Shortness of breath in a 12 year-old boy: a classic presentation of stage IV Hodgkin’s Disease?

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Shane is a 12 year-old boy who presents to your office with worsening shortness of breath on exertion. His father explains that his son had severe asthma when he was younger. He was admitted to hospital when he was 2 years old and put on a ventilator in the intensive care unit when he was 4. His symptoms have been much better since then. In fact, Shane hasn’t had to use puffers very much at all up until a few months ago. He started using Ventolin again while playing soccer and does get some relief with this.

IS IT ASTHMA?
You take a thorough history from Shane’s father. He notes that the shortness of breath has come on gradually over the last few months to the point where it causes Shane difficulties several times per week. There is no history of productive cough, and no fever, night sweats or weight loss. Shane has no other medical conditions, no known allergies, no previous surgeries, and his vaccinations are up to date. His parents are from Barbados but he has never been out of the country himself. Shane’s 13 year-old brother had a cough recently but there are no other sick contacts.

On examination, Shane is a lean-looking child but otherwise appears well. Head circumference and height are above the 50th percentile and weight is above the 25th percentile. He has no cervical, supraclavicular, infraclavicular, axillary, or inguinal lymphadenopathy. His respiratory exam is significant for mild wheeze throughout but no crackles or areas of decreased breath sounds.

You explain that Shane’s symptoms most likely represent worsening asthma. You give Shane a prescription for inhaled steroids and encourage him to use it twice per day. You also give him a refill for Ventolin and explain that he can use it whenever he feels short of breath. Shane’s father agrees to follow-up with you in one month.

IS IT INFECTIOUS?
You see Shane and his father back in clinic one month later. His father looks very concerned. The shortness of breath continues to be an issue and now Shane has a rash. The rash started behind his knees and has spread to his trunk, arms, and neck. The rash is pruritic and bothers Shane quite regularly.

On examination, Shane has an anterior cervical and supraclavicular lymphadenopathy. The nodes are nontender, rubbery and range in size from 1 to 2.5 cm. Respiratory exam is significant for wheeze but there are no crackles or areas of decreased breath sounds.

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WHAT ELSE COULD IT BE?
Shane is seen by your colleague in Infectious Disease six weeks later. Shane has now developed a dry cough. The rash is still present although the itchiness is relieved somewhat by the topical hydrocortisone. A review of systems reveals that Shane has now lost about 5 pounds since the worsening of shortness of breath began. Shane denies fevers and night sweats, but his father says that, “he’s been feeling really unwell recently.” Physical examination reveals anterior cervical and supraclavicular lymphadenopathy. The nodes are not tender, rubbery and range in size from 1 to 2.5 cm. Respiratory exam is significant for wheeze but there are no crackles or areas of decreased breath sounds.

Your colleague explains that he needs to get a chest x-ray as part of his workup. He agrees that Shane is quite sick and will need more tests. He sends Shane to the Pediatric Emergency Department for further evaluation.

HOW BAD IS IT?
Shane is assessed in the Emergency Department later that afternoon. He has a fever of 38.5 degrees Celsius, tachycardia with a heart rate of 105, and oxygen saturation of 94% on room air. The Emergency Physician orders a chest x-ray (see Figure 2) and bloodwork. The chest x-ray reveals mass-like pulmonary opacities in both lungs and enlargement of the hila and superior mediastinum.

Bloodwork is significant for a white blood cell count of 32.0, which consists of 24.0 neutrophils and 4.1 eosinophils. Hemoglobin is decreased slightly at 129. Platelets are elevated at 551, C reactive protein is 111.8, and erythrocyte sedimentation rate is 54. Lactate dehydrogenase is high at 616 but urate and calcium are normal.

Figure 1.
Crusted papules measuring 3-5 mm consistent with pityriasis lichonoides [4].
Shane is admitted to hospital by the inpatient Pediatrics team for further workup. The differential includes infection, vasculitis, and malignancy. He is placed on airborne contact precautions and admitted to a negative pressure room until tuberculosis can be ruled out.

**IS IT CANCER?**

Shane undergoes a CT scan of the pelvis, abdomen and thorax the following day (see Figure 3). The CT reveals multiple solid nodules in both lungs, as well as mediastinal and hilar lymphadenopathy. Enlarged nodes are seen in the para-aortic area but there are no signs of a primary tumor.

General surgery in consulted to obtain a biopsy. Shane and his parents remain anxious over the next few days as they wait for a spot to open up in the operating room. In the meantime, Shane's white blood cell count remains in the high 20s and platelets rise up to 762. Shane goes to the operating room three days after his admission for biopsy of a superficial supraclavicular lymph node and skin under general anesthetic. Frozen section of the lymph node is positive for malignancy but flow cytometry is normal. A definite diagnosis is deferred until permanent sections can be processed.

Over the next few days, Shane's shortness of breath worsens. The vasculitic bloodwork comes back normal and acid-fast cultures are negative for tuberculosis. The final pathology report is released one week later indicating Hodgkin’s Disease, Nodular Sclerosing subtype.

**IS THIS STORY TYPICAL FOR HODGKIN’S DISEASE?**

Shane’s story may seem somewhat convoluted but his symptoms are actually quite typical. In children, less than 20% of patients present with one of the classic “B” symptoms of Hodgkin’s Disease (weight loss, fevers, and drenching night sweats) [1]. In fact, the most common presentation in children consists of painless cervical lymphadenopathy (which occurs in 70-80% of cases) and/or a mediastinal mass (in 50% of cases) [2]. Shane’s initial chief complaint was shortness of breath due to the mass effect of mediastinal lymphadenopathy. This eventually progressed to a cough and hypoxia. The lesions in the lungs represent a combination of contiguous spread from hilar lymphadenopathy and metastases to lung parenchyma [3].

The rash and itchiness that Shane experienced isn’t that unusual either. In fact, some patients will give a history of insidious itchiness for months before being diagnosed with Hodgkin’s Disease [2]. The skin lesions in this case most likely represented pityriasis lichenoides, which is associated with lymphoma [4].

Shane’s initial bloodwork is classic for Hodgkin’s Disease. At first glance, the elevated white blood cell count consisting almost entirely of neutrophils would seem to suggest an infectious etiology. This is certainly supported by the high platelet count, C reactive protein, and erythrocyte sedimentation rate. (Indeed, in this case, Shane remained on airborne contact precautions until tuberculosis was formally ruled out with a negative acid-fast bacilli culture.) Nevertheless, a complete blood count characterized by neutrophilia, eosinophilia and thrombocytosis is classic for Hodgkin’s Disease in children, and is not due to underlying infection [1, 2, 5].

The presence of elevated lactate dehydrogenase would lead to some suspect tumor lysis syndrome. The elevated levels seen in this case actually represent a hemolytic anemia, which is not uncommon in Hodgkin’s Disease [6]. The normal serum electrolytes and urate levels seen here stand against the presence of ongoing tumor lysis.

**WHAT IS THE PROGNOSIS?**

Shane has stage IVB Hodkin’s Disease according to the Ann Arbor Staging Classification [5]. He has diffuse involvement of 1 or more extralymphatic organs (stage IV) and has B symptoms (B). This places Shane in the high-risk category [5, 7]. Even so, with proper treatment and monitoring the 5-year survival for children like Shane is up to 90% [7, 8]. Shane was started on induction therapy while in hospital, consisting of cyclophosphamide, vincristine (Oncovin), procarbazine, and prednisone (COPP). He was discharged home once his breathing improved and will complete three more courses of treatment before receiving radiation therapy.
REFERENCES