



A 12-Year-Old Boy with Pars Planitis

Robert Listernick, MD

A 12-year-old boy complained of a “floater” in his right eye. He first noticed it 3 months ago. He says the floater used to blur his vision but no longer does. He has no floaters in the left eye. His vision is good and he has worn glasses for 3 years. His eyes occasionally become red but his mother feels it is due to his frequent video game playing. He has no headaches, light sensitivity, flashes of light, or history of trauma. His eye examination was normal and new lenses were prescribed.

Robert Listernick, MD, moderator: I’ve been meaning to ask this question for my entire 36 years in medicine but I’ve never gotten around to it: what are floaters?

Hawke Yoon, MD, pediatric ophthalmologist: As we get older, the vitreous in our eye decompensates and the protein comes out of solution, causing floaters. It’s not pathologic in the older population. However, the rapid onset of multiple floaters or flashing lights might be the initial signs of a retinal detachment.

Dr. Listernick: How about in children?

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Dr. Yoon: If an articulate child says he has a persistent floater, he should undergo a complete ophthalmologic examination including funduscopy. Still, most of the time I expect that nothing would be found.

Dr. Listernick: Continuing on, 6 months later he developed sharp, left-sided head pain that was treated with nonsteroidal anti-inflammatory medication. On the day he was to see an ophthalmologist, he awoke and was unable to see out of his left eye. He was diagnosed with bilateral pars planitis and prescribed prednisone eye drops and oral prednisone. At that time, he had no systemic complaints other than headache. I have been waiting 36 years to ask “what is pars planitis?”

Dr. Yoon: Anatomically, the pars plana is the space behind the ciliary body and anterior to the retina. Pars planitis is generally defined as inflammation of that space for which no cause is found. If we find systemic involvement, we usually use the term intermediate uveitis. The vast majority of cases of uveitis in children either will be idiopathic or related to juvenile idiopathic arthritis (JIA). Most of these cases will involve the anterior segment.

Dr. Listernick: How does uveitis generally present in children with JIA?

Dr. Yoon: Usually, it is asymptomatic with a quite insidious onset.

Megan Curran, MD, pediatric rheumatologist: Young antinuclear antibody (ANA)-positive children with oligoarticular JIA are at highest risk for the development of uveitis. We stress that this group

needs to see an ophthalmologist every 3 to 4 months as the uveitis can be silent but quite damaging if not detected early.

Dr. Listernick: How do you evaluate a child with uveitis?

Dr. Curran: We look for any symptoms or signs of systemic disease such as JIA, sarcoidosis, or Behcet’s disease. If there are none, the ophthalmologist will treat the child with topical corticosteroids.

Dr. Listernick: Should infections be considered in the differential diagnosis of “idiopathic” uveitis?

Stanford T. Shulman, MD, pediatric infectious disease physician: There are many infections that cause uveitis, such as tuberculosis, fungal disease, *Bartonella*, and others. Most will have other signs or symptoms that point to the specific infection. Still, they need to be considered in “idiopathic” cases.

Dr. Listernick: This patient’s pain and vision improved and the steroids were tapered. The following tests were normal: chest X-ray, ANA, rheumatoid factor, complete blood count, erythrocyte sedimentation rate, C-reactive protein, Lyme disease titers, and interferon-gamma release assay for tuberculosis. His fluorescent treponemal antigen test-absorbed (FTA-absorbed) was positive.

Several weeks later, he developed vertigo and muffled hearing in his left ear. He was found to have high-frequency hearing loss. He also complained of a metallic taste in his mouth and decreased appetite, which were ascribed to postnasal

drip. Reportedly, physical examination at that time was significant for left-sided facial droopiness and slight deviation of the tongue to the left. Magnetic resonance imaging (MRI) of the brain was said to be normal.

Review of systems was negative for any other symptoms. Family history was remarkable for his mother who has ductal carcinoma in situ. There's no history of relatives who have autoimmune or immunologic diseases. When first seen here, his vital signs and growth parameters were unremarkable. His eyelids were described as "puffy." Otherwise, his general physical examination, including complete neurologic examination, was normal. The ophthalmologist noted a granular appearance of his vitreous.

We need to comment on the positive FTA-absorbed.

Dr. Shulman: Although it may represent old acquired or congenital syphilis, I suspect it's a false positive. The non-treponemal tests such as the rapid plasma reagin (RPR) and venereal disease research laboratory (VDRL) are the ones that are more often false positives.

Dr. Listernick: It was repeated, and it was negative the second time. What are we to make of this history of facial droopiness that apparently disappeared upon a now-normal neurologic examination?

Doug Nordli, MD, pediatric neurologist: As neurologists, we first try to localize the lesion. The history of facial nerve weakness, vertigo, and hearing loss suggests a lesion near the cerebellopontine angle given that cranial nerves VII and VIII are so close together there. Cranial nerve XII is only 1 cm away. This points to a process involving multiple cranial nerves on one side, perhaps a growing mass or basilar meningitis.

Dr. Shulman: The timeline is a bit too long here, but anytime you hear the term "basilar meningitis," you need to consider the possibility of tuberculosis. However, the fact that he received systemic steroids certainly should influence our thinking be-

cause the prednisone may have considerably altered the course of many different diseases. Fortunately, we know that his interferon-gamma release assay (IGRA) for tuberculosis was negative.

Dr. Listernick: Let's look at the neuroimaging performed at our hospital.

Michael Rozenfeld, DO, pediatric neuroradiologist: Centered near the left cerebellopontine angle, there's an enhancing infiltrative lesion that involves the dura and the adjacent occipital bone. This process extends toward the brain in a globular manner, although it's difficult to determine whether it's invading the brain parenchyma or simply compressing it with resultant edema. There's extension into the left hypoglossal canal to which his tongue symptoms can be attributed. It also slightly extends into the left internal auditory canal but I don't see any clear involvement of cranial nerves VII or VIII. Although very subtle, I believe we can see the beginning of this process on the first MRI as well.

Dr. Listernick: Can you give us a neuroradiologic diagnosis?

Dr. Rozenfeld: The list should include meningioma, lymphoma, and granulomatous processes both infectious (tuberculosis, fungal diseases) and rheumatologic, particularly sarcoidosis.

Leon Epstein, MD, pediatric neurologist: I know that I'm stating the obvious, but parsimony would dictate a single diagnosis unifying the pars planitis and the central nervous system (CNS) process. Sarcoidosis rises way to the top of this list.

Dr. Listernick: Agreed, but we still have to make a diagnosis. Tell me if you agree with this statement: we don't perform enough brain biopsies. We tend to do them after a long diagnostic odyssey during which the patient often becomes sicker.

Art DiPatri, MD, pediatric neurosurgeon: There are brain biopsies and there are brain biopsies. This lesion is within the posterior fossa, which in many cases can make the procedure more complicated and potentially more risky than performing a biopsy of a cortical lesion in the frontal

Panelists



Robert Listernick, MD
Moderator



Hawke Yoon, MD
Pediatric ophthalmologist



Megan Curran, MD
Pediatric rheumatologist



Stanford Shulman, MD
Pediatric infectious disease physician



Doug Nordli, MD
Pediatric neurologist



Leon Epstein, MD
Pediatric neurologist



Art DiPatri, MD
Pediatric neurosurgeon



Rishi Lulla, MD
Pediatric neurooncologist

Not pictured: Michael Rozenfeld, DO, pediatric neuroradiologist; Nitin Wadhvani, MD, pediatric neuropathologist; Lily Marsden, MD, pediatric pathologist.

All panelists practice at the Ann & Robert H. Lurie Children's Hospital of Chicago, IL, where this discussion, part of a weekly series, was recorded and transcribed for *Pediatric Annals*.

lobe. My preference would be to avoid performing a biopsy near the cranial nerves or

Key Learning Points

1. The pars plana is the space behind the ciliary body and anterior to the retina. Pars planitis is generally defined as inflammation of that space for which no cause is found.
2. Most cases of uveitis in children will be either idiopathic or related to juvenile idiopathic arthritis.
3. Young antinuclear antibody-positive children who have oligoarticular juvenile idiopathic arthritis are at highest risk for the development of uveitis.
4. Sarcoidosis is a diagnosis of exclusion after infections and other granulomatous diseases are excluded. Classically, the histology is non-necrotizing granulomas.
5. Neurosarcoid often presents as basilar meningitis with multiple cranial nerve involvement. Mass lesions and infiltrative optic nerve disease also have been described.

brainstem unless it was absolutely necessary. Certainly if there's an easier way to make a diagnosis in lieu of craniotomy, it should be performed first. If a child has a rapid deteriorating course or if there are profound deficits of unknown cause with unusual-appearing neuroradiologic lesions, we'd be more likely to perform an early biopsy. This child was having severe debilitating headaches with an unusual course, which prompted the biopsy.

Nitin Wadhvani, MD, pediatric neuropathologist: I'd also comment that unless the lesion is clearly a tumor on imaging, our diagnostic yield on brain biopsies has been low historically.

Dr. Curran: We're often faced with this dilemma in a child whom we believe has isolated CNS vasculitis. We believe the child has an inflammatory process, the neuroimaging is suspicious but far from diagnostic, and we know the yield on biopsy is low. On occasion, we've treated children for inflammatory diseases without clear pathologic evidence. Even though we were highly suspicious of a rheumatologic disease in this case, in particular sarcoidosis, we felt strongly that we would like to establish a pathologic diagnosis before starting treatment.

Dr. Listernick: I believe oncology was consulted prior to the biopsy?

Rishi Lulla, MD, pediatric neurooncologist: Yes we were. We felt that this lesion was very unlikely to be either a primary CNS tumor or metastatic disease from both its appearance and its association with uveitis. The question of primary

CNS lymphoma was raised. Once again, this is extremely rare in children and the lesion hadn't responded to systemic steroids given for the uveitis, so we thought it highly unlikely.

Dr. Listernick: Can we please see the pathology?

Lily Marsden, MD, pediatric pathologist: We received multiple core biopsies. There was no normal brain tissue; it was all highly cellular inflammatory tissue. We call this geographic necrosis because there are sharp dividing lines between the granulation tissue and the necrosis. The granulation tissue has multinucleated giant cells, lymphocytes, neutrophils, and spindle cell histiocytes that are trying to wall off the areas of necrosis. All the biopsies, including those from the cerebrum, cerebellum, cerebellopontine angle and dura, had this histology.

Dr. Listernick: And your interpretation?

Dr. Marsden: These were necrotizing granulomas. Sarcoidosis is a diagnosis of exclusion; the granulomas should be non-necrotizing. All the stains for infectious agents such as fungi or mycobacteria were negative. There was no evidence of vasculitis as should be seen with primary granulomatous angiitis or Behcet's disease. Even though we performed special stains for lymphoma, the histology was completely inconsistent with that diagnosis. So our final diagnosis was "necrotizing granulomatous inflammation."

Dr. Listernick: He underwent lumbar puncture that revealed 35 white blood

cells/mm³ (54% lymphocytes, 46% neutrophils) with normal opening pressure, glucose, and protein. The following tests were all negative: HLA-B51 (conveys genetic predisposition for Behcet's disease), antineutrophil cytoplasmic antibodies, antiphospholipid antibodies, urine histoplasma and blastomyces antigens and antibody titers for toxoplasmosis, histoplasmosis, blastomycosis, *Toxocara canis*, and *Bartonella*. Repeat testing of serum and cerebrospinal fluid for syphilis was negative.

So are we left with sarcoidosis?

Dr. Curran: Once again, sarcoidosis is a diagnosis of exclusion. There are no specific diagnostic criteria for sarcoidosis. We have excluded infections to the best of our ability.

Dr. Listernick: How does neurosarcoidosis generally present?

Dr. Curran: The classic neurosarcoid presentation is that of a basilar meningitis with multiple cranial nerve involvement. Mass lesions, such as in this child, and infiltrative optic nerve disease also have been described.

Dr. Listernick: There's always confusion about the utility of serum angiotensin-converting enzyme (ACE) levels in making the diagnosis of sarcoid.

Dr. Curran: ACE levels in healthy children are much higher than the stated reference for adults. ACE levels may be helpful in assessing disease activity in a child with a known diagnosis but, they are a very poor for establishing a new diagnosis.

Dr. Listernick: So we're going to go with the diagnosis of sarcoid. Treatment?

Dr. Curran: First, I make sure that there is no evidence of other end-organ involvement such as arthritis or myocarditis. In children with CNS disease, steroids are useful due to their rapid onset and efficacy in reducing inflammation. However, we add steroid-sparing agents as soon as possible, such as the tumor necrosis factor inhibitors like infliximab. When we use steroids, we generally opt for dexamethasone, which reportedly has better CNS penetration.

Dr. Listernick: Thanks everyone.