.2 kg/m^2). There was no fever, weight loss, night sweats, respiratory symptom or peripheral lymphadenopathy.

Laboratory investigation showed marked systemic inflammation: white blood cell count 10.2 × 10^9/L (neutrophils 6.63 × 10^9/L), haemoglobin 118 g/L, platelet count 450 × 10^9/L, C-reactive protein (CRP) 86.63 mg/L, erythrocyte sedimentation rate (ESR) 61 mm/h and serum amyloid A 762 mg/L (Table 1); serum albumin was mildly reduced at 37.1 g/L. Liver and renal function were otherwise normal. Immunoglobulin testing showed a

normal IgA level with mildly increased IgG, IgM, C3 and C4, consistent with the inflammatory state; immunofixation electrophoresis was normal, and antinuclear antibodies, antineutrophil cytoplasmic antibodies, rheumatoid factor, anti-cyclic citrullinated peptide antibodies and HLA-B27 were negative. Testing for human immunodeficiency virus and hepatitis B and C was negative, and T-SPOT.TB was negative.

Imaging

Imaging demonstrated multifocal skeletal disease. Lumbar computed tomography (CT) on 10 July 2025 showed irregular destruction of the L2 and L3 vertebral bodies with narrowing of the adjacent disc space and mild paravertebral soft-tissue swelling (Figure 2A, C). Chest CT on 11 July 2025 showed cortical thickening, partial destruction and periosteal reaction of the left third, fourth and sixth ribs, and pelvic CT on 16 July 2025 showed multifocal destruction of both iliac bones and the sacrum. Magnetic resonance imaging (MRI) on 19 August 2025 showed abnormal signal involving the L2–L5 vertebral bodies, the upper sacrum and both iliac bones, most marked at L2–L3, with narrowing of the L2–L3 disc space (Figure 3A). CT on 19 October 2025 documented lesions of the left third, fourth and sixth and the right fifth and seventh ribs, the right T1–T2 and left T8 appendages, the T2 and T9 vertebral bodies, the L2–L3 vertebral bodies and the inferior angle of the left scapula (Figure 4A, C).

Initial investigations and the working diagnosis of SAPHO syndrome

Biopsy of the right L2 vertebral body was performed on 10 July 2025. Histopathology showed necrotic bone fragments, proliferating cartilage and spindle cells with marked

crush artefact, without evidence of tuberculosis or malignancy, and acid-fast staining was negative (Table 2). Testing of the specimen was negative for *M. tuberculosis* and NTM DNA, *M. tuberculosis* RNA and *M. tuberculosis* complex DNA (*rpoB*); Xpert MTB/RIF was negative, routine bacterial and fungal cultures showed no growth, and a mycobacterial liquid culture (BACTEC MGIT 960) showed no growth after 42 days of incubation. Because the clinical and radiological picture — multifocal osteitis of the spine, ribs, sacroiliac region and iliac bones with acneiform skin lesions and a negative first biopsy — was compatible with an autoinflammatory bone disease, a multidisciplinary meeting concluded that the evidence for tuberculosis was insufficient and that SAPHO syndrome should be considered; sulfasalazine was started empirically on 23 July 2025 while an infectious cause was still being pursued.

Second biopsy and identification of *Mycobacterium intracellulare*

Given the history of recurrent mycobacterial infection and the inconclusive first evaluation, a second vertebral biopsy (right L3) was performed on 18 July 2025. Histopathology showed fragmented necrotic bone, marrow fibrosis, fibrous tissue proliferation and a sparse chronic inflammatory infiltrate, without evidence of tuberculosis, metastatic carcinoma or Langerhans cell histiocytosis; reticulin staining was markedly increased (MF grade 3) and Congo red staining was negative. Acid-fast staining and routine bacterial culture were again negative, but a mycobacterial liquid culture became positive after nine days of incubation and the isolate was identified as *M. intracellulare* (Table 2). The working diagnosis of SAPHO syndrome was therefore abandoned, and multidrug antimycobacterial treatment was planned.

Genetic diagnosis of MSMD

Because of the early onset and lifelong recurrence of mycobacterial disease, genetic testing was performed. Targeted sequencing of genes associated with inherited immunodeficiency in peripheral blood identified a heterozygous frameshift variant in *IFNGR1*, NM_000416:c.819_822del, p.(Asn274HisfsTer2) (chr6:137522057, GRCh37). The variant is absent from population databases, is recorded in the Human Gene Mutation Database as a disease-causing variant and was classified as pathogenic according to ACMG criteria. Family testing showed that the patient carried the variant (AT/−) whereas both parents were homozygous for the reference allele (AT/AT), indicating a de novo origin. This established a diagnosis of immunodeficiency 27B (OMIM 615978), that is, AD partial IFN-γR1 deficiency. Two additional heterozygous *TYK2* missense variants (p.Arg703Trp, inherited from the father, and p.Arg701Thr, inherited from the mother) were reported as supplementary findings; neither has been established as pathogenic in this patient, and no functional studies were performed.

Treatment, adverse events and follow-up

Antimycobacterial treatment was started in August 2025 with azithromycin 500 mg daily, amikacin 600 mg daily intramuscularly, rifabutin 300 mg daily and linezolid 600 mg twice daily, and was adjusted in early September 2025 at a tertiary referral centre to azithromycin 500 mg daily, amikacin 600 mg every other day, rifabutin 300 mg daily, linezolid 600 mg every other day and ethambutol 750 mg daily (Table 3). Treatment was complicated by pruritus attributed to ethambutol in September 2025, which improved after ethambutol was withdrawn; linezolid was stopped in November 2025 because of fatigue and anorexia, and ethambutol was reintroduced without recurrence of pruritus;

amikacin was discontinued in December 2025. The maintenance regimen consisted of azithromycin 500 mg, rifabutin 300 mg and ethambutol 1000 mg daily, with ethambutol omitted from some prescriptions. Therapeutic drug monitoring in August 2025 showed a linezolid trough concentration of 8.53 μg/mL (reference 2–8 μg/mL) and a rifabutin peak concentration of 0.28 μg/mL (reference 0.45–0.9 μg/mL). Mild neutropenia (absolute neutrophil count 1.57×10^9/L) and intermittent elevation of alanine aminotransferase (49 U/L) were observed, with stable renal function throughout.

The clinical response was favourable: back pain resolved and mobility returned. CRP fell from 86.63 mg/L at presentation to 2.63 mg/L by October 2025 and remained within the normal range thereafter, while ESR fell from 61 mm/h to 6–9 mm/h (Table 1, Figure 5). CT on 17 January 2026 showed increased bone density at the L2–L3 level (Figure 2B, D), MRI on 16 June 2026 showed regression of the previously abnormal marrow signal (Figure 3B), and CT on 16 August 2026 showed partial improvement of the thoracic, rib, scapular and sternal lesions compared with October 2025 (Figure 4B, D), although residual bone lesions persisted. At the last clinical review on 16 August 2026 the patient had no back pain, pruritus or lower-limb paraesthesia, and antimycobacterial treatment was still ongoing in September 2026. No interferon-γ therapy or haematopoietic stem cell transplantation was given.

Discussion and Conclusions

Multifocal osteitis mimicking SAPHO syndrome

Multifocal osteitis of the spine, ribs, sacroiliac region and iliac bones with acneiform skin lesions and a negative first biopsy made SAPHO syndrome a reasonable initial diagnosis. SAPHO syndrome is defined by osteoarticular manifestations together with palmoplantar pustulosis, severe acne or hidradenitis suppurativa, and its diagnosis requires the exclusion of infection, tumour and other causes of condensing bone disease, because neither laboratory tests nor imaging findings are specific [2,3]. Imaging does not resolve the ambiguity: vertebral corner lesions, paravertebral ossification, sacroiliitis and hyperostosis overlap with the features of infectious spondylitis [3]. Chronic multifocal osteomyelitis caused by MAC has been reported in adults in whom the diagnosis was reached only after repeated sampling [19], and in a multicentre cohort of patients with bone and joint NTM infection the clinical presentation overlapped substantially with that of non-infectious inflammatory bone disease, while outcomes differed according to immune status [20]. In our patient infection was ultimately demonstrated only by culture, after immunosuppressive treatment had already been started.

Why the first evaluation was negative, and why repeat sampling matters

Mycobacteria grow slowly and may be present in low numbers in bone, so that culture sensitivity depends on the amount and quality of tissue obtained, on previous antimycobacterial exposure and on the duration of incubation [4–6]. Acid-fast staining has low sensitivity, and *M. tuberculosis*-specific assays such as Xpert MTB/RIF and

rpoB-based tests do not detect NTM [5,6]. In our patient the first specimen was negative on all of these tests and remained culture-negative after 42 days, whereas a subsequent specimen became positive after nine days of incubation; histopathology was equally unhelpful, showing necrotic bone, fibrosis and sparse non-specific inflammation without granulomas, and the marked reticulin fibrosis (MF grade 3) prompted a recommendation for bone marrow examination. Vertebral osteomyelitis due to NTM is uncommon and indolent, and diagnosis is typically delayed by months [6,21,22]. Culture-independent methods such as metagenomic next-generation sequencing can improve pathogen detection in bone and joint infection and in osteoarticular tuberculosis with negative conventional cultures [7,8], but they do not replace prolonged mycobacterial culture and remain dependent on the sampled tissue. Our case therefore supports a practical rule: when multifocal bone lesions are accompanied by any history of mycobacterial disease, a single negative biopsy should not be accepted as evidence of a sterile process.

The underlying inborn error of immunity

Recurrent bone and joint disease beginning with BCG-associated lymphadenitis at two months of age was the decisive clue to an underlying immunodeficiency. MSMD comprises inborn errors of immunity caused by pathogenic variants in genes of the IL-12/IFN-γ circuit; all of them impair IFN-γ production or the cellular response to IFN-γ, resulting in selective susceptibility to weakly virulent mycobacteria including BCG and environmental NTM [9,10], with a clinical spectrum that depends on the gene affected and on residual IFN-γ signalling [9–11].

Our patient carried a heterozygous *IFNGR1* frameshift variant that was shown to be de novo. Heterozygous *IFNGR1* variants producing a truncated receptor with residual signalling cause AD partial IFN-γR1 deficiency, which, compared with complete autosomal recessive deficiency, has a later age at first mycobacterial infection (mean approximately 13 years), a milder course and a striking predilection for MAC osteomyelitis [12–15]. This genotype–phenotype relationship fits our patient, who had recurrent bone and joint disease from infancy that was repeatedly treated as tuberculosis and who presented in adolescence with multifocal MAC osteomyelitis. Adult-onset MSMD is increasingly recognised, and adults may present with isolated or multifocal bone disease rather than with the classic disseminated infection of infancy [23,24]; recurrent mycobacterial osteomyelitis has been reported in an adult with an AD *IFNGR1* variant and overexpression of the receptor [25], the allele identified here has been described in a child with disseminated *M. intracellulare* infection, and partial dominant IFN-γR1 deficiency with disseminated MAC infection has been reported in another child [17,26]. Together with reports of BCG osteomyelitis in patients with defects of the IFN-γ axis [27,28], these observations indicate that MSMD is under-recognised in adolescents and adults who present with bone disease rather than with classic disseminated BCG infection.

Table 4 summarises published cases of skeletal mycobacterial disease in patients with inherited defects of IFN-γ immunity. In the largest series, which included 38 patients with dominant partial IFN-γR1 deficiency and 22 with recessive complete deficiency, MAC osteomyelitis was far more frequent in dominant deficiency (22/28 [79%] vs 1/8 [13%]; p = 0.002), osteomyelitis without involvement of other organs occurred exclusively in dominant deficiency (9/28 [32%]), and the mean age at the first

environmental mycobacterial infection was 13.4 years compared with 3.1 years in recessive deficiency [12]. In a systematic review of adult-onset MSMD, bone or joint involvement was present in 5 of 12 patients (41.7%) and the median delay in diagnosis was 2.5 years [23]. Our patient differs from most published cases in two respects: the presenting syndrome was multifocal osteitis that closely mimicked SAPHO syndrome, and the microbiological diagnosis was obtained from a second vertebral biopsy with prolonged culture rather than during an episode of overtly disseminated disease. Two practical points follow. First, every child with recurrent, culture-negative "tuberculosis" of bone or joints, particularly after BCG vaccination, should be evaluated for an inherited defect of IFN-γ immunity. Second, our diagnosis was made with a targeted immunodeficiency gene panel rather than whole-exome sequencing and without functional studies; measurement of IFN-γR1 surface expression, IFN-γ-induced STAT1 phosphorylation and IL-12/IFN-γ production would be needed to define the functional impact of the variant.

TYK2 variants of uncertain significance

The sequencing panel also identified two heterozygous *TYK2* missense variants located in *trans*. Biallelic loss-of-function *TYK2* variants cause an autosomal recessive form of MSMD (immunodeficiency 35) [29], but neither variant identified here has been shown to cause disease, no functional testing was performed, and the phenotype is fully accounted for by the pathogenic *IFNGR1* variant. They are reported for completeness so that a second, modifying genetic lesion can be excluded in future analyses.

Treatment considerations

There are no controlled data on the treatment of NTM bone and joint infection, and recommendations for NTM disease are extrapolated from pulmonary and disseminated disease [5]. Regimens combine a macrolide with a rifamycin and ethambutol or another active agent for a prolonged period, guided by in vitro susceptibility, clinical response and drug tolerance [5,30]. Our patient received an initial four-drug regimen including amikacin and linezolid followed by maintenance azithromycin, rifabutin and ethambutol; treatment was limited by pruritus attributed to ethambutol, fatigue and anorexia during linezolid treatment, mild neutropenia and intermittent transaminase elevation, and therapeutic drug monitoring showed a slightly high linezolid trough concentration and a low rifabutin peak concentration, illustrating that drug exposure may be inadequate or excessive during long-term therapy. Recombinant IFN-γ is used as adjunctive therapy in MSMD, but its benefit is uncertain when the defect lies in the receptor itself, and it was not used in our patient. Haematopoietic stem cell transplantation is the only curative option and has been performed successfully in children with IFN-γR1 deficiency and disseminated mycobacterial disease, but it carries substantial risk and is generally reserved for patients with severe or refractory disease [30].

Limitations

This report describes a single patient, and the early history was reconstructed from records that lacked microbiological confirmation. Functional immunological testing, the bone marrow examination recommended by the pathologist and susceptibility testing with a standardised reference method were not performed, and the units and

interpretive criteria of the susceptibility panel require confirmation. The correspondence between the accession numbers of the positive culture and the species identification report should be verified with the clinical microbiology laboratory. Finally, follow-up extends to approximately 13 months of treatment, which is sufficient to document a partial response but not to establish cure or to define the optimal duration of therapy.

Conclusions

Multifocal bone lesions with non-specific histopathology and negative initial microbiology are usually attributed to CNO or SAPHO syndrome, but invasive NTM disease can produce the same picture. Mycobacterial infection should be excluded by repeat biopsy with prolonged culture and molecular testing before immunosuppressive treatment is started, and recurrent or culture-negative mycobacterial disease, particularly BCG-associated infection in infancy, should prompt genetic testing for MSMD. In our patient, a second vertebral culture that yielded *M. intracellulare* and a de novo pathogenic *IFNGR1* variant explained 18 years of recurrent bone and joint disease and redirected treatment, with a favourable clinical and partial radiological response after approximately 13 months of antimycobacterial therapy.

Declarations

Ethics approval and consent to participate. The study was conducted in accordance with the Declaration of Helsinki. Ethical approval for the publication of this case report was granted by the Ethics Committee of Hangzhou Red Cross Hospital (Approval

No. 2026-056-001). Written informed consent to participate was obtained from the patient.

Consent for publication. Written informed consent for the publication of this case report and of the accompanying clinical images was obtained from the patient. A copy of the consent form is available for review by the editorial office.

Availability of data and materials. All data generated or analysed during this study are included in this published article and its additional file. The raw sequencing data are not publicly available because of patient confidentiality but can be obtained from the corresponding author on reasonable request.

Competing interests. The authors declare that they have no competing interests.

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Authors' contributions. Huan Yang and Yuxia Yu contributed equally to this work. Huan Yang and Yuxia Yu collected the clinical data and drafted the manuscript. Meng Li performed and interpreted the microbiological and genetic investigations. Bin Sima and Yuanyuan Chen conceived the report, supervised the clinical management of the patient and critically revised the manuscript. All authors read and approved the final manuscript.

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Abbreviations. AD, autosomal dominant; AFB, acid-fast bacilli; BCG, bacille Calmette-Guérin; BMI, body mass index; CNO, chronic non-bacterial osteomyelitis; CRMO, chronic recurrent multifocal osteomyelitis; CRP, C-reactive protein; CT, computed tomography; ESR, erythrocyte sedimentation rate; HSCT, haematopoietic stem cell transplantation; IFN-γ, interferon-γ; IFNGR1, interferon-γ receptor 1; MAC, *Mycobacterium avium* complex; MGIT, mycobacteria growth indicator tube; MRI, magnetic resonance imaging; MSMD, Mendelian susceptibility to mycobacterial disease; NTM, non-tuberculous mycobacteria; SAPHO, synovitis, acne, pustulosis, hyperostosis and osteitis; TDM, therapeutic drug monitoring; TYK2, tyrosine kinase 2.

CARE checklist. This case report was prepared in accordance with the CARE guidelines [18]; the completed checklist is provided as Additional file 1.

Additional file 1. CARE checklist (DOCX). Completed CARE checklist for this case report, indicating where each checklist item is addressed in the manuscript.

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Tables

Table 1. Laboratory findings at presentation and during follow-up

Date	CRP	ESR	WBC	ANC	Hb	PLT	ALT	AST	Cr
10 Jul 2025†	86.63	61	10.2	6.63	118	450	9	9	50.3
17 Jul 2025	38.71	56	10.2	7.04	106	457	8	9	56.7
19 Aug 2025	45.69	51	8.7	5.2	112	434	9	9	53
26 Aug 2025	22.22	61	6.5	5.18	119	407	9	10	44.8
19 Oct 2025	2.63	19	3.8	1.25	128	203	35	32	51.2
16 Nov 2025	3.88	11	4.1	1.77	129	185	69	57	50.5
21 Dec 2025	1.21	7	3.9	2.08	129	213	40	42	46.6
17 Jan 2026	2.11	8	5.7	2.82	134	230	42	43	47
24 Feb 2026	1.25	8	4.1	1.57	136	198	36	33	51.7
19 Apr 2026	6.45	6	6.9	3.60	131	208	28	24	56.4
19 May 2026	2.49	9	5.5	2.25	136	213	49	35	51.8
16 Jun 2026	Not measured	7	5.6	2.13	127	221	37	30	52.1
14 Jul 2026	2.19	7	5.5	2.57	130	209	20	19	49.8
16 Aug 2026	2.1	10	5.9	2.87	134	207	34	22	48.5

Units and reference ranges: CRP mg/L (0–3.3; high-sensitivity CRP 0–5.0 for values from 19 October 2025 onwards); ESR mm/h (0–26); WBC 10^9/L (3.5–9.5); ANC 10^9/L (1.8–6.4);

Hb g/L (110–150); PLT 10^9/L (100–300); ALT U/L (7–40); AST U/L (13–35); Cr µmol/L (41–111). Dashes indicate that the test was not performed. Serum amyloid A was 762 mg/L at presentation (reference 0–10 mg/L). Therapeutic drug monitoring performed on 28 August 2025 showed a linezolid trough concentration of 8.53 µg/mL (reference 2–8 µg/mL) and a rifabutin peak concentration of 0.28 µg/mL (reference 0.45–0.9 µg/mL). ANC, absolute neutrophil count; ALT, alanine aminotransferase; AST, aspartate aminotransferase; Cr, creatinine; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; Hb, haemoglobin; PLT, platelets; WBC, white blood cell count. †Presentation.

Table 2. Investigations performed on the vertebral biopsy specimens and characterisation of the isolate

Specimen / date	Investigation	Result
First vertebral biopsy (right L2), 10 Jul 2025	Histopathology (reported 17 Jul 2025)	Necrotic bone fragments, proliferating cartilage and spindle cells with severe crush artefact; no evidence of tuberculosis or malignancy; immunohistochemistry: CK−, CAM5.2−, CK8/18−, S-100−, CD1a−, CD34−, CD138−, MUM-1−, LCA−
	Acid-fast staining (16 Jul 2025)	Negative

Specimen / date	Investigation	Result
	M. tuberculosis and NTM DNA; *M. tuberculosis* RNA; *M. tuberculosis* complex (*rpoB*)	Negative
	Xpert MTB/RIF	Negative
	T-SPOT.TB (peripheral blood)	Negative
	Routine bacterial and fungal cultures	No growth
	Mycobacterial liquid culture (MGIT 960), 42 days	No growth
Second vertebral biopsy (right L3),	Histopathology (reported 24 Jul 2025)	Fragmented necrotic bone, marrow fibrosis, fibrous tissue proliferation and sparse chronic inflammatory cells; no evidence of tuberculosis, metastatic carcinoma or Langerhans cell histiocytosis; reticulin markedly

Specimen / date	Investigation	Result
18 Jul 2025		increased (MF grade 3); Congo red negative
	Acid-fast staining (22 Jul 2025)	Negative
	Routine bacterial culture	No growth
	Mycobacterial liquid culture (MGIT 960)	Mycobacterial growth after 9 days of incubation (reported 5 Aug 2025)
Isolate characterisation	NTM species identification	*Mycobacterium intracellulare*
	Drug-susceptibility panel (values as reported by the laboratory)	Clarithromycin 4; rifampicin 4; rifabutin ≤0.5; linezolid 16; amikacin 32; moxifloxacin 4; ciprofloxacin >4; minocycline 8; doxycycline >16; tigecycline >8; imipenem 32; meropenem 64; cefoxitin >128; tobramycin 16; amoxicillin/clavulanate 64/32; trimethoprim/sulfamethoxazole 2/38
Genetic	Targeted	Heterozygous *IFNGR1* NM_000416:c.819_822del,

Specimen / date	Investigation	Result
testing (peripheral blood, reported 30 Aug 2025)	sequencing of inherited immunodeficiency genes and family study	p.(Asn274HisfsTer2) (chr6:137522057, GRCh37); patient AT/−, both parents AT/AT, consistent with a de novo pathogenic variant; two heterozygous *TYK2* missense variants reported as additional findings (p.Arg703Trp, paternal; p.Arg701Thr, maternal)

MGIT, mycobacteria growth indicator tube; NTM, non-tuberculous mycobacteria. The units and interpretive criteria of the drug-susceptibility panel should be confirmed with the reporting laboratory (see Discussion).

Table 3. Antimycobacterial treatment, adverse events and monitoring

Period	Regimen	Comments
23 Jul 2025	Sulfasalazine started while SAPHO syndrome was suspected	Empirical; the working diagnosis was subsequently revised
Aug 2025	Azithromycin 500 mg once daily; amikacin 600 mg once daily intramuscularly; rifabutin 300 mg once daily; linezolid 600 mg twice daily	Planned duration 18–24 months; started after *M. intracellulare* was identified
2–5	Azithromycin 500 mg once daily;	Diagnosis of MSMD established;

Period	Regimen	Comments
Sep 2025 (tertiary centre)	amikacin 600 mg every other day; rifabutin 300 mg once daily; linezolid 600 mg every other day; ethambutol 750 mg once daily	regimen individualised
19 Sep 2025	Ethambutol withdrawn	Pruritus without rash; cetirizine added on 19 Oct 2025
16 Nov 2025	Linezolid withdrawn; ethambutol reintroduced	Marked fatigue and anorexia during linezolid treatment
22 Dec 2025	Amikacin withdrawn	Clinical improvement; de-escalation to oral therapy
Jan–Jun 2026	Azithromycin 500 mg once daily; rifabutin 300 mg once daily; ethambutol 1000 mg once daily	Ethambutol omitted from the prescription in May 2026 and reintroduced in June 2026; mild neutropenia (Feb 2026) and intermittent transaminase elevation (May 2026)

Period	Regimen	Comments
Jul–Sep 2026	Azithromycin 500 mg once daily and rifabutin 300 mg once daily continued	Treatment ongoing at the last prescription (14 Sep 2026)

Table 4. Selected reports of skeletal mycobacterial disease in patients with inherited defects of IFN-γ immunity

Report	Genetic defect	Patients	Mycobacterial disease and skeletal involvement	Treatment and outcome
Dorman et al., 2004 [12]	*IFNGR1*, dominant partial and recessive complete deficiency	38 patients with dominant partial deficiency; 22 with recessive complete deficiency (international cohort)	MAC osteomyelitis in 22/28 (79%) of dominant vs 1/8 (13%) of recessive patients; osteomyelitis without other organ involvement only in dominant deficiency (9/28, 32%); mean age at first environmental mycobacterial infection 13.4 vs 3.1 years	Not reported in detail; mycobacterial disease was more frequent and more severe in recessive deficiency

Report	Genetic defect	Patients	Mycobacterial disease and skeletal involvement	Treatment and outcome
Jia et al., 2022 [17]	*IFNGR1* deficiency	3-year-old boy	Disseminated *M. intracellulare* infection with skin and soft-tissue disease, disseminated osteomyelitis and pulmonary disease	Azithromycin, rifampicin and ethambutol, with clinical and radiological improvement over more than one year
Shar ma et al., 2015 [26]	*IFNGR1* exon 6 heterozygous variant (partial dominant deficiency)	Child, India	Disseminated *M. avium* complex infection with multifocal osteomyelitis and BCG disease	Relapse during antibiotic therapy; subcutaneous IFN-γ added
Ri	Autosom	Adult male,	BCGitis at 2 years of age,	Antimycobacterial

Report	Genetic defect	Patients	Mycobacterial disease and skeletal involvement	Treatment and outcome
Vero-García et al., 2026 [25]	autosomal dominant *IFNGR1* variant with overexpression of the receptor	Mexico	tuberculous lymphadenitis at 3 years of age and recurrent osteomyelitis	treatment; further details not summarised here
Boudjemaa et al.,	*STAT1* exon 22 heterozygous variant	Twin sisters	Multifocal BCG osteomyelitis mimicking metastatic neuroblastoma	Not reported in detail

Report	Genetic defect	Patients	Mycobacterial disease and skeletal involvement	Treatment and outcome
2017 [27] Present case	*IFNGR1* c.819_822del, p.(Asn274HisfsTer2), de novo (partial dominant deficiency)	18-year-old woman	Multifocal *M. intracellulare* osteomyelitis of the L2–L3 vertebral bodies, ribs, thoracic vertebrae and appendages, sacrum, both iliac bones and the scapula, mimicking SAPHO syndrome	Azithromycin, rifabutin and ethambutol, with initial amikacin and linezolid; clinical and partial radiological improvement after approximately 13 months

530 BCG, bacille Calmette-Guérin; MAC, *Mycobacterium avium* complex.

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Figure legends

Figure 1. Timeline of the clinical course. Recurrent mycobacterial bone and joint disease from BCG-associated axillary lymphadenitis at two months of age through the episodes treated as tuberculosis in childhood, the presentation with multifocal bone lesions in July 2025, the two vertebral biopsies, the identification of Mycobacterium intracellulare, the genetic diagnosis of autosomal dominant partial IFN-γ receptor 1 deficiency, and the subsequent treatment and follow-up to September 2026.

Figure 2. Lumbar spine computed tomography before and after treatment. (A) Sagittal and (C) axial bone-window computed tomography (CT) on 10 July 2025 showing irregular destruction of the L2 and L3 vertebral bodies with narrowing of the adjacent disc space and paravertebral soft-tissue swelling. (B) Sagittal and (D) axial bone-window CT on 17 January 2026 showing sclerosis and partial healing at the same level. Arrows indicate the affected vertebral segments. The two studies were acquired with different fields of view; anatomically equivalent levels are shown.

Figure 3. Lumbar spine magnetic resonance imaging before and after treatment. (A) Sagittal T2-weighted magnetic resonance imaging (MRI) on 19 August 2025 showing abnormal hyperintense marrow signal involving the L2–L5 vertebral bodies and the upper sacrum, most marked at L2–L3 (arrow). (B) Sagittal T2-weighted MRI on 16 June 2026 showing regression of the abnormal marrow signal at the corresponding level (arrow). (C) Axial T2-weighted MRI at the L2 level on 19 August 2025 showing paravertebral soft-tissue swelling with involvement of the right psoas muscle. (D)

T2WI SPINE transverse view on June 16, 2026, showed marked improvement in soft tissue swelling at the L2 vertebral level and the infectious lesion in the right psoas major muscle compared to the previous scan.

Figure 4. Thoracic spine and rib involvement before and after treatment. (A) Axial bone-window computed tomography (CT) on 19 October 2025 and (B) on 16 August 2026 showing destruction of the right T2 vertebral appendage and the adjacent rib, with improvement after treatment (arrows). (C) Axial bone-window CT on 19 October 2025 and (D) on 16 August 2026 showing destruction of the right seventh rib and the left sixth rib, with pathological fracture at baseline and healing on follow-up (arrows). The two studies were acquired with slightly different fields of view.

Figure 5. Course of inflammatory markers during antimycobacterial treatment. C-reactive protein (CRP; squares) and erythrocyte sedimentation rate (ESR; circles) from presentation in July 2025 to the last measurement in June 2026. Treatment was started in August 2025 and continued throughout follow-up. CRP fell from 86.63 mg/L to within the reference range by October 2025, and ESR fell from 61 mm/h to 6–9 mm/h.

Figures

Figure 1. Timeline of the clinical course.

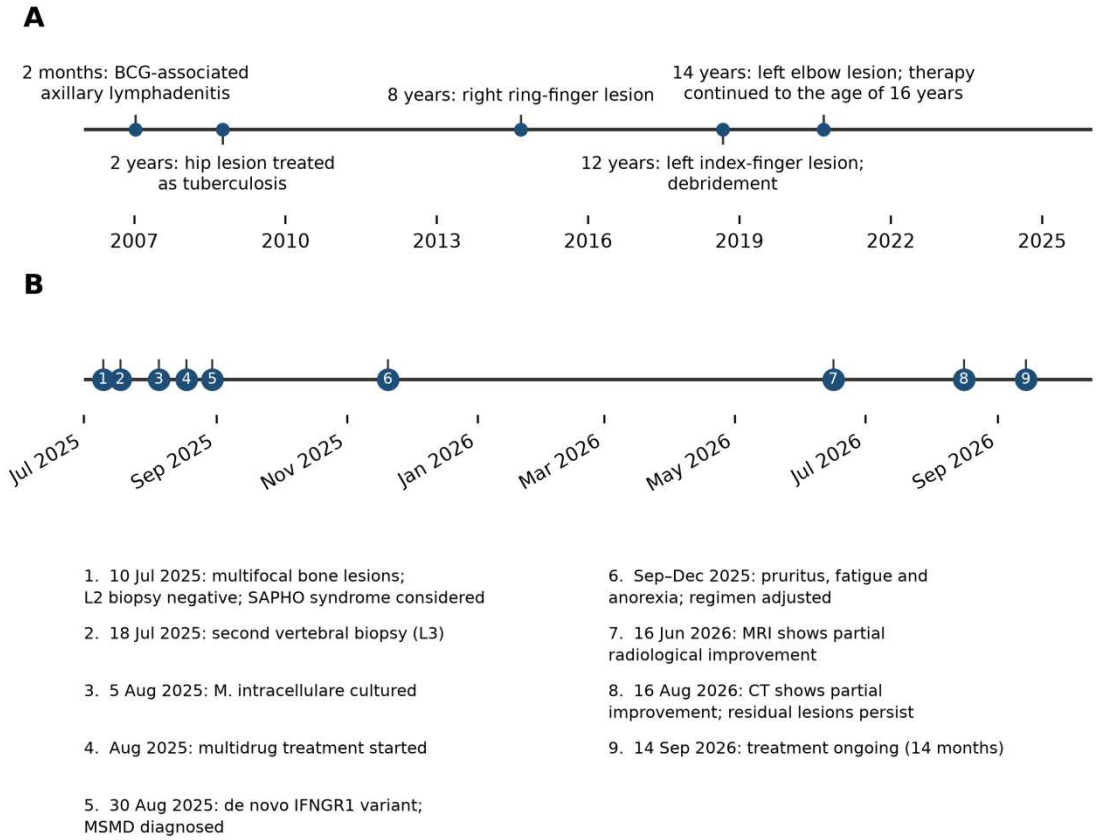


Figure 2. Lumbar spine CT before and after treatment.

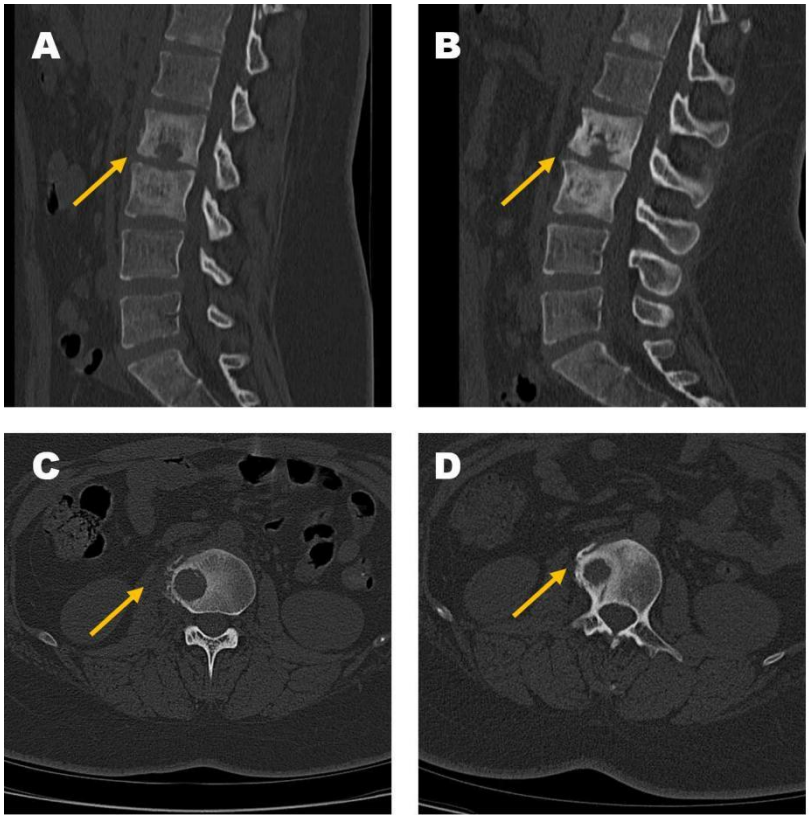


Figure 3. Lumbar spine MRI before and after treatment.

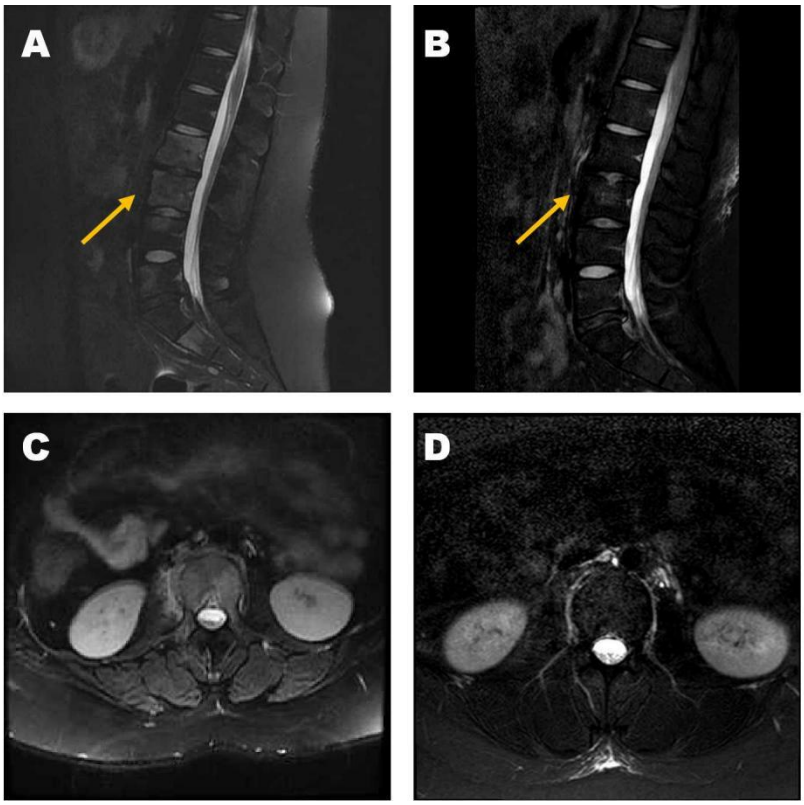


Figure 4. Thoracic spine and rib involvement before and after treatment.

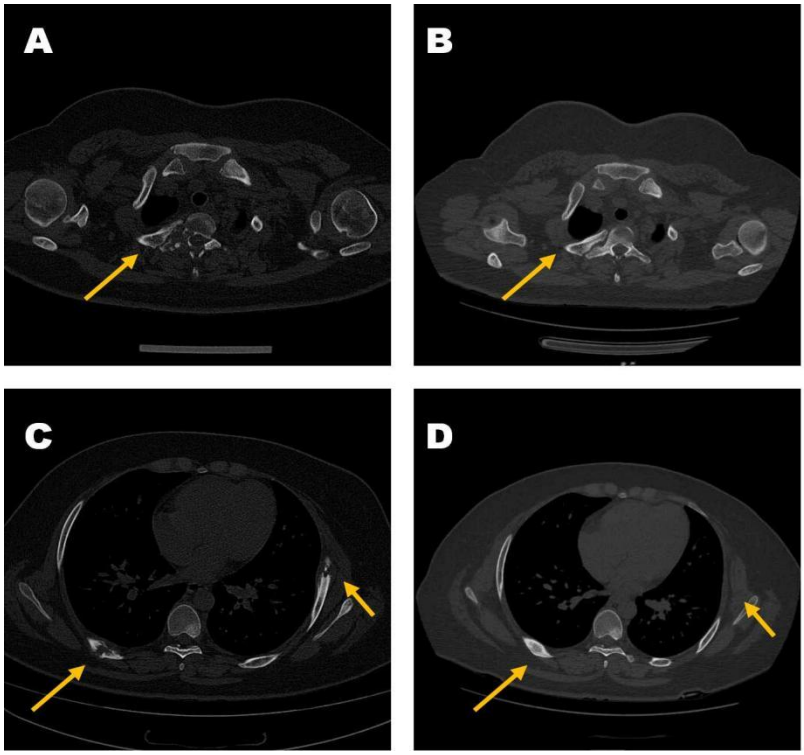
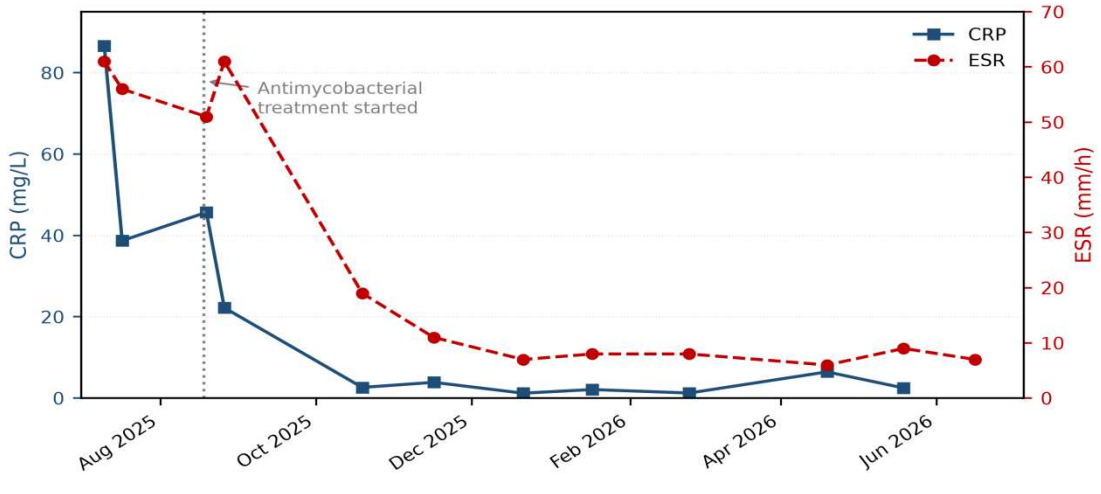


Figure 5. Course of inflammatory markers during antimycobacterial treatment.



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