A 10-Year-Old Girl with Arthritis

Robert Listernick, MD

A 10-year-old girl was seen at an outside hospital for evaluation of arthritis of 5 month’s duration. Initially she had intermittent swelling of both elbows, followed by swelling of her right knee and ankle. She complained of morning stiffness for about 20 minutes each day. On occasion, she had trouble combing her hair due to pain in the elbows.

Medical history was remarkable in that 1 year before this visit she developed intermittent swelling around her left eye. The area of swelling was painful to touch, and her mother had noticed some erythema just below her left lower eyelid. In addition, several months earlier she had several episodes of “tonsillitis,” leading to tonsillectomy. She received multiple courses of antibiotics without relief. There was no history of persistent fevers, anorexia, weight loss, or other symptoms.

She was diagnosed as having beta thalassemia trait several years previously. Family history was remarkable for many members with chronic tonsillitis. Her mother’s previous pregnancy was an infant who had both myelomeningocele and a chromosomal abnormality.

On exam, she was well-appearing. Vital signs were unremarkable. Weight was in the 20th percentile and height in the 25th percentile. She had an asymmetric face due to swelling of the left zygomatic arch at the lower lateral border of the orbit with a small nodule palpable underneath the skin. There was no warmth or erythema of this area. It was minimally tender to touch.

Her lungs were clear; cardiac exam was normal; and her abdomen was soft without masses or organomegaly. There was a large effusion of the right knee with 5 to 10 degrees of lost flexion; there was tenderness on flexion. There was warmth and ballotable effusions at both patellae.

The right ankle was swollen at the lateral malleolus with warmth and loss of flexion. There was bilateral elbow swelling and warmth, right greater than left. The right and left elbows had 10-degree flexion contractures with tenderness on flexion. Neurologic exam was unremarkable.

Laboratory evaluation included hemoglobin 10.5 g/dL and MCV 60, consistent with beta thalassemia trait; white blood cell count of 8,500/mm³ with 52% neutrophils and 41% lymphocytes; platelet count of 500,000/mm³; and erythrocyte sedimentation rate 60 mm/hour. Serum chemistries were normal.

Rheumatoid factor, antinuclear antibody, angiotensin-converting enzyme, and antinuclear cytoplasmic antibody were all negative. The diagnosis of juvenile idiopathic arthritis (JIA) was entertained. She was given intra-articular corticosteroid injections in the right knee and ankle and both elbows and started on naproxen twice daily, as well as penicillin three times daily for possible post-streptococcal reactive arthritis.

Robert Listernick, MD, moderator: Gestalt?

Megan L. Curran, MD, pediatric rheumatologist: She has a lot of arthritis! Etiology to be determined. Her pediatrician thought she might have post-streptococcal reactive arthritis because of an elevated antistreptolysin O (ASO) titer. My initial impression was that she most likely had polyarticular JIA.

Dr. Listernick: What about the elevated ASO?

Robert Tanz, MD, general academic pediatrician: Fifteen percent to 25% of children are chronic streptococcal carriers and will have moderately elevated ASO titers. The elevated ASO is due to past infections, not the streptococcal carriage.

Dr. Listernick: Is there any value in getting an ASO titer?

Dr. Tanz: All it means is that there was antecedent streptococcal infection sometime in the past 6 to 9 months. It doesn’t mean that it’s related to the child’s acute symptoms, whatever they are. If an acute streptococcal infection were suspected, I would recommend obtaining at least two separate streptococcal antigen antibody titers such as ASO, antihyaluronidase, or anti-DNAase B.

Dr. Listernick: What is the difference between post-streptococcal reactive arthritis and rheumatic fever?

Dr. Curran: There’s a subset of chil-
... who have arthritis following streptococcal infection without other stigmata of acute rheumatic fever, most notably carditis. Post-streptococcal arthritis occurs sooner following strep pharyngitis than does the arthritis of rheumatic fever, and the arthritis is not migratory like you see in rheumatic fever. The severity of arthritis can be quite marked and difficult to treat, as in this child. In general, post-streptococcal arthritis won’t respond to aspirin treatment as readily as does the arthritis of rheumatic fever.

Dr. Tanz: The magnitude of the risk of developing rheumatic carditis is unknown. Many experts still recommend that these children receive penicillin prophylaxis for a while.

Dr. Listernick: She was referred to a cardiologist who performed an echocardiogram. She was discovered to have mild mitral regurgitation without having a discernible murmur. Unfortunately, this further confused the picture.

Dr. Tanz: Echocardiographic evidence of cardiac disease in the absence of auscultatory abnormalities does not qualify as evidence of carditis in the modified Jones criteria.

Dr. Listernick: Is it necessary to obtain X-rays of the joints in a child who has arthritis in multiple joints?

Dr. Curran: X-rays are not necessary to establish the diagnosis of JIA; however, they may be quite helpful in atypical cases. For instance, erosive changes might suggest the possibility of a positive rheumatoid factor or cyclic citrullinated peptide arthritis. In these cases, we might initially be more aggressive with therapy.

Dr. Listernick: What is the role of intra-articular corticosteroid injections in the treatment of JIA?

Dr. Curran: Placing a corticosteroid inside a joint is the best way to treat synovitis because the medicine goes exactly where it’s needed. Some pediatric rheumatologists will inject every involved joint. There is minimal systemic absorption. The effect often lasts for 2 to 3 months. I generally use triamcinolone hexaconotide. This girl improved significantly. However, I was still quite concerned about the swelling on her face and I tried to identify its etiology through imaging.

Dr. Listernick: What would be the best way to image the area as described?

Jessie Aw, MD, pediatric radiologist: It really depends upon what you’re most concerned about. If you believe the focal point is the bone, computed tomography (CT) is the best test. Ultrasonography is better for a simple soft tissue abnormality, such as a cyst. However, for better detail of a soft tissue lesion or detailing bone and soft tissue, magnetic resonance imaging (MRI) is best.

Dr. Listernick: What imaging was performed?

Dr. Aw: Ultrasonography simply showed some soft tissue swelling. MRI indicated that, although there was a soft tissue component to the lesion, it appeared to originate in the bone of the left zygomatic facial plate. We entertained the possibility that this was either fibrous dysplasia, Langhans cell histiocytosis, or an aneurysmal bone cyst.

We wondered about an infectious/inflammatory process. However, the soft tissue component did not have the strands of enhancement we generally see in infection.

Finally, CT imaging was performed once it became clear that the process was centered in the bone. Once again, the epicenter of the process was within the left frontozygomatic plate extending into the anterior aspect of the left zygomatic arch. There were areas of bone that were clearly destroyed, with minimal soft tissue inflammation.

Dr. Listernick: After all these studies, did your differential diagnosis change?

Dr. Aw: At this point, we were most concerned about either chronic osteomyelitis or Langerhans cell histiocytosis. Less likely, we considered a sarcoma originating from the bone such as osteosarcoma.

Dr. Curran: When I saw these images, the first thing I did was review the pathology of the removed tonsils. There was no evidence of malignancy. I asked our otolaryngologist to biopsy the lesion. When he visualized the lesion in the operating room, he said, “It looks like the inside of a grape.” He had no idea what it was but he removed as much tissue as possible.

Agatha Bogard, MD, pediatric pathologist: In a nutshell, there were large areas of necrosis within which were multiple necrotizing granulomas. The top of our differential diagnosis was infection. The initial acid fast and fungal stains were
negative. The CD1A stain for Langerhans cells was negative, eliminating the possibility of Langerhans cell histiocytosis. In addition, we really don’t see this degree of necrosis in Langerhans cell histiocytosis.

**Dr. Listernick:** Do you have any data regarding the sensitivity and specificity of acid fast and fungal stains in this situation?

**Dr. Bogard:** The specificity is close to 100%. I would estimate that the sensitivity of these tests is around 50% each.

**Ben Z. Katz, MD, pediatric infectious disease specialist:** There’s nothing magical about these tests. The more severe the infection, the more organisms are present and the more likely the stain will be positive.

**Dr. Curran:** When I heard about the pathology, I also thought about the possibility of Wegener’s granulomatosis, now termed granulomatosis with polyangiitis. It is an ANCA (anti-neutrophil cytoplasmic antibody)-associated vasculitis. Her ANCA was negative.

**Dr. Listernick:** What now?

**Dr. Katz:** She recovered well from her biopsy and 1 month later we received a report that the culture was growing acid-fast organisms. When I saw her in clinic I had no idea about her history and just assumed she had “run-of-the-mill” tuberculosis (TB). It turns out that the literature describes a rare form of reactive polyarticular arthritis associated with TB called Poncet’s disease.

**Dr. Curran:** To be clear, the pathophysiology of reactive arthritis is due to immune system activation by circulating antigens cross-reacting with antigens in joints. It is not a direct infection. More common cases of reactive arthritis are due to gastrointestinal infections from *Salmonella* or other bacterial infections, or organisms such as *Chlamydia*. Most of these infections are self-limited or are treated, minimizing the arthritis. I assume this girl’s arthritis was severe because she had untreated tuberculosis.

**Dr. Katz:** The acid-fast organisms were ultimately identified as *Mycobacterium tuberculosis*. Her PPD (purified protein derivative) test was positive. It turns out that when this family emigrated to the United States from Mexico, the older daughter had a positive PPD test. The family was told that it was most likely due to her previous BCG (bacille Calmette-Guerin) vaccine but that she should take medication. The family interpreted this to mean that the medication wasn’t really necessary.

**Dr. Listernick:** How should a positive BCG be interpreted?

**Dr. Katz:** In the United States, where the prevalence of TB is low compared with that in the developing world, a history of receipt of BCG vaccine should not be taken into account when interpreting a positive PPD. While it’s true that BCG can cause a positive tuberculin skin test, we don’t care because it’s these same people who are at highest risk for having TB. The risk of not treating far outweighs the risk of overtreating a falsely positive PPD. The incidence of adverse reactions to anti-TB drugs in children is exceedingly low. We treat almost every child who has a positive TB skin test as if they have latent tuberculosis.

**Dr. Listernick:** So why the zygoma?

**Dr. Katz:** No idea. Bad luck? Maybe she had a little trauma there several years ago when she was bacillemic. It generally takes at least 2 years to develop TB osteomyelitis. Her chest X-ray was negative.

**Dr. Aw:** Facial involvement with TB is exceedingly rare.

**Dr. Listernick:** How will she be treated?

**Dr. Katz:** I started her on four anti-tuberculous drugs: isoniazid, rifampin, pyrazinamide, and ethambutol. Once we learned of the bacterium’s sensitivities, we were able to eliminate two drugs and treat her with isoniazid and rifampin alone. We’ll probably treat her for 1 year. The local Board of Health is investigating the possibility of other cases in the family.

**Dr. Listernick:** Thank you, everyone.