

This podcast can be accessed at www.pedscases.com, Apple Podcasts, Spotify, or your favourite podcasting app.

APPROACH TO MEDIASTINAL MASSES

Developed by Kiernyn Houlder and Dr. Beverly Wilson for PedsCases.com.
March 25, 2022

Introduction:

My name is Kiernyn Houlder, and I am a fourth-year medical student at the University of Alberta. This is a podcast on how to approach a pediatric patient presenting with a mediastinal mass. This podcast was developed with the help of Dr. Beverly Wilson a pediatric oncologist at the Stollery Children's Hospital.

Objectives

The objectives of this podcast are to:

1. Review an approach to a child presenting with a mediastinal mass including
 - a. Pertinent points in the history
 - b. Physical exam components
 - c. Initial investigations
2. Formulate a differential diagnosis for pediatric mediastinal masses
3. Discuss distinguishing features and treatment options for common causes of mediastinal masses

Mediastinum Anatomy

Firstly, let's do a quick review on the anatomy of the mediastinum. The mediastinum is the region between the lungs. It is defined anteriorly by the sternum and posteriorly by the vertebral column. It contains many important structures including the heart, thymus, portions of the esophagus and trachea, as well as the large vessels.

The mediastinum is commonly divided into 3 portions: anterior, middle and posterior. Where a mass is located within the mediastinum can help to determine the etiology of the mass. For the anterior compartment, the common differentials are the "Terrible T's" and include thymomas, teratomas, "terrible" lymphoma and thyroid masses. Middle mediastinal masses can include bronchogenic cysts (such as tracheal duplication cysts), Hodgkin's lymphoma, and teratomas. Finally, neurogenic masses are common in the posterior mediastinum.

Differential Diagnosis

For the purpose of this podcast, we have split the differential diagnosis into two main categories: neoplastic and non-neoplastic.

Developed by Kiernyn Houlder and Dr. Beverly Wilson for PedsCases.com.
March 25, 2022

Neoplastic

1. **Lymphoma** is the most common pediatric mediastinal malignancy. It can be broken into Non-Hodgkin (which makes up approximately 2/3 of lymphomas found in the mediastinum) and Hodgkin lymphoma. Constitutional symptoms are common among both subtypes. Diagnosis of both Hodgkin and Non-Hodgkin lymphoma is confirmed with an excisional biopsy of an enlarged lymph node. Extent of disease is often determined by CT and PET scans. Bone marrow biopsy may be conducted if there is suspicion of bone marrow involvement.
 - Hodgkin
 - Has a bimodal age distribution (peaks at 15-35 and then at greater than 50). Hodgkin lymphoma is rare in children under the age of 5.
 - Non-Hodgkin
 - More common in school aged children, and is more common in boys
 - Tends to be aggressive in clinical behavior. Symptoms develop quickly, and children may present in later stage disease than Hodgkin.
 - Because of its aggressive nature, there is the potential for Non-Hodgkin lymphoma to present as a medical emergency due to airway obstruction.
2. **Neurogenic** neoplasms include ganglioneuroma, ganglioneuroblastoma, neuroblastoma, and paraganglioma. This group of tumors arise from neural crest cells and can be either benign or malignant.
 - While the majority of neurogenic tumors are benign in adults, a great proportion are malignant in children
 - Presenting symptoms often include: cough, dyspnea, chest pain and Horner's syndrome
3. **Germ Cell Neoplasms** (teratoma or seminoma) can be both benign or malignant
 - Patients tend to present either as an infant or as a young adult. They are often more symptomatic as an infant as their softer tracheal cartilages are more easily compressed by a tumor
4. **Thymomas** are the second most common mediastinal mass in adults, however in children
 - Presentation can range from asymptomatic to chest pain, shortness of breath, superior vena cava syndrome, pleural and pericardial effusion
 - Diagnosis is usually confirmed with a CT

Non-Neoplastic

1. **Bronchogenic / Enterogenic Cysts** are congenital abnormalities.
 - In children these are usually symptomatic, with symptoms such as cough, dyspnea, wheeze, stridor or cyanosis
2. **Congenital Duplication Cysts**
3. **Thymic Cysts**

4. Infection
5. **Vascular Anomalies (hemangiomas, angiosarcomas, cystic hygromas)**

Case Presentation

Now let's move onto a clinical case to help work through this differential diagnosis:

You are a medical student completing your pediatric rotation. James, a previously well male comes into the clinic with his mother complaining of difficulty breathing, especially at night and well as difficulty swallowing.

What are the first steps that we need to take to determine the cause of James' symptoms? What is on your differential diagnosis?

History

Before we get into James' case it is important to note that mediastinal masses can present in a variety of ways. Neoplastic masses often present with respiratory symptoms such as dyspnea or shortness of breath, dysphagia or voice changes. In contrast to this, masses that are not malignant are often found incidentally, usually on Xray for an unrelated reason.

Firstly, given that mediastinal masses have the potential for airway obstruction and respiratory distress, ensure that the patient is stable before you continue with a history and physical exam. Do they need any immediate intervention?

While sitting up on the exam table James notes no difficulty breathing.

Your assessment can now start with a thorough history:

1. The patient's age can help narrow down your differential, as the most common etiologies change based on the age of the patient (ie. Infant, school-aged, adolescent)
2. The history will continue with a history on the presenting symptoms. How long have they noticed the symptoms for? Are they getting worse? Was there any incident that brought about these symptoms?
3. With mediastinal masses, the child and/or guardian will not actually feel the mass, but instead will present with symptoms due to the mass effect. If they do not mention it, ask specifically about
 - Respiratory symptoms such dyspnea/ shortness of breath, cough
 - Cyanosis
 - Dysphagia (difficulty swallowing)
 - Facial swelling
 - Hoarseness

4. Because there are a significant proportion of mediastinal masses that are malignant, it is also important to ask about constitutional symptoms. These include **fever, weight loss, night sweats**.
5. You should ask the patient, and their family member (if present) if they have noticed any lumps in their neck, and in the rest of their body. This can indicate **lymphadenopathy** and can also be a sign of malignancy. Remember that supraclavicular lymphadenopathy is malignant until proven otherwise.
6. Finally, ask about past medical and surgical history, as well as family history.
 - Does the child have any underlying genetic conditions such as Klinefelter's or Down Syndrome, as these can predispose them to malignancies?
 - Is there a family history of childhood cancer?

When you take James' history, he notes that other than the orthopnea and dysphagia he hasn't noticed any other symptoms. The issues began a few weeks ago and seem to be getting worse. He notes that getting up for school has been more difficult, and he feels like he can't get through the day without having to take a break or nap. He denies any fever or night sweats. Otherwise, he is a previously healthy kid, with no significant family or past medical history.

Physical Exam

Next, we move onto the physical exam. Examination of the chest and abdomen should look for signs of:

1. Respiratory distress or cyanosis
 - Blue discoloration of the mucous membranes
 - Delayed capillary refill
 - Difficulty breathing/ breathlessness while speaking
2. Hoarseness
3. Symptoms of **Horner's syndrome**
 - Ptosis (drooping eyelid)
 - Miosis (one pupil dilated in comparison to the other)
 - Decreased sweating
4. Facial/upper limb edema and/or venous distention
5. Hepatomegaly / splenomegaly
6. Lymphadenopathy

- Lymph nodes that are > 2 cm, fixed to underlying structures, and have a hard consistency are concerning for malignancy and must be investigated further

Finally, growth parameters should be assessed to ensure that there has been no impact on the child's development.

When doing the physical exam, it is important to screen all children for **Superior Vena Cava Syndrome**, which is a medical emergency. Superior vena cava syndrome occurs when there is an obstruction of the superior vena cava. Most commonly caused by malignant mediastinal masses, common symptoms of superior vena cava syndrome include dyspnea (shortness of breath), orthopnea, cough and wheezing, dysphagia, facial swelling, venous distention in the upper body, headache, anxiety, confusion and syncope.

- If suspected, urgent action must be taken. A Chest X-ray or CT Scan must be performed.
- Anesthesia should also be consulted, as these children can lose airway patency, and intubation can be extremely difficult
- Children with superior vena cava syndrome should not be laid flat, and sedation should be avoided if possible, as it can exacerbate airway symptoms
- Treatment can include steroids and ICU admission, radiation (especially for NHL), chemotherapy or surgery if the mass is not radio or chemo sensitive.

Other complications that are important to be aware of include:

- **Tracheal/ Bronchial Compression**
- **Right Ventricular Outflow Tract (RVOT) obstruction**
- **Pericardial effusion / tamponade**

It is also important to screen for **tumor lysis syndrome**, which is a rare complication but is also an oncologic emergency. Can cause electrolyte disturbances such as hyperkalemia, hyperphosphatemia, hyperuricemia, hypocalcemia.

When examining James, shortness of breath is observed when the exam table is lowered. Cervical and supraclavicular lymphadenopathy are noted. James cannot specifically remember when these "lumps" appeared, but has noticed them for awhile. They are not tender to palpation.

Investigations and Imaging

Chest Xrays are the primary imaging modality used in the visualization of mediastinal masses. A chest Xray allows us to see:

- The location of the mass as well as its relationship to adjacent structures
- The composition of the mass: fatty tissue, cystic, vascular, soft tissues
- If the mass is well circumscribed

Anesthesia is often consulted for pediatric patients with mediastinal masses regardless of the etiology because of the potential for these masses to compromise the airway. Whether it is for insertion of a permanent line, biopsies, or removal of the mass itself, it is important that they are involved in the care of these patients.

Initial investigations for mediastinal masses are determined based on the history and physical exam. Suspected malignant masses are often treated very differently than if a benign mass is suspected.

Malignant Masses

If a malignancy is suspected, pediatric oncology should be consulted as soon as possible. Pediatrics, like most medical disciplines is multidisciplinary and in this case, pediatric oncology can help to connect and coordinate other specialties for further work-up and treatment of the mass.

For most patients, initial investigations should include

- CBC and differential +/- peripheral smear
- Calcium, phosphate, PTH
- AFP and bHCG, LDH, Inhibin B
- Screening for tumor lysis syndrome : uric acid, electrolytes (potassium, phosphate, calcium)

Again, involving pediatric oncology prior to ordering extensive workup is crucial as they can help guide which investigations are necessary.

An ECHO and pulmonary function testing (if age appropriate) should be conducted to ensure that the mass is not compromising function of either of these systems.

A biopsy of the mass or of an enlarged lymph node is often carried out to more accurately classify the etiology of the mass.

Benign Masses

Once malignancy has been ruled out, pediatric surgery is often consulted as the treatment is often surgical excision.

Initial lab investigations are often very similar for non-neoplastic masses, and has often been done in the process of ruling out a malignancy. Pediatric surgery can assist with general pre-operative work-up.

The surgical team will also advise on any pre-operative imaging that needs to be done. All masses are imaged with CT scan, and if necessary an MRI is done. Cardiac ECHO is also completed if there is any suspicion of outflow obstruction.

James' chest Xray confirmed the presence of a mediastinal mass. His lab values were all within normal limits other than a slight leukocytosis. James' presentation

was suspicious for malignancy, specifically lymphoma. Pediatric oncology was involved and he underwent an excisional biopsy of an enlarged cervical lymph node. The diagnosis of Hodgkin's lymphoma was confirmed. James promptly began treatment and is currently in remission.

Treatment

Approximately 50% of mediastinal masses in pediatrics are malignant, and as mentioned previously pediatric oncology will help to coordinate and dictate treatment. With most malignant etiologies, surgical excision is not done. Instead, a multi-modal, multidisciplinary treatment strategy which can include chemotherapy and radiation is carried out.

Non-malignant masses such as thymomas, germ cell tumors and bronchogenic/enterogenic cysts will often be treated with surgical excision, especially if symptomatic.

Conclusion

What are some of the takeaway points from this podcast?

1. Symptoms that can indicate a mediastinal mass include: cyanosis, hoarseness, shortness of breath, orthopnea, Horner's syndrome and facial/ neck swelling. Sometimes, mediastinal masses can be found incidentally on imaging.
2. Screening for complications of mediastinal masses such as superior vena cava syndrome is extremely important, as these are oncologic emergencies and need to be treated urgently
3. Approximately 50% of mediastinal masses in the pediatric population are malignant, and therefore it is important to thoroughly investigate all masses that are found.
4. Lymphoma is the most common mediastinal malignancy. Attention should be paid to lymph nodes in the area when doing a physical exam. Excisional biopsy should be done if there is any suspicious lymphadenopathy.
5. Treatment for mediastinal masses is dependent on the etiology of the mass. For most malignant masses the treatment is non-surgical. In contrast, most masses that are not malignant are treated with surgical excision.

And this wraps up the podcast on mediastinal masses! Thank you so much for listening!

Resources

1. Up to Date: Overview of non-Hodgkin lymphoma in children and adolescents
2. Up to Date: Treatment and prognosis of neuroblastoma
3. Up to Date: Clinical presentation, diagnosis, and staging evaluation of neuroblastoma
4. Up to Date: Overview of Hodgkin lymphoma in children and adolescents

5. Jagers J, Balsara K. 2004. Mediastinal masses in children. Semin Thorac Cardiovasc Surg [Internet]. [cited 2021 Jan 10]; 16(3) : 201-208. Available from : <https://www.sciencedirect.com/science/article/abs/pii/S1043067904000541>
6. Michelle Lai. Tumor Lysis Syndrome. [cited 2021]. Available from : <https://learn.pediatrics.ubc.ca/body-systems/hematology-oncology/tumor-lysis-syndrome/>
7. The Editors of Encyclopaedia Britannica. [Internet]. 2020. Mediastinum. [cited 2021 Jan 10]. Available from : <https://www.britannica.com/science/mediastinum>
8. Stringer H. [Internet]. 2011. Approach to mediastinal mass. [cited 2021 Jan 10]. Available from : <https://learn.pediatrics.ubc.ca/body-systems/gastrointestinal/approach-to-a-mediastinal-mass/>
9. Pediatric Oncology Education Materials. [Internet]. 2008. Superior Vena Caval (SVC) Obstruction and Superior Mediastinal Syndrome (Central Airways Obstruction). [cited 2021 April 10]. Available from: <http://www.pedsoncologyeducation.com/basiconcologyemergency1.asp>