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Recurrent Still's Disease

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Abstract Adult-onset Still's disease (AOSD) is a systemic inflammatory disorder. Its clinical presentation is similar to the systemic form of Juvenile idiopathic arthritis (JIA). In this case report we explore a young female 22 years after a diagnosis of JIA and 4 years after her diagnosis of AOSD who presents with systemic inflammatory symptoms. Some of the symptoms consistent with her previous diagnosis and some new. Specifically the new symptom of her diffuse lymphadenopathy lead to a differential of possible lymphoproliferative disease. After a biopsy and multiple admissions with unrelenting symptoms the patient was diagnosed with a flare of AOSD. We explore her case in depth with the question in mind: Does one diagnosed with JIA remain on long term therapy to avoid recurrent flares and progression to AOSD, and if so for how long?

Keywords: *stills disease, juvenile idiopathic arthritis, lymphadenopathy*

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1. Introduction

Adult-onset Still's disease (AOSD) and Juvenile Idiopathic Arthritis have been associated together for over twenty years. Whether or not the two are the same continuation of one disease has yet to be determined [1]. There are theories that they are one disease with a change in phenotype over years and other theories that they are separate diseases with overlapping symptoms [2,3]. In this case report we describe a case of a patient with both diseases diagnosed.

The following criteria have been established to help diagnose AOSD [4]:

Table 1. DIAGNOSTIC CRITERIA FOR AOSD

Major Diagnostic Criteria	Minor Diagnostic Criteria
Fever of at least 39°C for at least a week	Sore throat
Arthralgia or arthritis for at least 2 weeks	Lymphadenopathy
Nonpruritic salmon colored rash on trunk/extremities	Hepatomegaly or splenomegaly
Granulocytic leukocytosis (10,000/microL or greater)	Negative tests for RF and ANA

Using the above criteria, a total of 5 features must be present and 2 of those being major diagnostic criteria. Diagnosis requires at least 5 features, with at least 2 of these being major diagnostic criteria. These are important to consider when evaluating patients as many of the symptoms overlap with infectious and oncologic disease. AOSD remains a diagnosis of exclusion, meaning it would be diagnosed after other diseases are ruled out and the above diagnostic criteria is met. Similarly JIA is a diagnosis of exclusion in children with inflammation in one or more joints lasting at least 6 weeks [3].

We report a case of extensive medical evaluation to diagnose a recurrent flare of AOSD in a patient with previously diagnosed JIA.

2. Case Presentation

A 27-year-old Female with a history of AOSD (diagnosed 4 years prior to her hospital admission) and Juvenile Idiopathic Arthritis diagnosed at 22 years prior presented to the hospital with 5 days of fever, chills, cough, congestion, nausea, vomiting, palpitations, chest pain, shortness of breath, headache, diffuse joint pain and a runny nose. This patient had been asymptomatic from an AOSD perspective and off of any medication for 2 years. She had previously taken methotrexate and prednisone in the past, which she self discontinued. Her vitals on presentation were significant for unremitting tachycardia (110s-130s), and fevers up to 102.8 F, normotensive and 99% O2 saturation. On exam she had significant lymphadenopathy throughout and a prominent diffuse scaly rash across her legs and chest. Labs were seen as followed.

Table 2. PATIENTS LABORATORY VALUES WITH UNITS

Lab	Patients values:	Normal range:
White Blood Cells	27	4.5-11 x 10^9/L
Eosinophils	3.92	<0.5 x 10^9/L
Hemoglobin	7.9	12.1 to 15.1 g/dL
Platelets	500	150-450 10^3/ μL
Prothrombin Time /International Normalized Ratio	14.5/1.22	10-13/<1.5 seconds
C-Reactive Protein	116	0-5 mg/L
Pro-calcitonin	0.17	0-0.25 μ/L
Lactate	1.2	0.5-1 mmol/L
Lactate Dehydrogenase	602	100-190 IU/L

Blood cultures and urine cultures were negative. Chest/Abdomen/Pelvis CT scan was significant for bilateral hilar lymphadenopathy, bilateral axillary lymphadenopathy and left supraclavicular lymphadenopathy and splenomegaly.

Echocardiogram was within normal limits. Her prior treating rheumatologist reported no prior evidence of lymphadenopathy or eosinophilia. She was started on standing Ibuprofen for symptom control with rheumatology, pulmonology, and hematology consults called for further evaluation of possible bronchoscopy and/or biopsy. Per recommendations of hematology/oncology a left axillary final need aspiration excisional lymph node biopsy was performed by general surgery. The patient was discharged from the hospital and asked to wait for the results of the biopsy before any medication was started. She was discharged with close follow up with outpatient rheumatology. However, prior to her appointment or receiving the results of her biopsy she was readmitted with further progression of tachycardia, fevers and similar symptoms 1 week after discharge. During that second admission, pathology resulted revealing florid reactive lymphoid hyperplasia with scattered eosinophils and large cells. It was concluded that the patient was not suffering from a malignancy based off of the biopsy and the symptoms stemmed from rheumatologic disease. Per recommendations she was started on prednisone 40 daily inpatient with significant and rapid improvement of symptoms. The patient became hemodynamically stable with resolution of her palpitations rash cough nausea and vomiting and was able to be discharged with close follow up.

At her follow up appointment, she was still on prednisone 40, with improvement of her symptoms overall. She continued to have tachycardia and a minor cough. She followed up with primary care, pulmonology and rheumatology. The patient expressed that she felt overall better since her discharge but felt some side effects of the prednisone and was eager to be tapered off of it. She felt anxious which was one of the main symptoms that caused her to self discontinue her prednisone in the past. After a full set of labs outpatient, she was started on methotrexate (MTX) 10 mg weekly, recalling that this was the therapy that helped her best in prior years. This patient saw much improvement after starting MTX and was able to be slowly tapered from her prednisone weeks later.

3. Discussion

Our patient presented with 4/4 major criteria of AOSD as mentioned in our introduction and ¾ minor criteria. As her evaluation involved biopsies and culturing, it can be said that it was a diagnosis of exclusion. However, it prompts considering if someone was previously diagnosed with AOSD/JIA and has remission of disease – do they need full evaluation ruling out other presentations to diagnose their flare up. This requires understanding the trajectory of JIA, and AOSD.

Multiple studies have been done using long term follow up to understand the trajectory and length of JIA. There are multiple hypothesis, one study showed 19-44% of patients with monocyclic courses with no relapses, 10-41% of patients with unpredictable exacerbations after months-years, 35-57% of patients with chronic progressive course [5]. It appears our patient has unpredictable exacerbations however, since she had worsening symptoms, it is possible she has a chronic progressive course. While biologic treatment response is the mainstay way of categorizing, it would take some years to fully understand what her disease fits under. Packham reports patients continued to have symptoms for a range of 13-27 years following initial diagnosis [4]. Sampalis states Still's disease has a duration of approximately 10 years, with 50% of patients requiring treatment after those ten years [6].

This patient specifically had relapsing and remitting effects for at least up to 22 years when considering both diagnosis she had. With the initial diagnosis of JIA patients should have continuous close follow up [7]. She was lost to follow up as her disease had remitted. The time period a patient with this disease would need to be on long term therapy to prevent recurrent disease, and whether Still's disease is the adult form of JIA is unknown due to the variety of presentation [8,9]. Perhaps patients with this diagnosis need much longer therapy than 2-3 years to prevent subsequent remission. The two diseases are associated due to similar presentations, and gene expression analysis [10]. Multiple studies have been done analyzing the similar patterns between the two diseases specifically. Inoue found that patients with both diseases had a common cytokine profile pattern and increase in IL-6 and IL18 specifically [11]. The similarity, and maybe even continuity helps the argument that the one disease is just the continuation of the other. When the two cytokine profiles were compared, it gave insight on which clinical symptoms patients suffered from more severely. While further analysis and studying is needed, this can help management and correlation of the two diseases, as certain studies have done by testing disease response to the same therapy [12].

4. Conclusions

While half of patients with a diagnosis of juvenile idiopathic arthritis have progression into adult hood, it is important to have consistent follow up throughout adulthood and heavily consider systemic symptoms as a flare of disease as seen in Packham's studies. Whether or not JIA always manifests to Still's or other diseases has not been established to date. Had our patient had better follow up and monitoring of her disease, perhaps the flare up would not have been so severe requiring hospitalization and lymph node biopsy. The American College of Rheumatology has created a set of documentation and questionnaires to help transition care from pediatric to adult care which our patient would have greatly benefited from the implementation of.

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