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Case report

NUT carcinoma of the thorax in a 7-year-old child ☆

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ABSTRACT

We present a rare case of NUT midline carcinoma of the thorax in a 7-year-old-male who presented with nonspecific abdominal pain. The patient was initially evaluated with an abdominal ultrasound, which was negative, followed by an abdominopelvic CT that demonstrated a partially visualized infiltrative mediastinal mass. Subsequent, chest CT showed a large, aggressive appearing heterogenous middle mediastinal mass with pulmonary parenchyma, hilar, and posterior mediastinal invasion. Given its epicenter in the middle mediastinum and its irregular and invasive appearance, the primary consideration was NUT midline carcinoma, subsequently confirmed on biopsy.

Introduction

NUT midline carcinoma (NMC) is a poorly differentiated, very aggressive tumor that primarily arises either in the head/neck region or from the middle mediastinal compartment. Thoracic NMC is a rare malignancy with only a few hundred cases reported in the literature. An analysis of 141 NMC patients demonstrated a median age at diagnosis of 23.6 years with a median overall survival after diagnosis of 6.5 months [1]. The sites of origin of these patients were 51% thoracic, 41% head and neck, 6% bone or soft tissue, and 1% other [1]. Males and females were similarly affected with females comprising 52% of the patients. There have been different genetic NUT fusion types identified with differences in prognostic timeline based on anatomic site and fusion type. However, regardless of fusion type, thoracic origin is associated with the worst survival [1]. Although very few cases have been reported, it is believed to be underdiagnosed due to its poor differentiation, with 1 study finding that 3.5% of the cases examined involving poorly differentiated carcinomas or unclassified mediastinal malignancies showed nuclear NUT expression [2].

Case report

A previously healthy 7-year-old male presented to his local emergency department with epigastric abdominal pain that was “poking” in nature and extended like a band to his right

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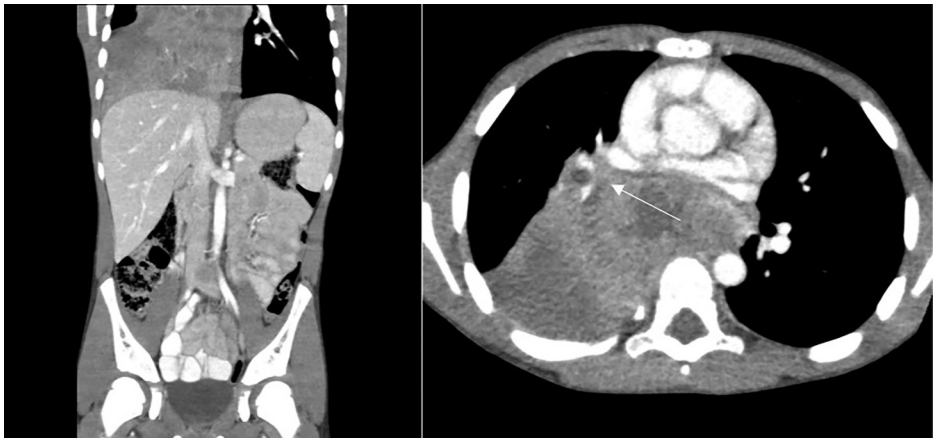

Fig. 1 – Contrast enhanced CT scan of the abdomen and pelvis at initial presentation to the ED. (A) Coronal CT demonstrates a partially visualized, large heterogenous mass involving the right lung base. (B) Axial CT demonstrates the mass with its epicenter located in the middle mediastinum and associated hilar (arrow) and posterior mediastinal invasion.

upper quadrant. The pain began the previous night, was worse with movement, and made it difficult to sleep. There was 1 episode of non-bloody emesis on the way to the ED. His mother reported that he had a poor appetite and lower energy for 1 week and had been getting short of breath with activity recently.

Upon arrival at the emergency department, he was tachycardic to 144 and initial physical exam demonstrated right-sided abdominal tenderness with guarding. Initial laboratory results showed leukocytosis (15.1 WBC count) with a left shift. There was also mild hypochloremia and hypocalcemia.

Initial ultrasound of the appendix and complete abdominal ultrasound demonstrated no sonographic abnormality. A computed tomography (CT) scan of the abdomen and pelvis was then ordered and demonstrated a partially visualized large heterogeneously enhancing mass centered in the middle mediastinum concerning for malignancy (Fig. 1). For further evaluation, a chest CT scan was obtained which showed the epicenter of the lesions located anterior to 1 cm posterior to the anterior border of the vertebral body, confirming that the lesion was middle mediastinal in origin. The mass infiltrated into the mid and lower pulmonary parenchyma, right hilum, and posterior mediastinum with scattered internal low-density areas throughout the mass (Fig. 2). The mass encased and partially effaced the traversing right pulmonary, hilar, and mediastinal vasculature as well as the suprahepatic IVC and esophagus. There was encasement of the trachea and mainstem bronchi with apparent occlusion of the bronchus intermedius (Fig. 3). Given it's CT appearance and compartment of origin, differential considerations included NUT midline carcinoma, lymphoma, metastatic disease, and fibrosing mediastinitis.

Following the initial CT findings, the child was transferred to our institution for further evaluation and treatment. Additional laboratory tests were obtained which demonstrated a markedly elevated Alpha-Fetoprotein of 167 (normal <8.4), LDH of 665, and minimally elevated Beta-HCG.

CT guided soft tissue biopsy was performed with 8 core biopsy samples obtained which were sent for laboratory examination. Cytology of the middle mediastinal mass demonstrated high-grade poorly differentiated carcinoma, consistent with NUT carcinoma of the thorax. A whole-body PET/CT was then ordered to assess the extent of the malignancy. It redemonstrated the middle mediastinal mass which was markedly FDG avid with a standardized uptake value (SUV) max measuring 10.7. There were additional FDG avid right and left paratracheal lymph nodes, including a left paratracheal lymph node with an SUV max of 10.9. There was no osseous or distant FDG avid metastatic disease. There was incidental moderate concentric FDG uptake within the cecum and ascending colon with SUV max 7.4 which was suggested to represent physiologic uptake vs focal colitis. Based on the PET/CT findings and pathology report, a PICC line was placed and a chemotherapy regimen was initiated.

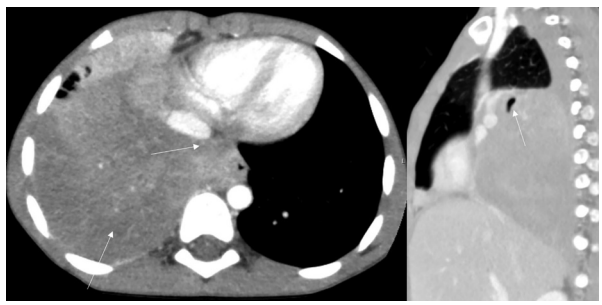

Fig. 2 – Contrast enhanced CT scan of the chest at initial presentation to the ED. (A) Axial CT demonstrates large, middle mediastinal, heterogenous soft tissue mass with involvement in the right lower and middle lobe parenchyma, right hilum, and posterior mediastinum with scattered low density/necrotic areas throughout the mass (arrows). (B) Sagittal CT in lung windows demonstrates airway compression on the right distal right mainstem bronchus (arrow) by the soft tissue mass.

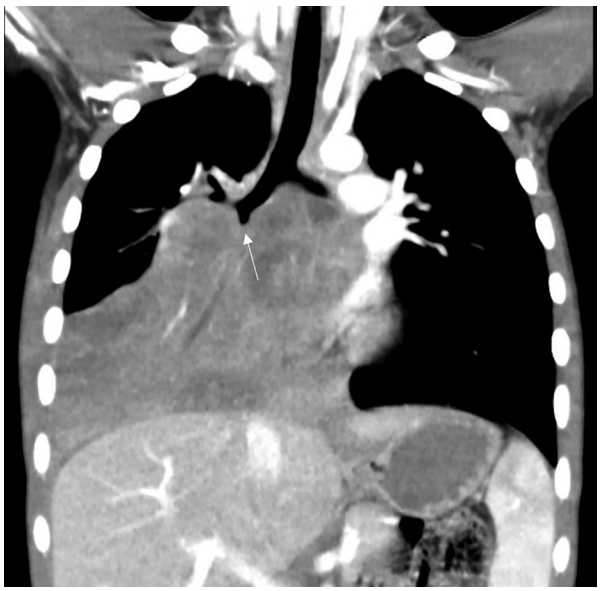

Fig. 3 – Coronal CT of the chest at initial presentation to the ED demonstrating encasement of the trachea and mainstem bronchi with occlusion of the bronchus intermedius (arrow).

Discussion

In this 7-year-old boy presenting with acute abdominal pain incidentally found to have a large heterogenous middle mediastinal soft tissue mass. CT guided biopsy was performed, and cytology as consistent with NMC of the thorax.

Although rare, NMC should be included in the differential for a radiographically infiltrative and rapidly aggressive soft tissue mass, particularly of the head and neck or thorax and mediastinum [3]. It is likely underdiagnosed and misdiagnosed in many circumstances secondary to poor differentiation, lack of awareness of the diagnosis, and paucity of reports in the medical literature. [2,4]. These lesions are classically described in young adults with a median age at the time of diagnosis of 16-30 years, however they can occur in all age groups [5]. Presenting symptoms of primary thoracic NMC are nonspecific. In this case, there was a history of dyspnea on exertion; however, other case reports have included presenting symptoms such as chest pain, cough, weight loss, lumbago, and coxalgia [5,6]. The lumbago and coxalgia were likely secondary to biopsy-proven bony metastases to the lumbar spine, femur, and pelvis [6]. As seen in this case, there can be an association with elevated AFP which may lead to a misdiagnosis of a germ cell tumor [7].

Secondary to rapid progression and late presentation, primary pulmonary NMC is often first visualized on chest radiographs as a large pulmonary opacity. It can mimic or present with lobar collapse and pleural effusion. CT is typically the next modality used for evaluation of the nonspecific radiographic findings. CT findings typically include a large heterogenous primary soft tissue mass that is locally aggressive and encasing surrounding structures with involved mediastinal and hilar lymph nodes and internal hypoattenuation secondary to necrosis and hemorrhage [4,5,8]. Calcifications may be seen within the soft tissue mass; however, they are not classic for NUT carcinoma [4]. A review of 7 cases demonstrated predilection for the lower lobes as well as right sided involvement in 5 of the cases. The contralateral lung was spared in all of the cases other than trace pleural effusions [8]. In a study of 10 patients with NUT midline carcinoma of the lung, the tumors had a mean attenuation of 64 Hounsfield Units (HU) on contrast-enhanced CT scans with a mean net contrast enhancement value of 26 HU [10] (Figs. 4–6).

MRI has been shown to be helpful in staging thoracic tumors, such as NUT carcinoma, as it can more easily delineate invasion into surrounding structures such as neuro-vascular or chest wall involvement [4]. Classically, NUT carcinoma will have low signal on T1-weighted images and intermediate-high signal on T2 weighted images with heterogenous enhancement [4].

PET/CT is helpful to evaluate for distant metastases which may be seen in cases of NUT carcinoma with bone metastases seen most commonly and often presenting as lytic lesions [8]. Other sites of metastases include subcutaneous soft tissue, liver, and retroperitoneal lymph nodes [8]. Primary NUT carcinoma as well as metastatic lesions will be FDG avid, with a range of 5-40 maximum SUVs and a mean of 12 in 1 study [10].

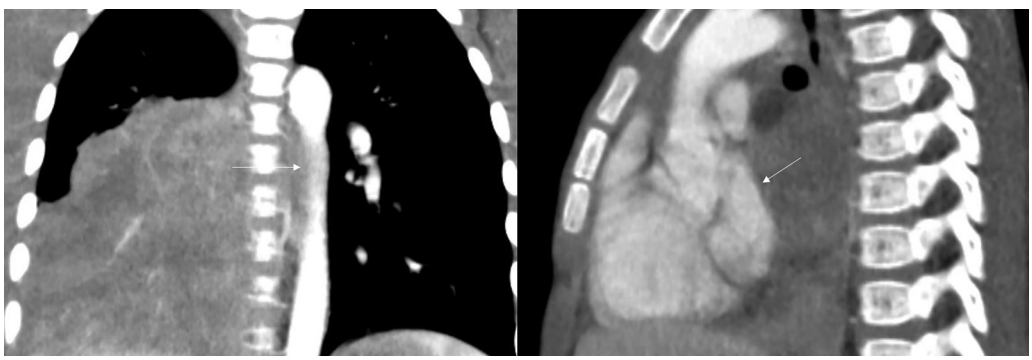

Fig. 4 – (A) Coronal CT of the chest demonstrating abutment of the descending aorta (arrow) by the middle mediastinal soft tissue mass. (B) Sagittal CT of the chest demonstrating abutment of the left atrium (arrow) by the soft tissue mass.

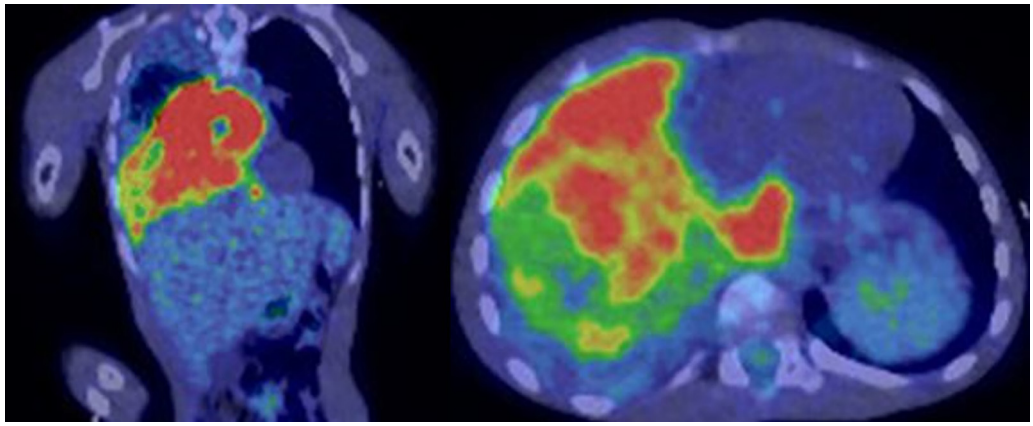

Fig. 5 – (A) Coronal and (B) Axial PET/CT demonstrating avid FDG uptake within the middle mediastinal mass. SUV max measured 10.7.

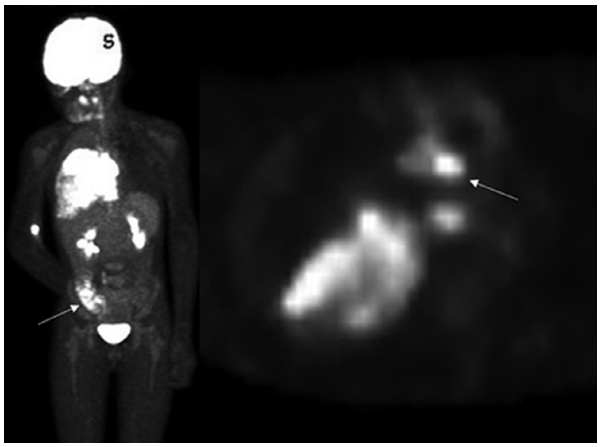

Fig. 6 – (A) FDG PET/CT MIP demonstrated avid uptake within the middle mediastinal mass. There is also focal uptake within the cecum and ascending colon (arrow) which may represent physiologic uptake vs infectious/inflammatory etiology. Physiologic uptake within the brain, kidneys, and bladder is also visualized. (B) Axial FDG PET/CT imaging demonstrating an FDG avid left paratracheal lymph node (arrow) with SUV max measuring 10.9. Multiple other FDG avid paratracheal lymph nodes are not visualized on this image.

NMC has a poor overall survival prognosis, with primary pulmonary NMC having the poorest prognosis. It is a fatal disease typically within the first year after diagnosis. There are currently no standardized treatment guidelines, however, management methods have included chemotherapy regiments initially developed for other cancers, surgical resection followed by radiotherapy, and molecular therapy. Use of a bromodomain and extra-terminal inhibitor targeting OTX015/MK-8628 in 4 patients demonstrated dramatic clinical and radiologic response with regression of the primary tumor in 2 of the 4 cases with overall survival of 19 and 18 months in those 2 cases as well as stable disease in 1 other case [9]. Early diagnosis and immunochemical testing are important for overall survival prognosis and may allow for use of targeted molecular therapies.

Conclusion

NUT carcinoma of the thorax is a rare, aggressive tumor that is likely under- and misdiagnosed. Presenting symptoms are typically nonspecific. However, imaging can be very helpful as imaging features are relatively characteristic and include middle mediastinal origin as well as its infiltrative and aggressive appearance out of proportion to other mediastinal processes. Knowledge of this entity is important as imaging often is more suggestive of the ultimate diagnosis given that histologic evaluation may not provide an accurate diagnosis. NMC should be included in the differential of a rapidly progressive, aggressive appearing tumor of the mediastinum and can occur in all ages, although young adults are classically described.

Patient consent

Written informed consent for the publication of this case was obtained from the patient and his legal guardian.

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