Behçet's Disease

Developed by Levi Ansell and Dr. Dax G. Rumsey for PedsCases.com
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Introduction:

Hi everyone, my name is Levi Ansell and I am a second-year medical student at the University of Alberta in Edmonton, Alberta, Canada. This podcast was developed in conjunction with Dr. Dax G. Rumsey, pediatric rheumatologist at the University of Alberta and Stollery Children's Hospital in Edmonton, Alberta, Canada.

Today we will be discussing pediatric Behçet's Disease or simply 'Behçet's'.
Objectives for this PedsCase are as follows:

1. Recognize the signs and symptoms of Behçet's
2. List the 6 classification criteria for pediatric Behçet's
3. Conduct a focused history for patients suspected to have Behçet's
4. Describe what you would look for on physical exam in a patient with suspected Behçet's
5. Discuss the investigations and management of patients with Behçet's

Definition:

Behçet's Disease is a multi-system inflammatory disease primarily characterized by recurrent oral ulcers (in 98-100% of cases) and genital aphthous ulcers. There may also be other cutaneous, ocular, neurological, gastrointestinal, articular, and vascular manifestations present. The disease is described as a variable vessel vasculitis, meaning that it can affect both arteries and veins. The clinical presentation of Behçet's is highly variable and appears to follow patterns based on geographic areas. The etiology of the disease is still largely unknown, but, as in many diseases, it is thought to be due to a combination of genetic factors and environmental triggers.

Epidemiology:

Although Behçet's can be seen all over the world, it tends to have the highest prevalence along the historical Silk Route from Japan to the eastern edge of the Mediterranean Sea. It is most commonly seen in Turkey and other parts of the Middle East. In pediatric Behçet's, boys and girls tend to be affected equally. The same is not true in adult Behçet's, where it is observed almost twice as often in men as compared to women. It is estimated that only about 5.4-7.6% of patients with Behçet's have their disease onset in childhood.

The Case:

You are a clerk doing an elective with a general pediatrician in a community clinic. You are seeing a 14-year-old boy with a 3-year history of sporadic oral ulcers. His mother was originally not concerned about these ulcers, presuming they were just canker sores, but they have increased in frequency and severity and her son has recently complained of genital ulcers over the last several months. The boy is otherwise healthy, has two healthy siblings, and is of Turkish descent. You begin to wonder if this could be Behçet's Disease. How would you approach this patient?

Classification Criteria:

Consensus classification criteria specific for pediatric Behçet's Disease were developed in 2015 in an effort to more accurately identify and describe Behçet's as it presents in children and adolescents (as opposed to using the adult criteria). Classification of pediatric Behçet's requires that patients have at least 3 out of 6 of the following categories of symptoms:

1. **Recurrent oral aphthosis (98-100%)**
- This describes oral ulcers and must occur at least 3 times per year
2. **Genital ulceration or aphthosis**
- The genital ulcers typically heal with scarring
3. **Skin involvement**
- There can be a number of presentations such as necrotizing folliculitis, acneiform lesions, and erythema nodosum
4. **Ocular involvement**
- Here we can see ocular inflammation in the form of anterior uveitis, posterior uveitis, and/or retinal vasculitis
5. **Neurological signs**
- *Isolated headache can occur, but is not sufficient to count as a criterion
- The rest of the neurologic signs are related to parenchymal or non-parenchymal (vascular) disease
- In parenchymal disease, it can present as encephalomyelitis (with pyramidal symptoms, extrapyramidal symptoms, and seizures)
- In non-parenchymal disease, it can present as papilledema often due to dural sinus thrombosis
- The most common neurologic presentation in children is **cerebral venous sinus thrombosis**
6. **Vascular signs**
- Such as venous and arterial thromboses and arterial aneurysms
- Pulmonary artery aneurysms are **highly associated** with Behçet's (yet, they are a rare presentation of this disease)

Of note, classification criteria are created for the purposes of research studies. They are not necessary or sufficient for diagnosis in all cases. However, they can be very helpful in guiding your approach to patients with suspected Behçet's.

Behçet's Disease History:

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Because some of the signs mentioned earlier are not specific to Behçet's, a good history and physical exam is crucial to teasing out important details. Questions that you might ask to help ascertain a diagnosis of Behçet's might sound like the following (the way you may phrase your questions is expressed in italics):

History of Presenting Illness:

- *Tell me a little bit more about your symptoms. How frequent are you getting sores in your mouth? What are these sores like and where are they located? Any triggers? When did you first notice the genital ulcers? Are you having any other symptoms or have you noticed anything else going on?*

Rheumatologic Review of Systems: Now that we have given our patient a chance to recall symptoms that they have noticed over the last few years, we want to direct the conversation toward some of the specific areas that may narrow our differential diagnosis and subsequent physical exam.

- Neurologic: *Have you had any headaches? Any associated nausea? How about ringing in your ears? Any abnormal movements?*
- Head and neck symptoms: *We already have the mouth ulcers on our radar, how about any changes in your vision? Do you ever get really dry, itchy, or red eyes (that feel like there is sand in your eyes)? Does bright light ever bother your eyes? Do you often feel like your mouth is so dry that you need an excessive amount of water, even through the night? Have you noticed any hair falling out? Any bald patches?*
- Chest symptoms: *Any chest pain? How about shortness of breath?*
- Gastrointestinal/Genitourinary: *So, we already know about the genital ulcers. Have you noticed any change in bowel or bladder function? Any diarrhea, constipation, or blood in your urine or stool?*
- Musculoskeletal: *Are you able to participate in gym class and after school activities? Can you keep up with the others in your class? Any joint pain, swelling, stiffness, or weakness?*
- Skin changes: *Have you noticed any new rashes, skin lesions, or anything else like that? Do you ever get a rash from exposure to the sun? How about any color changes of your hands or feet?*
- General: *How about any unexplained fevers, weight loss, or change in appetite?*

The remainder of the history shares characteristics with any general pediatric history.

- Medications
- Allergies
- Past Medical History
- Family History, with emphasis on rheumatologic/autoimmune conditions, as well as ethnicity and consanguinity
- Social History – important because of the differential diagnosis of sexually transmitted infections (STIs) for children/adolescents presenting with oral/genital lesions.
    - Adolescent (HEADSS) history

<u>Physical Exam for Behçet's:</u>

After the history, we should have a pretty good idea about what has been going on with our patient. Thus, we can then proceed with a physical exam. The physical exam should consist of the following:

- Head and Neck exam:
  - Inspecting for ulcers in the oropharynx and nose
  - Checking the eyes for lacrimation (tears) or hyperemia (excessive blood vessels)
  - Completing lymph node exam
- Full skin exam:
  - Looking for rashes, such as erythema nodosum, acneiform rash, signs of pathergy (which is a skin condition classically seen in Behçet's in which a minor trauma such as a bump or bruise leads to the development of skin lesions or ulcers)
  - Checking for signs of superficial thrombophlebitis
- Cardiovascular exam:
  - For signs of vasculitis (e.g. bruit, hypertension)
  - For signs of thrombosis
- Respiratory exam:
  - For signs of respiratory distress
- Neurologic exam:
  - Checking for papilledema
  - As well as assessments of strength, reflexes, spasticity, rigidity, and tremors
- Gastrointestinal exam:
  - Do a general abdominal exam and further exam or investigations guided by the history
- Pelvic exam for genital ulcers and/or scarring
  - This can be a very sensitive exam, especially in adolescents. Proper draping and communication are important, as well as having a chaperone present during the exam

Back to the case:

Following our thorough history, review of systems, and physical exam, we have now learned a lot about our patient. As mentioned before, our patient had complained of both oral and genital aphthous ulcers. Nothing else significant came out in the review of systems. Another thing that our physical exam yielded were several tender nodules on our patient's lower legs.

Differential Diagnosis:

Other possible diagnoses to consider based on our patient's presentation should include:

- Infection, infection, infection (STIs – e.g. HSV)
- Mucositis (post-infectious – e.g. Mycoplasma)
- Lipschütz ulcers
- Self-harm (less likely in this case)

Investigations:

There is no one laboratory test that is diagnostic for Behçet's. However, several investigations can help rule in/out other conditions and/or help support/refute the diagnosis of Behçet's.

Some investigations we may want to start with include:

- Swabs, urine, and blood work for infection (e.g. HSV, EBV, syphilis, chancroid)
- CBC + differential – we would expect to see signs of inflammation in active disease (thrombocytosis, neutrophilia)
- Inflammatory markers (such as ESR and CRP) are also typically elevated during active disease
- Think about getting an eye exam to screen for ocular involvement
- If a rash is present, then think about referring for a skin biopsy

Other investigations to leave for the rheumatology team are things such as:

- An HLA-B51 test
- More specialized imaging to look for things like vasculitis

Back to the case:

After undergoing initial testing, the swabs come back negative and we are able to rule out an HSV infection and other STIs. The inflammatory markers are elevated. Biopsy of the skin lesions demonstrates erythema nodosum. Our suspicion for Behçet's grows stronger. As we think about next steps, a referral to rheumatology is likely warranted at this time to initiate suitable treatment (if they are not already involved). It would also be the right time to consider follow-up with other specialties, such as ophthalmology, to ensure uveitis and other complications are diagnosed and managed appropriately, if present.

Treatment:

The treatment for Behçet's is largely dependent on the symptoms present.

For mucocutaneous involvement (e.g. ulcers), topical steroids are often used. In select cases, particularly ones where the dominant lesions are genital ulcers or erythema nodosum, colchicine can be used to prevent recurrence. Also, NSAIDs can be used for treatment of erythema nodosum and systemic steroids can be used to treat severe mucocutaneous flares.

Ocular involvement should be managed in conjunction with an experienced ophthalmologist. Uveitis should be treated with azathioprine, cyclosporine, or monoclonal TNF-inhibitor biologics. Systemic steroids could be considered in acute situations in combination with other systemic immunosuppressive medications.

Other symptoms can be managed with several immunosuppressants and more detailed information about this can be found in the 2018 update of the European League Against Rheumatism (EULAR) recommendations for the management of Behçet's syndrome.

Back to the case:

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Now that our patient has been started on some initial therapy (i.e. colchicine and topical steroids) and has seen some improvement after a few weeks, we should take some time to explain what the management plan will look like down the road. We would encourage our patient to follow up periodically with the rheumatology team, the ophthalmologist, and to see other specialists, as necessary. Monitoring will include regular clinic visits, lab work, eye exams, and other monitoring/investigations (e.g. imaging), as needed. Referral to other specialists depends on manifestations that are present, but could include referral to respirology, gastroenterology, and/or neurology. Psychology and/or psychiatry may also be useful to help the patient cope with the disease. Behçet's tends to have a lengthy course with the disease being managed, but not cured. Coordinated management is very important to ensure that the complications of Behçet's are minimized.

Take Home Points:

1. The most common presenting symptoms for Behçet's are oral and genital ulcers, but keep in mind some of the other less common and potentially more serious manifestations.
2. The 6 classification criteria for pediatric Behçet's were developed primarily for research purposes and include recurrent oral ulcers, genital ulcers, skin involvement, ocular symptoms, neurological signs, and vascular symptoms.
3. Be sure to capture a patient's ethnic background, various symptoms, and to perform a detailed rheumatologic review of systems.
4. Complete a thorough physical exam and ensure that your patient is comfortable.
5. Primary investigations should rule out infection and identify other serious symptoms. Although there is no specific test for Behçet's, elevated inflammatory markers and the absence of another clear cause of typical symptoms can point us in that direction. Management will vary depending on how the patient presents.

Thank you for taking the time to listen to this podcast. We hope you found the information helpful and that you feel more comfortable approaching a patient with Behçet's in the future.

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