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Approach to Pediatric Neck Masses

Developed by Asa Rahimi and Dr. Frederick Kozak for PedsCases.com.
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Introduction:

Hi everyone, my name is Asa Rahimi and I'm a fourth-year medical student at the University of British Columbia in Vancouver, Canada. This PedsCases podcast on 'neck masses' was developed with the help of Dr. Frederick Kozak, a pediatric otolaryngologist, clinical professor, post graduate education program director of the UBC Division of Otolaryngology – Head and Neck Surgery, and the former head of the division of pediatric otolaryngology at BC Children's Hospital.

This podcast was designed to address the following learning objectives:

1. Describe the typical clinical presentation of congenital and acquired neck masses.
2. Describe the causes of congenital and acquired neck masses.
3. Explore the approach to diagnosis and management of pediatric neck masses.
4. Review a detailed case presentation of a pediatric neck mass.

The case:

Before we dive into addressing the objectives, let's start with a case. Imagine you are a third year medical student working in the in-patient pediatrics ward, and you meet 'Aiden Lawfford' a 4 year old boy with a new neck mass. His father mentioned that he's had seven days of fever, irritability and has now developed a rash. You read in the medical record that Aiden had been recently seen at his family doctor's office for fever and sore throat. During that visit, his mother reported that a child at Aiden's preschool had been diagnosed with Streptococcus pharyngitis a few days before Aiden became sick.

Aiden was started on empiric amoxicillin, and a throat culture was obtained prior to starting antibiotics with results pending.

Let's address the first learning objective, that is, to describe a typical clinical presentation and the causes of congenital neck masses

We can't rule out the possibility of a congenital neck mass that until now, has not presented. So let's start off by understanding the typical clinical presentation of congenital neck masses. Timing, location and size are key characteristics that can give you clues on whether this is a congenital problem, or something acquired. A mass present since birth or discovered during the neonatal period is likely congenital. However, some congenital masses may present later in life with growth over time or with superimposed infection.

The location of the neck mass provides many clues. The most common midline cystic neck masses are thyroglossal duct cysts or dermoids. Thyroglossal duct cysts are often found in close proximity to the hyoid bone and elevate with tongue protrusion or on swallowing. Whereas dermoids typically move with the overlying skin and present as painless skin-coloured or yellow tinged lumps.

Q: So, what are thyroglossal duct cysts? And how do they come about?

A: Well, a thyroglossal duct cyst is a congenital defect. When the thyroid gland forms during embryonic development, it begins at the base of the tongue and descends down the neck through a canal called the thyroglossal duct. This duct normally regresses once the thyroid reaches its final position in the neck. Sometimes, portions of the tract or duct remain that result in a thyroglossal cyst along the descent path. These cysts can fill with fluid or mucus and may enlarge if they become infected.

Dermoids occur during embryonic development when the skin layers do not properly grow together. A dermoid is lined with epithelium, which contains tissues and cells normally present in skin layers, including hair follicles, sebaceous, and sweat glands. These glands and tissues secrete their normal substances which collect inside the cyst, causing it to grow and enlarge.

Masses found in the lateral neck include branchial cleft anomalies and vascular or lymphatic malformations. For example, a lymphatic malformation, previously known as a cystic hygroma, is a deep subcutaneous cystic swelling filled with lymph, but is blocked from the rest of the lymphatic system. Vascular hemangiomas are benign vascular tumors derived from blood vessel cell types.

A: Now to talk about branchial cleft anomalies, we need to get into some embryology.

Branchial clefts are defects that result from incomplete involution of branchial cleft structures. Around the fourth week of gestation, neural crest cells migrate into the future head and neck region where the remaining five pairs of branchial or also known as pharyngeal arches begin to develop. They are structurally composed of mesoderm that is covered externally by ectoderm and is internally lined by endoderm. The arches are separated by depressions known as clefts which represent the ectoderm surface and pouches which represents the endoderm surface. There are typically 4 pharyngeal clefts. These buried clefts become ectoderm-lined cavities that will usually involute

completely by 7 weeks of gestation. But if the clefts do not involute, they will form pathological remnants of an epithelium-lined cyst containing keratinous debris inside, with or without a sinus tract over the skin. Cysts have a mucosal or epithelial lining without external openings. Sinus tracts may communicate either externally with skin or internally with the pharynx, compared to fistulae that connect to both.

Embryologically this is a complicated process. We've provided a reference on the pedscases website that will give you a detailed overview of what occurs embryologically in utero.

Lastly all congenital masses have the potential to have a superimposed infection which can present as tenderness, swelling and redness of the mass.

Now let's describe the typical clinical presentation and the causes of acquired neck masses

Now briefly going back to the case, it appears that Aiden wasn't born with the neck mass, but instead that it was a 'new' finding during this illness.

In terms of timing, acquired neck masses are not present at birth. A new rapidly growing mass is usually inflammatory, and a mass persistent for weeks or enlarging after initial antibiotics should be concerning for a potential neoplasm. A slowly enlarging mass over months to years suggests benign lesions like lipomas, fibromas and neurofibromas.

A generalized term used to describe diseases of the lymph node is lymphadenopathy. Lymphadenopathy due to Inflammatory aetiologies is often associated with rapidly enlarging tender masses with overlying erythema. For example, lymphadenitis, which is direct inflammation of a lymph node, usually due to infection and caused by a virus, bacteria or fungus.

An upper respiratory tract infection with common symptoms like runny nose, nasal congestion and discharge, sneezing, sore throat, cough and malaise preceding the onset of the mass suggests possible reactive lymphadenopathy. Reactive lymphadenopathy from an upper respiratory tract infection often presents as multiple small lymph nodes. These lymph nodes are not directly infected, therefore won't be tender or have overlying erythema. But they will be enlarged due to the upregulation and activity of immune cells in these nodes due to infection elsewhere, likely a virus, but it can also be due to a neoplastic, bacterial or parasitic process in the body. However, neoplastic presentations will not present with cold-like symptoms.

Lymphadenopathy due to malignancy, and primary malignancy neck masses are often asymptomatic and non-painful unless there is an acute infection on a necrotic malignant lymph node. Constitutional symptoms such as fever, weight loss, night sweats and malaise suggest malignancy. A hard irregular, firm or rubbery mass that is fixed to the

deep tissues of the neck may indicate malignancy, either from a primary lymphoma or metastasis. Malignant anterior neck masses can be caused by thyroid cancer, although this is relatively rare in the pediatric population. Other primary malignancies to consider are neuroblastoma, rhabdomyosarcoma and head and neck cancer. We must not forget the possibility of metastatic spread from cancers such as acute lymphoid leukemia.

It should be noted that cervical lymph nodes up to 1 cm in size are normal in children younger than 12 years of age. Persistent enlarged lymph nodes greater than 2cm that do not respond to empiric antibiotic therapy should be suspicious for malignancy.

Lymphadenopathy with a several day history of high fever, oral mucosal changes with a strawberry tongue and bilateral nonpurulent conjunctivitis is suggestive of Kawasaki disease.

Medications should be reviewed. For example, phenytoin (Dilantin) which is known to cause pseudolymphoma or lymphadenopathy associated with anticonvulsant hypersensitivity syndrome. And this should be remembered.

Lastly, recent exposure to an ill child, animals, specifically cat scratch or feces, tick bites and foreign travel, should be considered and may inform an infectious etiology.

Cat-scratch disease (CSD) is an infectious disease that results in regional lymphadenopathy from a scratch or bite of a cat. Symptoms typically begin within 3-14 days following infection. Cat-scratch disease is caused by the bacterium Bartonella henselae which is believed to be spread by the cat's saliva.

Now let's go over our diagnostic approach for Aiden

In order to make a diagnosis we need to characterize the mass, meaning we need to take a thorough history and physical examination.

We know that the chief complaint is neck mass, but now we have to learn more about its course. When did the mass appear, did it have a slow and insidious onset, or did it appear quickly? Is it changing in size, if so, how quickly? Is there any associated pain or change of colour? Is there any notice of other masses in the neck or the rest of the body? Has the child had any fevers, night sweats, recent weight loss? What's their energy/mood or appetite like lately? Lastly, a review of systems should be performed to identify any loci of infection.

Like other histories, you want to ask past medical and surgical history including the child's prenatal, and birth history. You want to ask about immunizations, medication, allergies, family history and social history.

Now let's get back to Aiden.

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After speaking to Aiden's dad, this is what you find out about his history. Aiden's neck mass showed up suddenly about 7 days after the onset of his fever. It's sizeable and only on the left side of his neck. It has grown in size since its onset, and dad thinks it looks red and swollen and is causing Aiden some grief. Aiden and his dad haven't noticed any lumps or masses anywhere else. He hasn't had any weight loss or night sweats.

Although Aiden has had fevers before, they have never lasted this long or been up to 40 C (104 F) so often. His temperature comes down slightly in response to appropriate doses of acetaminophen and ibuprofen, but quickly goes back up. He has been much more irritable than normal, not interested in playing with his toys and crying a lot more than he typically does. He has not been sleeping very well, either. He hasn't eaten well for almost a week because he's been too crabby to eat. But he has been drinking fluids and his urine output has been normal. His dad noticed a rash about four days ago, starting in the groin area but now it covers his entire body; even his arms and legs. His dad says it looks like a bunch of red spots all over his body. He doesn't seem to be scratching it at all. Aiden's eyes have also been red over the past several days. And now dad tells me his mouth has been hurting and his tongue looks red.

Aiden's past medical history is unremarkable. He was born via a spontaneous vaginal delivery at term from a Gravida 2, parity 1 mother with no pregnancy or perinatal complications. He was diagnosed *with acute otitis media at 18 months of age, but it resolved appropriately with oral antibiotics. He has had no surgeries and received all his required immunizations. His family history is non contributary. Aiden lives with his parents and brother. He has not recently travelled, and there are no animals or smokers at home. He attends preschool but no one seems to be ill at school*

Physical exam:

Moving on to the physical examination. You want to start off by checking the vitals, followed by doing a head to toe assessment. You want to ask yourself, 'does this child look unwell?' That is, are they sweaty, working hard to breath, pallor or particularly thin?

Specifically, you want to inspect and palpate the neck mass or masses. Take notice of where they are located, and how many you are seeing. Palpate the mass – is it soft, hard, fluid filled? Is it mobile or matted down? Does the child grimace in pain when it's touched, or do you see any surrounding swelling or redness?

Check the rest of the body from head to toe for signs of infection or malignancy. Specifically palpate the cervical, axillary, epitrochlear and groin areas for evidence of lymphadenopathy. Also palpate the spleen and assess for enlargement. Signs of infection include swelling and redness of the area with accompanied tenderness on exam. Malignancy can present as a non-painful palpable mass elsewhere if it has metastasized or in cases of lymphoma.

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Now back to the case.

Aiden looks irritable and you immediately notice a rash on his arms. He's febrile at 39.7 degrees Celsius, tachycardic at 150 bpm, and tachypneic at 24 breaths/min. His blood pressure is 95/60 mm Hg. His weight is 19 kg and his height is 108 cm.

Aiden's eyes are red but not purulent and not painful. His tongue is bright red, and the left side of his neck is red and swollen to the size of a golf ball, with a diameter of 2.5 cm. When you palpate the neck mass it's tender and you can feel a cluster of smaller 1 cm lymph nodes, but you note that it's a difficult exam due to the surrounding swelling.

Looking closely at his rash, you note that it has spread to multiple locations, including his neck, trunk, arms, legs and groin area. The rash consists of red non-raised blanching spots, also described as an erythematous macular blanching eruption. Aiden's palms and soles seem to be swollen as well.

The remainder of the exam is normal.

Differential:

Before we move any further in our diagnostic approach, we should amalgamate the information in order to create a differential diagnosis. Remember, Aiden is a 4-year-old boy with a 7-day history of fever, increased irritability, cervical lymphadenopathy, who has recently been treated for presumptive streptococcus pharyngitis. He now presents with a diffuse, blanching macular rash, and red eyes.

Inflammatory etiologies should be high on the differential because of the recent onset of the mass. We should consider: Reactive lymphadenopathy from a systemic infection, cervical lymphadenitis due to bacterial infection, or Kawasaki's disease, which is a medium sized artery vasculitis. Congenital lesions are much less likely due to the time course and systemic symptoms, but branchial cleft cysts can appear later and can become infected. Reactive lymphadenopathy due to neoplasm is less likely with the acuity of the symptoms and their inflammatory nature. Primary neoplasm would be highly unlikely for the same reasons.

We should also consider other more life-threatening presentations that present with a rash such as meningitis.

A: The most likely diagnosis at this point is Kawasaki disease.

Investigations:

The final step to approaching diagnosis is ordering the needed investigations.

Initially we would order a complete blood count with a differential to look for signs of infection, malignancy, hemolysis and platelet consumption. In inflammatory and infectious etiologies, we would expect a high white blood cell count.

Pancytopenia with blast cells is suggestive of leukemia and atypical lymphocytosis can occur in mononucleosis. An ESR or CRP would be useful to assess as a marker of inflammation. However, these markers play a more useful role in following a disease process. Liver and kidney function tests should also be ordered to evaluate any systemic involvement. An elevated transaminase level can be seen in infectious mononucleosis. A blood culture should also be drawn to rule out bacteremia.

After routine laboratory investigations, more specific testing can be done.

A fine needle aspirate of the tissue could be performed and sent for gram stain and culture to evaluate bacterial etiologies. It can also be used in suspected malignancy to avoid an open biopsy of the lymph node or tissue. Monospot or EBV serologies could be performed to diagnose infectious mononucleosis. Bhenselae serologies or Bartonella henselae titers could be done to investigate catscratch disease. Measurement of titers for cytomegalovirus, human immunodeficiency virus, and toxoplasmosis also should be considered if the history suggests possible exposure or if a presumed inflammatory mass is not responding to antibiotics.

Imaging with ultrasound, CT or MRI has its role in characterizing the mass, its extent of involvement to adjacent tissues, and with planning for invasive intervention such as surgery. For example, in the context of suspected neoplasm and its needed excision. Ultrasound is the preferred initial imaging study in an afebrile child with a neck mass or a febrile child with a palpable neck mass. Ultrasound should be the initial imaging study for the evaluation of a thyroid mass, when a thyroglossal duct cyst is suspected, or in order to determine the presence of a normal thyroid gland. CT with intravenous contrast media is preferred for evaluation of a malignancy or a suspected retropharyngeal or deep neck abscess that may require surgical drainage.

MRI imaging can better define soft tissue anatomy, and avoids radiation exposure from CT; however, the expense and frequent need for sedation often limits its use as an initial imaging modality. It is however the imaging study of choice when a vascular malformation is suspected.

Keeping in mind the diagnosis of Kawasaki disease, we would order a series of tests investigating infectious/inflammatory causes, and this would include a complete white count with differential, CRP or ESR, and blood culture. We would expect a high white blood cell count. Normocytic anemia and thrombocytosis are also common, with thrombocytosis occurring normally in the second week of illness. A negative ESR would argue strongly against Kawasaki disease while an elevated transaminase level and a urinalysis showing sterile pyuria secondary to sterile urethritis is associated with Kawasaki disease.

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It would be of high importance to order an echocardiogram for suspected Kawasaki Disease as it's known to affect the coronary arteries and can cause aneurysms and pericardial effusions that can be life threatening. There would be no need for any further imaging or a fine needle aspirate.

Now let's jump back to the case, and review Aiden's investigations.

Because of the sudden onset of the neck mass, and the swollen and red nature of it, inflammatory etiologies were suspected. Initial testing performed was blood work.

Aiden's CBC showed 17 billion cells per liter with a left shift. His ESR is elevated at 78 mm/hr, normal being between 0-15 mm/hr. There is no evidence of anemia or thrombocytopenia, in fact his platelets were noted to be elevated. His liver function and kidney function are normal. Blood culture is negative. Urinalysis shows sterile pyuria and his throat swab was negative for streptococcus. Seeing that Kawasaki's is our working diagnosis, he had an echocardiogram performed. The scan was normal and there was no evidence of coronary artery aneurysm.

Based on these findings, Kawasaki's disease is still a strong possibility. Let's chat about Kawasaki's disease.

Kawasaki disease is an acute inflammatory pan-vasculitis of any blood vessel but with a preference for small and medium sized blood vessels. It is of unknown etiology, but the disease is thought to result from an autoimmune response to an unidentified infectious trigger. Kawasaki disease is a disease of childhood, with the typical age of patients between 15-18 months old. Eighty percent of Kawasaki disease patients are under the age of 5 years. Kawasaki disease "outbreaks" follow seasonal patterns, being higher in the winter. And children of Asian descent have a higher incidence of Kawasaki disease, suggesting both infectious and genetic influences.

There are three distinct phases of illness with the acute phase lasting 10 days. Fever and clinical findings are present, with evidence of systemic inflammation seen through an elevation of acute phase reactants. The subacute phase is between days 10 and 21. Fever resolves and clinical findings largely subside, often with peeling of hands and feet. Serologic evidence of inflammation continues. The final convalescent phase is between week 3 through to week 6-8. All clinical findings have resolved however, there can be continued serologic evidence of inflammation. Beyond 6-8 weeks, serologic evidence for inflammation has resolved. Seeing that Kawasaki disease has a predilection for small and medium-sized vessels, and especially the coronary arteries for unclear reasons, this vasculitis can lead to aneurysmal dilation, particularly during the subacute phase of illness.

But to truly diagnose Kawasaki's disease, we need to use the diagnostic criteria which states that

the patient has to have a history of fever for greater than or equal to 5 days AND at least four of the five
following clinical criteria need to be met.

1. Changes in the peripheral extremities (erythema of the palms and soles; edema of the hands and/or feet; or periungal desquamation)
2. A polymorphous rash
3. Bilateral bulbar conjunctival injection without exudate
4. Changes in the lips and oral cavity (erythema and/or cracking of the lips' strawberry tongue; diffuse erythema of the oropharynx)
5. Cervical lymphadenopathy (>1.5 cm diameter, usually unilateral)

AND the disease cannot be explained by another disease process.

Summary of case:

Just to give you a re-cap, Aiden is a 4-year-old boy with a 7-day history of fever, irritability, and new onset unilateral swollen lymph nodes. He presents with a diffuse, blanching macular rash, red watery eyes, and a red painful mouth. He was recently treated for presumptive streptococcus pharyngitis. Investigations show evidence of inflammation. Aiden meets all the criteria for Kawasaki disease.

Management approach:

Ok, so now knowing that Aiden has Kawasaki disease, we need to begin treating him to prevent any complications such as coronary aneurysms. Aspirin and intravenous immune globulin (IVIG) have been standard therapy for Kawasaki disease for many years.

High dose aspirin is administered for its anti-inflammatory properties. Aspirin shortens the febrile course of the illness but has no effect on the development of aneurysms. Following defervescence, low dose aspirin is administered for its anti-platelet effects, as Kawasaki Disease can cause thrombocytosis. Aspirin is discontinued altogether after a total of six-eight weeks if no coronary artery changes are seen in follow up echocardiograms. If there are coronary artery abnormalities, low dose aspirin is continued indefinitely as an anti-platelet agent.

IVIG in KD has decreased the incidence of coronary artery aneurysm from 20-25% to 2-4%. If coronary artery aneurysm is to develop, they usually do so during the subacute phase of illness and almost always by four weeks of onset of acute illness. A follow up visit at one to two weeks is recommended with cardiology.

Other antipyretics are usually not effective for fever control. Furthermore, use of ibuprofen has been shown to antagonize the irreversible platelet inhibition induced by aspirin and should be avoided.

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The role of steroids is unclear. Newer studies suggest they may have a role in acute management. But no treatment has been proven superior to IVIG and aspirin, which remains the standard of care.

If Aiden did not have Kawasaki disease, management would be much different, and would vary on the diagnosis. Observation is recommended for children with cervical lymphadenitis bilaterally, whose lymph nodes are smaller than 3cm and are not red or swollen. However, an empiric course of antibiotics should be considered for patients with systemic symptoms such as fever or chills, unilateral lymphadenopathy, redness, tenderness or if their lymph nodes are greater than 2-3 cm. Common antibiotics prescribed include oral cephalexin (Keflex), amoxicillin-clavulanate or clindamycin because most organisms are staphylococcus aureus or group A streptococcus. For presumed reactive lymphadenopathy, observation is acceptable, with a course of empiric antibiotics if things worsen or fail to improve.

Children with congenital neck masses should be referred to a specialist, such as a head and neck surgeon to consider definitive excision. Excision would be recommended to confirm the diagnosis and to prevent future growth or secondary infection. Those with suppurative lymphadenitis or a neck mass not responding to oral antibiotics should be referred for possible incision and drainage or intravenous antibiotics or further workup.

If malignancy is being considered, that is, the lymph nodes are rubbery, firm, immobile, and have been present for longer than six weeks, or are growing, in the context of a course of antibiotics, the child should be referred to a pediatric head and neck surgeon for urgent evaluation and possible biopsy. Malignant lesions, albeit rare, can occur, such as lymphoma, rhabdomyosarcoma, thyroid carcinoma, and metastatic nasopharyngeal carcinoma.

Conclusion:

Now, let's get back to the case. Aiden starts on the high dose aspirin and gets a dose of IVIG. Thirty six hours later, he is afebrile with increased activity and eating well. He shows you that the skin on his fingers is peeling, and you explain to him that this commonly occurs in Kawasaki disease. Aiden will require follow up with cardiology in one-to -two weeks and given a prescription for high dose aspirin. Once the febrile phase of Kawasaki Disease passes however, Aiden is to take low dose aspirin for another 6-8 week. Since aspirin can cause gastrointestinal bleeding, his parents should watch for warning signs, such as a stomach ache or blood in the stool. He will also require a repeat echocardiogram, and generally it's scheduled 6 weeks after the child is afebrile. Repeat blood work should be performed as well, to be used as another tool to evaluate resolution of the disease process.

Now let's review the take home points

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1. Neck masses can be congenital or acquired and gathering information regarding their timing, location, consistency, and size can help narrow the possibilities.
2. Remember, congenital neck masses are often present at birth, such as a thyroglossal cyst, which can be found in the midline position, and a branchial cleft cyst is often lateralized.
3. Rapidly growing masses are often inflammatory in nature, and multiple small sized lymph nodes palpated bilaterally is likely reactive lymphadenopathy.
4. Initial investigations often start with labs including a CBC, kidney function and liver function tests. A CRP or ESR is also useful for inflammatory etiologies.
5. Management will vary depending on the etiology, but as a rule of thumb, infectious bacterial etiologies, like a lymphadenitis will require a course of antibiotics, while neoplastic or congenital anomalies may need referral to a head and neck surgeon for possible surgical intervention.

Thank you everyone for listening to our podcast on an approach to neck masses!

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