JUVENILE IDIOPATHIC ARTHRITIS – A case based study

By: Michael Zhanel

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Supervisor: Dr. Nader Shenouda

Abstract

Juvenile idiopathic arthritis (JIA) is a chronic inflammatory joint disease affecting children less than 16 years of age. The International League of Associations for Rheumatology (ILAR) has categorized JIA into sub-classifications including systemic arthritis, RF-positive polyarthritis, RF-negative polyarthritis, oligoarthritis, enthesitis-related arthritis, and psoriatic arthritis. In this case, a 2-year-old Caucasian female originally presented to the emergency department with painful, swollen wrists. Follow up by the family physician prompted further investigations and subsequently a consultation with a rheumatologist. A diagnosis of RF-negative polyarthritis was supported by patient history, physical exam, laboratory findings, and imaging.

Background

Juvenile idiopathic arthritis (JIA) is a chronic inflammatory joint disease affecting children less than 16 years of age (1). Symptoms including joint swelling, pain, and impaired range of motion in the joints most commonly present between ages 1-3 and persist into adulthood (2). Arthritic symptoms must persist for ≥6 weeks in at least one joint in order for a diagnosis of JIA to be considered (1). JIA has an incidence of 13.9 cases per 100,000 per year in the United States and is twice as likely to affect females in comparison to males (2). There appear to be ethnic differences in prevalence of the disease; for instance, there are higher rates of disease amongst Indigenous Canadians compared to Caucasian Canadians (2). JIA appears to have only a mild hereditary link with members of the proband being at a slightly increased risk of acquiring the disease (2).

Diagnostic investigations

Laboratory testing is often used to support the clinical diagnosis of JIA. The presence of antinuclear antibodies (ANA), rheumatoid factor (RF), an elevated erythrocyte sedimentation rate (ESR), elevated C-reactive protein, anti-CCP antibodies, synovial fluid analysis, and HLA typing can aid in diagnosis and allow for sub-classification of the disease (1,3,4). Imaging modalities including MRI, X-ray and bone scans are also helpful (1). Juvenile idiopathic arthritis was previously recognized as juvenile rheumatoid arthritis (JRA) in the United States and juvenile chronic arthritis (JCA) in Europe; however, JIA underwent reclassification by the International League of Associations for Rheumatology (ILAR) in the late 1990's in order to standardize nomenclature (3). The ILAR criteria categorizes JIA into sub-classifications including systemic arthritis, RF-positive polyarthritis, RF-negative polyarthritis, oligoarthritis, enthesitis-related arthritis, and psoriatic arthritis (3). Characteristics of each ILAR classification of JIA can be seen in Table 1.

Table 1. Key characteristic features of juvenile idiopathic arthritis sub-classifications as outlined by the International League of Associations for Rheumatology (ILAR) [a].

ILAR Classification	Percentage of total JIA cases (%)	Peak Age of onset (years)	Clinical features	Key laboratory findings
Systemic arthritis	5-15	1-5	≥1 joints affected; Fever, rash	Anemia; elevated ESR[b], CRP[c] and WBCs[d]
Polyarthritis				
RF[e]-positive	<10	9-12	≥5 joints affected	Mild anemia; elevated ESR
RF-negative	20-35	2-4	≥5 joints affected	Mild anemia; ANA[f] positive in ~40% of cases; elevated ESR
Oligoarthritis	50	2-4	1-4 joints affected	ANA positive in ~60% of cases
Enthesitis-related arthritis	5-10	9-12	Predominantly affects lower limb joints	80% positive for HLA-B27
Psoriatic arthritis	5-10	2-4	Asymmetrical arthritis; Psoriasis in 50% of cases	Mild anemia; ANA positive in 50% of cases; elevated ESR

[a] Data adapted from reference (4,5)
[b] Erythrocyte sedimentation rate, [c] C-reactive protein, [d] White blood cells, [e] Rheumatoid factor
[f] Anti-nuclear antibody

Treatment

Although there is no cure for JIA, a number of treatment regimens have demonstrated efficacy in managing disease progression and in symptom management. Treatment regimens vary slightly depending on the ILAR sub-classification. Non-steroidal anti-inflammatory drugs (NSAIDs) are the cornerstone of treatment for most forms of JIA including RF-positive and RF-negative polyarthritis, oligoarthritis and systemic arthritis (4,6). Some patients may benefit from intraarticular corticosteroid injections if NSAIDs are ineffective (4). For patients that do not benefit from NSAIDs or intraarticular corticosteroid injections, disease-modifying antirheumatic drugs (DMARDs) such as methotrexate, sulfasalazine, and leflunomide can be used (4,6,7). Various biologic agents are also available including tumor necrosis factor alpha (TNFα) antagonists such as etanercept and adalimumab, T-cell modulators such as abatacept, and interleukin-1 (IL-1) and interleukin-6 (IL-6) receptor antagonists including anakinar (4,6,7) . These agents have demonstrated a significant reduction of morbidity of the disease. Systemic corticosteroids are only recommended in select patients or as bridging therapy prior to initiation of DMARDs (8).

Case presentation

Overview

A 2-year-old Caucasian female originally presented to the emergency department with painful, swollen wrists. The girl's parents first became aware of the issue when they noticed their child excessively crying at night and clutching her wrists. X-rays taken in the emergency department did not reveal any apparent pathology. The patient was discharged with a suspected soft tissue injury. The patient was then followed up by her family physician. A history and physical exam revealed that the patient had experienced multiple episodes of intermittent atraumatic bilateral wrist swelling over the course of several months. Further investigations including bloodwork and MRIs revealed both laboratory and structural abnormalities which prompted a consult to a rheumatologist.

History

The patient's history was gathered from the parents of the child. The parents noted that they first noticed signs of pain in their daughter's joints about 3 months ago in June of 2018. The parents originally became concerned when their daughter was staying awake at night crying and clutching her wrists in pain. The parents deny presence of any systemic symptoms including fatigue, malaise, weight loss, or loss of appetite. The parents note that their daughter is often in the least amount of pain in the morning, worsening throughout the course of the day with use and movement of her joints. For several months, the parents have also been concerned about skin lesions in the patient's genital area. These skin lesions have yet to be diagnosed. There is no history of any type of arthritis or psoriasis in the family aside from the patient in question.

The patient has been taking Naproxen daily since June, 2018 as instructed by the family physician. Despite some symptom management, the patient's condition has continued to worsen. Greater pain and arthritic involvement of previously unaffected joints have been reported over the course of three months. The daughter is now beginning oral prednisone for 3 weeks and ongoing subcutaneous methotrexate injections.

Physical exam

On physical exam, the patient looked generally well with no signs of failure to thrive. No apparent atrophy of muscle was observed. Mild swelling could be observed over several joints including the joints of the patient's left wrist and right knee. The patient had a total of thirteen affected joints, mostly small joints of the left hand and wrist. The patient's left wrist and right knee felt warm to the touch. No erythema was present. The patient walked with a limp appearing to favour her right leg. Active and passive range of motion were limited in the patient's right knee as well as the small joints of the patient's left hand and wrist. According to a recent ophthalmic exam, the patient has no early signs of uveitis and vision is intact. The rheumatologist reports no signs of pleuritis, pericarditis, or peritonitis. No hepatomegaly, splenomegaly, or lymphadenopathy were noted on exam.

Laboratory testing

The patient's bloodwork revealed a hemoglobin of 113 g/L with an MCV of 75.9 fL, an MCH of 24.3 and an MPV of 8.5 fL suggesting a mild normocytic anemia. An elevated ESR of 35 mm/h was noted. Antinuclear antigen (ANA) was positive and rheumatoid factor (RF) was negative. Results of HLA-B27 are pending.

Imaging

MRI findings revealed significant joint effusions with associated synovial thickening and enhancement involving the following joints of the right hand and wrist: (i) The first, third and fourth metacarpal-phalangeal (MCP) joints, (ii) the first, second, third and fourth carpometacarpal (CMC) joint compartments, (iii) the radiocarpal joint, (iv) the intercarpal joints, and (v) the proximal interphalangeal (PIP) joint of the fourth digit. Additionally, tendon sheath dilatation and enhancement involving the flexor pollicis longus, flexor pollicis brevis, extensor pollicis brevis, and extensor pollicis longus tendons of the right hand were noted.

MRI findings of the left hand and wrist revealed significant join effusions with associated synovial thickening and enhancement involving the following joints: (i) The second, third and fourth metacarpal-phalangeal (MCP) joints, (ii) the first, fourth and fifth carpometacarpal (CMC) joint compartments, (iii) the radiocarpal joint, (iv) the ulnocarpal joint, and (v) the intercarpal joints. Additionally, enhancing bone marrow edema involving the right third finger was noted.

Discussion

This patient was ultimately diagnosed with juvenile idiopathic arthritis, specifically RF-negative polyarthritis. The diagnosis of JIA was based on the clinical presentation of the patient including the patient's symptoms, age, and chronicity of arthritis in her joints. MRI imaging confirmed synovitis in >5 joints supporting a diagnosis of polyarthritis. Laboratory findings including an elevated ESR, a mild anemia, the presence of ANA, and the absence of rheumatoid factor all further supported the diagnosis of RF-negative polyarthritis. At this time, a diagnosis of psoriatic arthritis cannot be excluded as an alternative diagnosis in this patient until the skin lesions in the patient's genital area have been evaluated by a dermatologist.

Based on the patient's diagnosis, treatment with methotrexate has been advised by a rheumatologist. The patient had been taking Naproxen and Nexium at the onset of arthralgia as advised by the family physician. The patient had little improvement in symptoms with NSAID use. The continued progression of arthritis into previously unaffected joints prompted a more aggressive treatment approach. The patient has been prescribed a 3-week course of oral prednisone as a bridging therapy. Subcutaneous methotrexate injections will be used as an ongoing treatment for 2 years or until remission is achieved.

JIA increases the likelihood of developing uveitis. In fact, as many as 80% of cases of anterior uveitis in the pediatric population are associated with JIA (9). Regular ophthalmic exams to screen for uveitis in patients are recommended. Patients who are female, RF-negative, ANA positive, and have an early age of onset of disease, are at higher risk of developing uveitis (9). Patients with polyarthritis, however, are three times less likely to develop uveitis than patients with oligoarthritis (9). Cumulatively, the risk of developing uveitis in patients with polyarticular arthritis is 4.3% (9). In this patient, routine ophthalmic exams every three months have been recommended.

Immunizations, if incomplete, can become problematic in some patients with JIA due to contraindications with immunosuppressive therapies. Patients on immunosuppressive

medications including DMARDs are advised not to receive live vaccines. Intranasal influenza, varicella, oral typhoid, yellow fever, oral polio virus, smallpox, Bacillus Calmette-Guerin and rotavirus are generally not recommended in patients taking methotrexate (10). In this case, it was recommended that the patient receive all necessary vaccinations including the MMRV vaccine prior to initiation of treatment with methotrexate.

Recommendations

Early detection and diagnosis of JIA is crucial. It is important to recognize the varying presentations of patients with JIA. Appropriate imaging and bloodwork should be conducted in order to rule out other causes of arthritic symptoms. Ultimately, a diagnosis should be made based on clinical signs and symptoms. With appropriate and timely treatment, the morbidity of JIA can be reduced. Despite this, up to 50% of patients with JIA will have symptoms persisting into adulthood and endure severe physical limitations throughout their lifetime (4). NSAIDs are the first-line therapy in patients with JIA. If NSAIDs are insufficient, intraarticular steroid injections should be tried. If symptoms continue to be uncontrolled or if disease progression continues, DMARDs should be initiated. Methotrexate is often the drug of choice. Systemic corticosteroids are only recommended in cases of severe systemic illness or as bridging therapy while DMARDs are taking effect. Long term oral corticosteroid treatment poses a variety of risks including toxicity, development of Cushing syndrome, growth retardation, and osteopenia (4). A combination of pharmacological and non-pharmacologic treatments such as physiotherapy are recommended to achieve the best possible outcomes for patients with JIA. Routine ophthalmic exams are recommended to screen for uveitis.

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