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A Case Report of Still's Disease in the Adult

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Abstract

Adult Still's disease (ASD) is a rare systemic inflammatory disorder of unknown etiology, typically characterized by a clinical triad (daily spiking high fevers, evanescent rash, and arthritis) and a biological triad (hyperferritinemia, hyperleucocytosis with neutrophilia and abnormal liver function test). There are no specific diagnostic tests for ASD, so the diagnosis of ASD remains one of exclusion and the differential diagnosis may be lengthy. We present a case of an adult-onset Still's disease with previous admissions for fever of unknown origin with a 2-month history of fever and systemic symptoms. The patient posteriorly presented polyarthralgies and cutaneous rash. The study disclosed anemia, inflammatory markers and hepatic enzymes elevation, and negative serological and immunological studies. The introduction of corticotherapy resolved symptoms and laboratories alterations. Adult-onset Still disease is a heterogeneous and rare disease and the lack of serologic markers as a true gold standard makes diagnosis difficult.

Keywords: Adult Still's disease; Fever; Rash; Hyperferritinemia; Polyarthralgies

Introduction

Adult Still's disease (ASD) is a systemic inflammatory disorder of unknown etiology, typically characterized by a clinical triad (daily spiking high fevers, evanescent rash, and arthritis) and a biological triad (hyperferritinemia, hyperleucocytosis with neutrophilia and abnormal liver function test) [1].

ASD is a rare disorder, known to exist worldwide, with equal distribution between the sexes, and with three quarters of patients reporting disease onset between 16 and 35 years of age [2].

The laboratory findings in ASD reflect the systemic inflammation and cytokine cascade present, and none of the findings are specific for ASD. There is no association with rheumatoid factor or antinuclear antibody positivity [3].

There are no specific diagnostic tests for ASD. The diagnosis of ASD remains one of exclusion and the differential diagnosis may be lengthy. Infectious, neoplastic, autoimmune diseases or drug hypersensitivity reactions can mimic the clinical manifestation of ASD. Therefore, several sets of different classification criteria have been proposed for ASD [3, 4]. The classification criteria proposed by Yamaguchi et al published in 1992 are the most widely used [1].

Treatment options include non-steroid anti-inflammatory drugs (NSAIDs) and aspirin, glucocorticoids, and immunomodulating drugs. Most patients require steroids at some point in the course of their ASD; the usual prednisone dose is 0.5 - 1.0 mg/kg/day. Responses to steroid therapy range from 76% to 95% [2, 5].

Case Report

We present a case of a 26-year-old female patient, admitted in our outpatient hospital with a constitutional syndrome, with fever, asthenia and polyarthralgia 2 months long. At the moment of the first appointment, arthritis of small joints, axillary and cervical adenopathies, with anemia, thrombocytosis, neutrophilia and elevation of inflammatory markers (C-reactive protein and erythrocyte sedimentation rate) and transaminases were noted. The patient was already on steroid therapy (prednisolone 20 mg per day) since the clinical outbreak. A CT scan was therefore realized to further evaluation, having confirmed axillary, cervical and mediastinal adenopathies with 10 - 30 mm; no hepato- or splenomegaly was documented. Hence, a biopsy to one for the cervical lymph nodes was preformed, yet with no certain conclusions, since the histologic features were compatible with Hodgkin's lymphoma, but in terms of immunophenotyping characteristics, it was in favor of a large B-cell lymphoma. The patient was then hospitalized to better understand the clinical features. During the time of admission, patient had high fever with no patterns, unresponsive to therapeutics, associated with maculopapular evanescent rash. An anatomopathological review of the first histological sample was requested, having shown a reactive lymphadenitis. The possibility of an infectious disease was studied and excluded; the autoimmune laboratorial workout was also negative.

At the moment, we have a patient with a high fever, associated with polyarthritis, evanescent rash and reactive lymphadenitis. Infectious and lymphoproliferative conditions were excluded. The laboratorial workout showed inflammatory

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Table 1. Yamaguchi Criteria - Five or More Criteria With at Least Two Major Positive

Major criteria	Minor criteria
Fever (> 39 °C)	Pharyngitis
Arthralgia (over 2 weeks long)	Lymphadenopathy/splenomegaly
Cutaneous rash	Hepatic dysfunction
Leucocytosis with neutrophilia	ANAs and RF negative

markers and transaminases elevation. Therefore, the possibility of an ASD was accessed. Further laboratorial study showed hyperferritinemia of 5,339.9 µg/dL. The patient scored on Yamaguchi criteria, having the ASD diagnosed. Prednisolone 0.5 mg/kg/day was then started, and great response to steroid therapy was shown, with total resolution of the clinical manifestations.

Discussion

Despite the improvement in diagnostic techniques, the undetermined febrile syndrome (UFS) remains a challenge to overcome, comprising 50% of the cases without clear etiology [6]. ASD represents one of the possible diagnoses among UFS, only accessible excluding a long list of other possibilities. Hence, until today, ASD remains a difficult diagnosis, relying in six different sets of classification criteria (Glodman, Calabro, Cush, Reginato, Kahn and Yamaguchi) [7]. The Yamaguchi criteria (Table 1) are the ones recognized for their superior accuracy, as it was shown in Masson et al study in 1996 [7]. The two greatest obstacles concerning these criteria are: the fact that, despite being a diagnosis of exclusion, there is not a clear set of diagnosis to exclude before assuming ASD, nor helpful complementary diagnosis techniques to help supporting the hypothesis; the other limitation is the absence of ferritin levels (or its glycosylated form) in the criteria [8].

Therefore, the frequent delay on the diagnosis brings no surprises and our case is no exception. The lack of specificity of the symptoms and signs, and their absence of synchronicity concerning the cutaneous manifestations, represent a strong contributor to the difficulties on this diagnosis [9-11].

In our case, after excluding other causes of febrile syndrome, we recognized six aspects of Yamaguchi criteria: high fever with more than 3 weeks of evolution, leucocytosis with neutrophilia associated with atypical cutaneous rash (major criteria); splenomegaly, transaminases and rheumatoid factor elevation and negativity antinuclear antibodies (minor criteria). We have to enlighten the long period of clinical evolution (5 years) without compromising the patient's general well-being [12].

The search for a sensible/specific biochemical marker for this disease is still a long awaited discovery. Consistent data towards the predominant role of macrophage activity in Still's pathophysiology have been found, since high levels of ferritin, IL-6, -8, -18 and the TNF-alpha are frequently recognized [13].

The treatment generally relies on NSAIDs and steroids, requiring no further more potent immunosuppressors. In some refractory cases, hydroxychloroquine, gold salts, methotrexate and cyclosporine have been used with limited data [14, 15].

In our case, with a mild articular damage (known for being the major indicator of a poorer prognosis), low-dose corticoid and NSAIDs were used with resolution of all symptoms. During a 2-year follow-up, no recurrences were found.

Conclusion

We present this case of ASD to enlighten the difficulties concerning the diagnosis and the need of more accurate classification criteria. The lack of high sensibility methods to recognize ASD delays the diagnosis, therefore comprising the correct treatment to improve the outcome. The intricacy of the symptoms and the lack of accurate diagnostic techniques make the clinical approach to ASD patients the hallmark to the right management of this condition.

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