Massively elevated serum ferritin in an ill man with abnormal liver function tests

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A 55-year-old man presented with a 3-week history of sore throat, muscle aches, arthralgia, lethargy, night sweats and rigors. On direct questioning he admitted to a previous episode 22 years ago which had been extensively investigated with no cause found. It had taken approximately 6 weeks to resolve and he had been symptom-free since then. On examination he was pyrexial (37.5°C), mildly icteric without lymphadenopathy or stigmata of chronic liver disease. Initial investigations revealed grossly deranged liver function tests and elevated serum inflammatory markers as shown in the table. Abdominal ultrasound was normal except for an enlarged spleen at 15 cm. Liver biopsy showed mild nonspecific inflammatory changes, and biopsy stains were negative (hepatocyte iron, copper-associated protein, hepatitis BsAg and α 1-antitrypsin). Admission chest X-ray showed a small left-sided pleural effusion with borderline cardiomegaly.

Table Summary of investigations (normal range in brackets)

Alkaline phosphatase (IU/l)	1181 (30–140)
Gamma glutamyl transferase (IU/l)	417 (<65)
Alanine transaminase (IU/l)	63 (<45)
Albumin (g/l)	33 (35–50)
Bilirubin (μ mol/l)	28 (1–17)
Blood haemoglobin (NNI)	11.2
Leucocytes ($\times 10^9/l$)	17.8 (neutrophils $16.0 \times 10^9/l$)
Platelets ($\times 10^9/l$)	412
Plasma viscosity (cp)	2.04 (1.5–1.72)
C-reactive protein (mg/l)	309 (0–6)
Serum ACE (IU/l)	40.5 (14.1–36.6)

Following admission his temperature continued to show high spiking fevers in the evening, often accompanied by rigors, which returned to normal in the mornings. On the second day of his admission his breathlessness worsened and he became acutely distressed and unwell. Physical examination and electrocardiogram revealed fast atrial fibrillation, and a new onset pericardial rub. An echocardiogram showed a pericardial effusion with no valvular vegetations seen. He was treated with amiodarone and his atrial fibrillation settled. His spiking fevers and rigors persisted, particularly in the evenings. He developed a widespread maculopapular rash over his trunk, neck and back. His arthralgia, myalgia and general malaise persisted. A full infection and autoimmune screen was negative. Serum ferritin was grossly elevated at 55 950 μ g/l (15–300).

He remained under observation in hospital and his fevers, arthralgia, myalgia, rash, pericardial and pleural effusions, raised inflammatory markers and abnormal liver function tests gradually settled over the 5 weeks following admission. He was discharged and has remained well with normal blood tests and no further symptoms during 6 months of follow-up.

Questions

- 1 What is the most likely diagnosis?
- 2 What are the diagnostic criteria for diagnosis?
- 3 What treatment is indicated?
- 4 What is the prognosis?

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Answers

QUESTION 1

The patient is probably suffering from adult Still's disease, a relatively rare condition (incidence 1:100 000¹), and the only condition in which very high serum ferritins have consistently been reported.²⁻⁴ A raised serum ferritin can occur in a variety of inflammatory conditions, liver diseases, malignancies and iron overload, but figures over 10 000 µg/l are rare. Measurement of serum ferritin is well correlated with iron stores in healthy individuals, but high values do not necessarily indicate iron overload because there are two other mechanisms which can increase serum ferritin. Firstly, damage to ferritin-rich tissues can release large amounts of cellular ferritin into the serum, and secondly, ferritin synthesis can be increased in inflammatory conditions.

QUESTION 2

The diagnosis is based on the suggested criteria shown in the box.⁵ For a positive diagnosis, five or more criteria including at least two major criteria are required, together with exclusion of infection, malignancy, and rheumatic disease. The case reported here had all eight major and minor criteria. During the acute phase, he also had a grossly elevated serum ferritin.

QUESTION 3

Treatment with aspirin, other non-steroidal anti-inflammatory drugs, oral steroids and even pulsed intravenous methyl prednisolone are sometimes required to control this disease.⁴ The condition did respond to high-dose

Adult Still's disease: diagnostic criteria

Major criteria

- fever of 39°C
- arthralgia
- maculopapular rash
- neutrophil leucocytosis

Minor criteria

- sore throat
- lymphadenopathy or splenomegaly or both
- liver dysfunction
- negative rheumatoid factor and antinuclear antibody

steroids which had been prescribed 22 years previously, although the diagnosis at that time was unknown. The fact that he recovered in the same time on this occasion without steroids suggests that supportive treatment only may suffice in many cases.

QUESTION 4

The prognosis of adult Still's disease is variable. The case presented here seems to have made a full recovery, with serum ferritin and other disease markers returning to normal without steroids. Other patients with the same condition may be much more difficult to manage.²

Final diagnosis

Adult Still's disease.

Keywords: Still's disease; serum ferritin

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