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ADULT-ONSET STILL'S DISEASE PRESENTING WITH ATYPICAL KIKUCHI-FUJIMOTO DISEASE-LIKE HISTIOCYTIC NECROTIZING LYMPHADENITIS: A DIAGNOSTIC PITFALL

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ABSTRACT

Background: Adult-onset Still's disease (AOSD) is a rare systemic autoinflammatory disorder and a diagnosis of exclusion. Kikuchi-Fujimoto disease (KFD) is a benign, usually self-limiting necrotizing histiocytic lymphadenitis. The clinical and histopathological overlap between the two can be diagnostically challenging.

Case report: A 24-year-old female presented with a 6-week history of quotidian fever, migratory polyarthralgia, a fleeting salmon-coloured rash, and cervical lymphadenopathy. Initial workup revealed pronounced leucocytosis, highly elevated C-reactive protein, and critically high serum ferritin (6,500 µg/l). An excisional lymph node biopsy, performed to exclude malignancy, demonstrated features consistent with KFD. Active hemophagocytic lymphohistiocytosis (HLH) / macrophage activation syndrome (MAS) was ruled out as the calculated H-score was low (5), indicating a low probability of HLH, and the patient did not have the cytopenias and organomegaly necessary for a diagnosis of HLH/MAS. The patient's presentation was ultimately confirmed as AOSD based on the Yamaguchi criteria.

Conclusion: This case illustrates a rare presentation where AOSD was masked by KFD-like lymphadenitis. Extreme hyperferritinaemia appears to serve as a vital, specific biomarker to establish the correct diagnosis of AOSD and ensure timely, life-saving immunomodulatory treatment. Also, prompt calculation of the H-score and the strict application of clinical and laboratory criteria are critical steps when managing patients with extreme hyperferritinaemia and systemic inflammation.

KEYWORDS

Adult-onset Still's disease, Kikuchi-Fujimoto disease, hyperferritinaemia, autoinflammatory syndrome

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LEARNING POINTS

- Adult-onset Still's disease (AOSD) may, in rare cases, present with the histopathological features of Kikuchi-Fujimoto disease, posing a significant diagnostic challenge and potentially leading to error.
- The persistence of systemic symptoms (spiking fever, severe polyarthralgia) and most critically, extreme hyperferritinaemia (often >5,000 µg/l) necessitate the immediate calculation of the H-score. A low H-score and the presence of neutrophilic leucocytosis are key factors in differentiating AOSD from macrophage activation syndrome (MAS) and hemophagocytic lymphohistiocytosis.
- This case highlights the necessity of rapid initiation of targeted immunosuppressive therapy (e.g., IL-1 inhibitors) to treat the underlying AOSD and prevent complications like MAS.

INTRODUCTION

Adult-onset Still's disease (AOSD) is an uncommon systemic disease characterized by triad of high fevers, arthralgia, and an evanescent rash, often accompanied by leucocytosis and systemic inflammation. The diagnosis relies on the strict exclusion of infections, malignancies, and other rheumatic diseases. Kikuchi-Fujimoto disease (KFD) is another rare condition causing self-limiting fever and regional lymphadenopathy[1]. The differential diagnosis in patients presenting with fever, arthralgia, and marked hyperferritinaemia must always include AOSD, KFD, as well as the potentially life-threatening conditions hemophagocytic lymphohistiocytosis (HLH) and its rheumatologic variant, macrophage activation syndrome (MAS). Distinguishing between them is critical, as AOSD requires prompt immunosuppressive therapy, while KFD typically resolves spontaneously.

CASE DESCRIPTION

A previously healthy 24-year-old woman presented to the Internal Medicine department with a 6-week history of daily temperature spikes up to 39.5°C, typically spiking in the evening. The fever was associated with severe, migratory polyarthralgia affecting the knees and wrists, and a fleeting, non-pruritic, salmon-coloured rash on the trunk. She also reported painless, firm swelling of the anterior cervical lymph nodes. Physical examination confirmed polyarthralgia and bilateral cervical lymphadenopathy. There was no evidence of hepatosplenomegaly.

Initial laboratory tests revealed a pronounced inflammatory response: leucocytosis (18.5 $\times 10^9$ with neutrophilia), erythrocyte sedimentation rate of 75 mm/h, and C-reactive protein of 150 mg/l. Liver transaminases were mildly elevated. Crucially, serum ferritin was severely elevated at 6,500 µg/l (reference <250 µg/l). Extensive infectious and autoimmune workups (antinuclear antibodies, rheumatoid factor, anti- cyclic citrullinated peptide) were negative.

Given the persistent fever and adenopathy, an excisional lymph node biopsy was performed to rule out a lymphoproliferative disorder. Histopathology revealed foci of necrosis surrounded by activated histiocytes and a lack of neutrophils—findings considered pathognomonic for KFD[1]. Differential diagnosis with MAS and HLH was initiated immediately. The H-score was calculated to assess the probability of secondary HLH. Based on the patient's parameters (fever: +1, ferritin >6000: +4, cytopenia: 0, hepatomegaly: 0, fibrinogen/triglycerides: 0), the total H-score was 5. This score corresponds to a very low probability of HLH (less than 1% probability).

The lack of fulfilment of other HLH-2004 criteria (specifically, the absence of cytopenia in two or more lineages, normal fibrinogen/triglycerides, and the absence of clinical organomegaly) provided sufficient evidence to exclude active HLH/MAS. The patient fulfilled the required criteria of the Yamaguchi Classification Criteria for AOSD.

Treatment was initiated urgently with high-dose intravenous methylprednisolone (1 g daily for 3 days), leading to rapid clinical response and defervescence within 48 hours. Oral prednisolone (1 mg/kg/day) was then started, and a subsequent plan for the IL-1 receptor antagonist anakinra was made to manage the disease long-term and prevent steroid dependence[2].

DISCUSSION

AOSD and KFD are both systemic inflammatory conditions that share clinical features such as high fever, lymphadenopathy, and elevated inflammatory markers. They are both diagnoses of exclusion. The co-existence or a preceding KFD diagnosis in patients who later develop AOSD has been rarely reported[1,3]. Crucially, AOSD, KFD, MAS, and HLH share core features including persistent fever, hyperferritinaemia, and lymphadenopathy, placing their differentiation among the most challenging in internal medicine.

This case emphasizes the significance of extreme hyperferritinaemia in the differential diagnosis of systemic febrile illnesses with lymphadenopathy. The low calculated H-score (5) and the presence of neutrophilic leucocytosis were decisive factors in steering the diagnosis away from HLH/MAS, highlighting that clinical and laboratory parameters can be sufficient for initial classification and treatment initiation, even without the most invasive procedure. The extreme hyperferritinaemia helped override the potentially misleading KFD biopsy result, establishing the correct diagnosis of AOSD[4]. Differential diagnosis (KFD vs. AOSD vs. HLH/MAS):

- KFD is typically self-limiting and shows necrotizing histiocytosis without neutrophils. Ferritin is usually only mildly elevated.
- HLH/MAS are life-threatening conditions, which require bi- or tri-lineage cytopenia, organomegaly, and/or evidence of haemophagocytosis. The low H-score and the lack of fulfilment of HLH diagnostic criteria definitively excluded active HLH/MAS, despite the extremely high ferritin level.
- AOSD is distinguished by the characteristic rash, arthralgia, and, importantly, neutrophilic leucocytosis, which strongly argues against active HLH/MAS.

The significance lies in the therapeutic urgency. Misdiagnosis based solely on the KFD biopsy could have led to inappropriate expectant management, delaying crucial immunosuppressive therapy required for AOSD. Untreated AOSD carries a risk of significant morbidity and life-threatening complications, such as MAS. The dramatic clinical and laboratory response to glucocorticoids confirmed the autoinflammatory nature of the disease, and the fulfilment of the Yamaguchi criteria explained the patient's condition and the need for AOSD-specific therapy.

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