CASE REPORT

RARE THORACOPULMONARY NEOPLASM IN A YOUNG FEMALE: A CASE REPORT.

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ABSTRACT

Askin tumor is a rare malignant neoplasm that arises within the thoracopulmonary region. It is a type of peripheral primitive neuroendocrine tumor that is most commonly seen in children and adolescents. Askin tumors are frequently misdiagnosed due to their low incidence and nonspecific presentation. The tumor presents with symptoms of dyspnea, cough, chest tightness and discomfort. It may also present with a painful or painless chest wall mass, rib fractures and erosions, pleural effusion, empyema and localized lymphadenopathy.[1] Due to these signs and symptoms, Askin tumors are often misdiagnosed as tuberculosis, lymphoma and small cell tumors.[2] There is no clear-cut diagnostic criteria or treatment regimen for this tumor and amulti-disciplinary approach is essential for management. We report a case of a young female who was diagnosed with metastatic Askin tumor at the time of presentation and discuss the diagnosis according to imaging results and histopathological analysis.

KEYWORDS: Ewing sarcoma, Askin tumor, PNET, neuroectodermal tumors

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INTRODUCTION

The Ewing sarcoma family of tumors (EFT) comprises a group of neoplasms that includes Ewing sarcoma and peripheral neuro-ectodermal tumors (PNET). Although primitive neuro-ectodermal tumors were originally described as malignant small round cell tumors arising from primitive nerve cells[3] most commonly in the central nervous system, they may also arise in peripheral nervesthe chest wall, pleura, pelvis and limbs.[1] This rare tumor is most prevalent in children and young adults[4] and presents with a wide array of symptoms. The main investigations required for diagnosis include computed tomography (CT) scan, histopathological analysis and immunohistochemistry. The treatment depends on the extent of disease and metastasis and usually requires a combination of surgery, chemotherapy and radiotherapy.

CASE REPORT

A 25-year-old female was admitted via the emergency department with complaints of progressive shortness of breath for 8 months. She also complained of left sided chest pain for 3 months and dry cough plus weight loss for one month.

According to the patient, shortness of breath initially occurred only with moderate exertion but symptoms were now present even at rest. Chest pain was pleuritic, left-sided and aggravated by movement. The cough was dry and non-productive. Weight loss was subjective and undocumented.

She initially consulted her general physician who diagnosed her with pulmonary tuberculosis on the basis of clinical presentation and chest x-ray findings.The patient was prescribed anti-tuberculous therapy, however, she discontinued therapy when she did not see an improvement in her symptoms.

She had no history of fever, edema, oral ulcers, photosensitivity, rash, hair loss, skin tightening, joint pains, history of recurrent abortions or DVT. Additionally, there was no history of exposure to organic or inorganic dust.

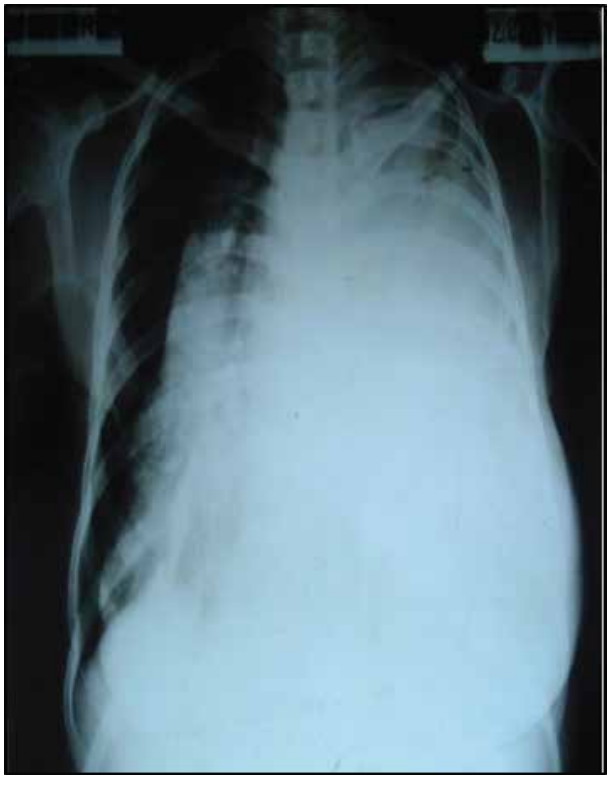
On physical examination, the patient was dyspneic at rest and unable to lie in the supine position. Her temperature was 99 F, pulse was 100/min, blood pressure was 100/60 mmHg and respirations were 30/min.

On respiratory examination, tenderness was elicited over the left anterior chest wall and trachea was deviated to the right. Both chest expansion and breath sounds were diminished over the left lung. The systemic examination was otherwise unremarkable.

Her CBC showed microcytic hypochromic anemia, which may be as a result of anemia of chronic disease. Her renal function tests, LFTs and coagulation profile were all normal. Serum ANA, dsDNA, ANCA, rheumatoid factor and anti-CCP were all negative, therefore ruling out an autoimmune etiology.

A diagnostic pleural tap was done which showed hemorrhagic pleural fluid, with hematocrit >50%. Pleural biopsy and chest intubation were subsequently planned, however the incision for biopsy resulted in profuse bleeding, resulting in the procedure being postponed. Instead, a CT chest was done.

CT chest showed massive left hydro-pneumothorax with complete collapse of the left lung



with a circumferential lobulated pleural thickening extending posteriorly. A large confluent para-aortic mass with mediastinal and left supraclavicular lymphadenopathy were seen indicative of extensive metastasis.

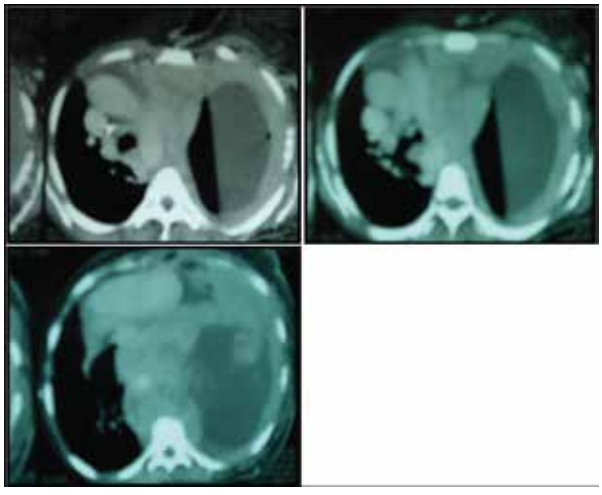


Figure 2(a,b,c): Chest CT

A CT guided biopsy was performed and subsequent histopathological analysis showed that the tumor was of ectodermal origin and stained positive for the CD99 gene (encoding the MIC2 cell surface glycoprotein) specific for Askin tumor. The diagnosis for Askin tumor was confirmed.

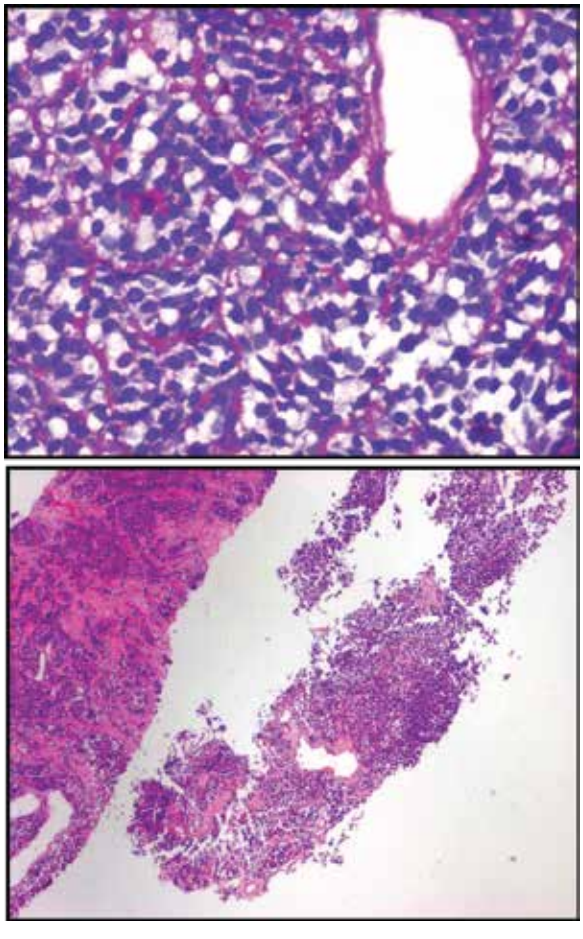


Figure 3 (a,b): Histopathological slides

The patient was subsequently referred to the oncology department for further management. Due to extensive spread of disease, only palliative treatment was planned. She was given one dose of radiotherapy, beyond which the patient did not survive.

DISCUSSION

The Ewing sarcoma family of tumors encompasses a spectrum of neoplastic diseases including the classic Ewing sarcoma of the bone, extra skeletal Ewing sarcoma, peripheral primitive neuro-ectodermal tumors (PNETs) and Askin tumors. Askin tumor was first named in 1979 by Askin et al who studied the histopathological characteristics of the tumor in 20 Caucasian patients.[5] Prior to this study, the tumor was classified as a "malignant small round cell tumor of undetermined histogenesis" due to its lack of characteristic microscopic findings usually seen in known small cell carcinomas such as neuroblastoma, rhabdomyosarcoma or Ewing's sarcoma.[6] The tumor was identified primarily in the thoracopulmonary region and PNETs arising in this region were thus described as Askin tumors. Although the incidence is rare, Askin tumors are the most common chest wall tumors found in children and adolescents[7] with a mean age of presentation of 14.5 years (range 4-39 years) and median survival of 8 months.[2] They are more commonly seen in females.

Although most patients with Askin tumor present with a painless soft tissue swelling of the chest wall (70%), it may also present as a painful palpable mass (32%) and dyspnea with or without palpable swelling (16%).[2] As the symptoms largely vary and a specific diagnostic criterion cannot be defined on the basis of current data on Askin tumor, timely diagnosis is challenging and requires extensive testing. This not only exacerbates the present condition, it also delays diagnosis resulting in local spread of disease and metastasis. Additionally, generalized symptoms such as fever, fatigability and acute onset of cough may steer the diagnosis towards an infectious etiology further precluding adequate investigation. Due to these limitations, our patient was also initially misdiagnosed with tuberculosis, resulting in inappropriate treatment and delays in diagnosis.

The tumor is poorly differentiated, aggressively growing and metastasizes rapidly. Prognosis is grave with a 2- and 6- year survival rate of 38% and 14%, respectively.[8] It commonly recurs locally and may involve lungs, pleura, ribs, mediastinal and retroperitoneal lymph nodes. Additionally, extensive distant and remote metastases also occur. Vessel metastasis is common, along with spread of disease to bones, brain, mediastinum, liver and adrenal glands.[9] Pleural invasion may present as pleural effusion, which may be moderate or large. However, mediastinal involvement is rare. Our patient had hydro-pneumothorax with collapsed lung and mediastinal involvement, which is an atypical finding on chest CT.

Diagnosis involves a multidisciplinary approach starting with imaging studies like CT/MRI/PET scan. These imaging techniques are used to localize the mass, assess extent of disease and eventually as an aid in estimating response in patients undergoing chemotherapy and radiotherapy. Initial CT scans typically show non-uniform pleural thickening with a soft tissue density as was also seen in our patient's scan. IV contrast administration demonstrates a heterogeneous mass with non-enhancing necrotic or cystic components.[10]

Histopathological analysis and immunohistochemistry are essential for confirmation of diagnosis as it is difficult to differentiate Askin tumor from other tumors using light microscopy alone. Histopathology typically reveals small round cells with scanty cytoplasm and Homer-wright rosettes with layers of fibrillary material.[9] However, as these findings may be seen in other small cell tumors, immunohistochemical staining needs to be done. Immunohistochemical staining demonstrates high levels of a glycoprotein MIC2 surface antigen or p30/32 MIC2, which is encoded by the CD99 gene. An additional potential marker that has been identified for Ewing sarcoma family of tumors is the NKX2.2 gene, which may also be a finding in Askin tumor. Moreover, the chromosomal translocations t(11;22) (q24; q12) seen in cytogenetic studies done on PNET tumors are also commonly seen in molecular genetic analyses done on Askin tumor.[1]

Timely diagnosis and treatment of Askin tumor proves to be challenging due to multiple contributing factors, however, the rarity of the condition plays the most vital role. Due to a low incidence, there is a scarcity of available data that is relevant, concise and specific. In 1989, Marina et al proposed a possible diagnostic criterion that can be used to confirm the diagnosis of Askin tumor. The criteria were compiled by analyzing pathological characteristics, electron microscopy and immunohistochemical findings as well as response to therapy, to determine if the tumor had a unique presentation. The criteria are as follows:

- Development of the tumor from a peripheral nerve;
- Identification of Homer-Wright rosettes;
- Expression of NSE and Leu-7;
- Existence of cytoplasmic neurosecretory granules and microtubules
- Identification of t(11;22) (q24;q12)
- Detection of proto-oncogenes (N-myc, C-myb, C-ets-1)
- Activity of neurotransmitter biosynthetic enzymes

(tyrosine hydroxylase, dopamine B hydroxylase and acetylcholine transferase)

These diagnostic criteria, however, have limitations as they focus primarily on findings seen on histopathological and immunohistochemical analyses, allowing clinicians to solely use them to retain the diagnosis of Askin tumor once it has already been made. The criteria may be difficult to fulfill due to lack of available resources for extensive testing and financial constraints, especially in the underdeveloped world where a large majority of patients come from low socio-economic backgrounds. Moreover, clinical diagnosis is obscured due to a range of non-specific signs and symptoms that may point towards a number of infectious, autoimmune or neoplastic disease processes, resulting in delays leading up to a biopsy. In light of this, a diagnostic criteria incorporating both clinical presentation and histopathological findings should be made.

The treatment of Askin tumor involves a multimodal approach and generally includes a combination of poly-chemotherapy combined with extensive surgical resection and external beam radiotherapy to control primary disease and metastasis. As our patient was initially misdiagnosed, there was extensive metastasis at the time of presentation and demise of the patient occurred shortly after initiation of radiotherapy. Therefore, unfortunately, the effectiveness of different treatment modalities could not be assessed. Surgical resection of the tumor and reconstruction of the chest wall may be an effective strategy for controlling local disease and preventing recurrence. Multiple studies suggest that the most effective treatment strategy involves chemotherapy combined with complete resection of the primary tumor. Although radiotherapy with 40-60 Gy for 4-5 weeks and chemotherapy using different combinations of vincristine, doxorubicin, cyclophosphamide, etoposide, cisplatin and actinomycin are commonly used, not enough research has been done to determine an effective and reliable treatment regimen.[9]

Askin tumor due to its aggressive growth, progression to metastatic disease and poor prognosis, should be included in the differential diagnoses when assessing children and young adolescents with chest wall tumors. Furthermore, due to paucity of data available on its characteristic presentation and diagnosis, a high index of suspicion is required when diagnosing patients presenting with a soft tissue swelling of the anterior chest wall and symptoms of lower respiratory tract disease. More extensive research needs to be done to streamline and simplify diagnosis as well as determine effective treatment regimens in order to improve survival.

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