Still looking for the cause of fever?

Jeremy Cohen

Clinical record

A 49-year-old man with no significant past medical history was transferred to our unit from another facility. He had become unwell 9 days previously, initially with a sore throat, followed by generalised muscle aches, primarily over his shoulders, legs and chest. These symptoms were accompanied by fevers, headache, and worsening breathlessness. Despite initial management by his local doctor with non-steroidal anti-inflammatory drugs, the man's pain progressed to the point that he was unable to walk, and he was admitted to hospital. He was treated with broad-spectrum antibiotics for presumed community-acquired pneumonia. However, his condition deteriorated, with breathlessness, agitation and fever, and he was intubated, ventilated, and transferred to our ICU.

He had been working recently as a carpenter at a mine site in northern Queensland. A co-worker had complained of symptoms which were similar but much less severe. The patient gave no history of foreign travel or exposure to animals or toxic substances.

On examination, he was noted to be febrile (temperature, 39.8° C) and to have generalised muscle tenderness, particularly over the upper body. A faint papular rash was evident on the upper back. No joint swelling or neck stiffness were noted. Chest x-ray showed scattered bilateral alveolar shadowing.

The results of relevant investigations during the patient's hospital course are shown in Table 1. In addition, no abnormalities were found on:

- repeated cultures of blood, urine and sputum;
- culture of cerebrospinal fluid;
- examination and culture of synovial fluid aspirate from the knee;
- serological testing for legionella, chlamydia, mycoplasma, brucella, toxoplasma, coxiella, cytomegalovirus, Epstein–Barr virus, rickettsia, syphilis, streptococci, leptospirosis and hepatitis;
- autoimmune screen for rheumatoid factor, antineutrophil cytoplasmic antibodies (ANCA), antinuclear antibodies (ANA), extractable nuclear antigen antibodies (ENA), and dsDNA, glomerular basement membrane and cardiolipin antibodies;
- computed tomography of the head, chest and abdomen;
- transthoracic echocardiography; and
- bone marrow examination.

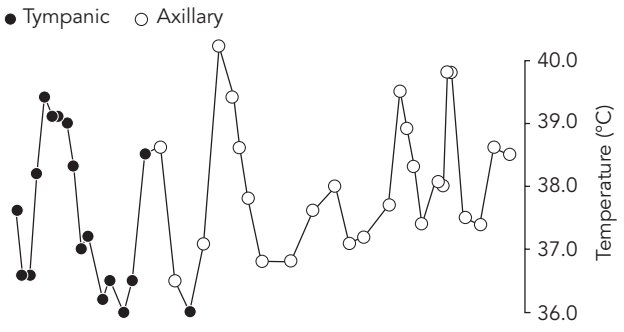
Therapy was begun with meropenem and azithromycin, but the patient continued to have daily spiking fevers (temperature > 40° C), and the leukocyte count remained elevated. However, he had no evidence of organ system dysfunction, and was successfully extubated after 5 days of ventilation. Following extubation, the daily fever spikes continued, as did the leukocytosis. The patient complained of muscle pains over his right shoulder and knee, as well as intermittent breathlessness.

A representative portion of the temperature chart is shown in Figure 1.

Table 1. Results of relevant investigations

	Test result	Reference range
Haemoglobin (g/L)	105	120–180
White cell count (cells/L)	25.9×10^9	$3.5–11 \times 10^9$
Platelet count (cells/L)	347×10^9	$140–400 \times 10^9$
Electrolytes, urea and creatinine	Normal	
Bilirubin (μmol/L)	10	< 20
Alkaline phosphatase (U/L)	126	40–110
γ-Glutamyl transferase (U/L)	181	< 50
Alanine aminotransferase (U/L)	145	< 45
Aspartate aminotransferase (U/L)	54	< 40
Lactate dehydrogenase (U/L)	216	110–250
Creatine kinase (U/L)	118	< 200
Ferritin (μg/L)	32 200	30–300

Figure 1. Representative portion of the patient's temperature chart



Diagnosis: adult-onset Still's disease

Adult-onset Still's disease (AOSD) is an extremely rare rheumatological condition, characterised by myalgias, fevers and a pathognomonic rash. Diagnosis is difficult, as there is no specific test for the disorder, so the clinician must rely on clinical signs and the exclusion of other potential causes.

A number of diagnostic criteria have been advocated; one of the most widely accepted sets of criteria is that proposed by Yamaguchi et al[1] (Table 2).

The fever is classically described as quotidian, with temperature spiking once a day to 39° C or higher, and returning to normal between spikes. Still's rash is a salmon pink evanescent rash, associated with the fever spikes and usually affecting the trunk.

While high serum ferritin levels are not included in these diagnostic criteria, elevated levels are commonly reported in patients with AOSD, and markedly elevated ferritin values (> 4000 µg/L) have been reported as very specific for AOSD in patients with compatible clinical syndromes.[2,3] Levels as high as those observed in our patient are extremely rare.

Based on a likely diagnosis of AOSD, therapy was begun with daily prednisolone treatment, and antibiotics were ceased. The patient's fever and leukocytosis abated over the next 48 hours, and myalgia decreased. He continues to do well in the general ward.

Table 2. Diagnostic criteria for adult-onset Still's disease

More than five criteria are required for the diagnosis, of which two must be major.[1]

Major criteria	Minor criteria
• Fever (temperature > 39° C)	• Sore throat
• Arthralgia > 2 weeks	• Lymphadenopathy or splenomegaly
• Still's rash	• Liver dysfunction
• Neutrophilic leukocytosis	• Negative rheumatoid and antinuclear factors ◆

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References

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