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Case Report

Bilateral pulmonary metastases of papillary thyroid carcinoma in a 12-year-old child–A case report and review of the literature

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ABSTRACT

Metastatic disease of the lung has been extensively documented in the adult patient population. The most common primary sources for pulmonary metastases include breast, colon gastrointestinal including pancreas and urinary bladder. Malignant lung tumors in pediatric population is extremely rare. However, like in adult patient population, metastases are more common than primary tumors in lung in pediatric patients. Metastatic spread of tumors can occur both by way of hematogenous spread and lymphatic pathways. We present a rare case of biopsy proven metastatic thyroid carcinoma in the lung in a 12-year-old male child masquerading as bilateral miliary nodules on imaging studies. The importance of recognition of this entity in terms of prognosis and treatment is discussed.

Case presentation

A 12-year-old male with a recent diagnosis of hyperthyroidism presented with cough and difficulty breathing. He had developed a mild cough, runny nose, and fatigue 3 months prior that has been persistent despite starting Singulair, and antibiotics. He had a 2-pound weight loss over the last year. The night before he was brought to ER, he woke up from sleep with worsening cough, dyspnea and feeling a "tickle" and fluid in his throat. He was found to be hypoxic at 74% saturation, and chest x-ray (CXR) showed diffuse bilateral pulmonary nodules (Fig. 1). CT further confirmed diffuse bilateral pulmonary nodules in a miliary pattern of distribution (Fig. 2). Clinical suspicion for Langerhan's histiocytosis was high on the list of differential diagnoses followed by infectious etiologies including Tuberculosis. A wedge biopsy of the lung was performed, and the specimen was sent to Pathology for histologic evaluation and cultures to rule out infectious etiologies including fungal infections and tuberculosis. On histologic evaluation, an infiltrative tumor was identified composed of sheets and groups of epithelial cells with occasional papillary formations (Fig. 3). Psammoma bodies were readily identified (Fig. 4). The cells exhibited high NC ratios with clearing of nuclear chromatin and rare nuclear groves. Intranuclear inclusions were not apparent. Immunohistochemical stain against TTF-1 was diffusely and strongly positive (Fig. 5) and Napsin was negative in tumor

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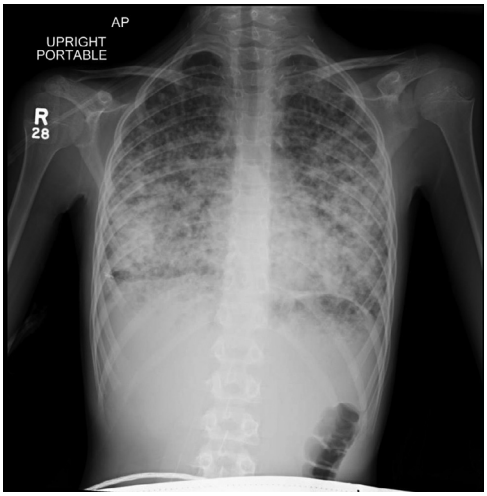

Fig. 1 – AP view of chest showing diffuse opacity of multiple nodules.

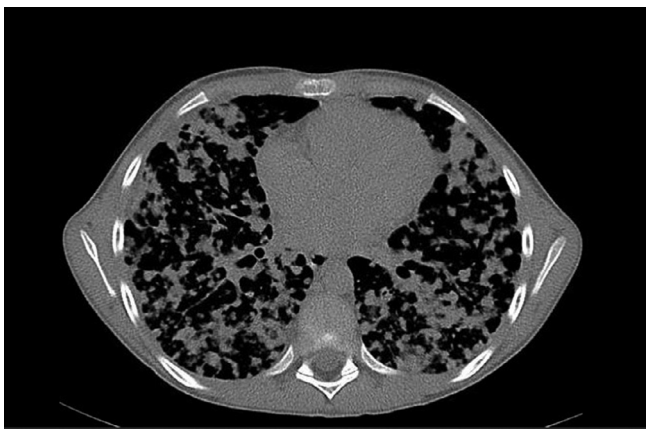

Fig. 2 – Axial CT of chest with contrast showing bilateral miliary nodules.

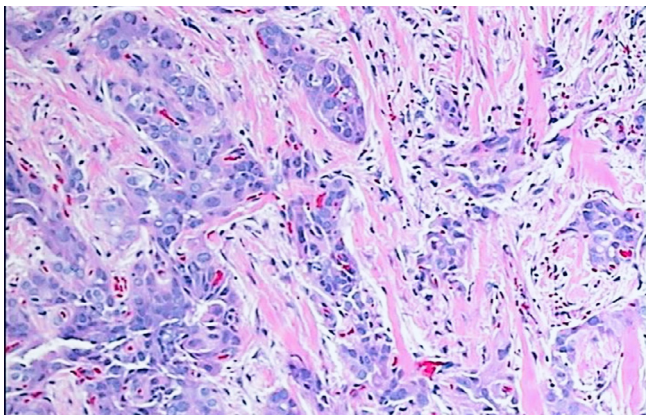

Fig. 3 – Wedge biopsy of lung showing papillary tumor consistent with thyroid primary (H&E X20) magnification.

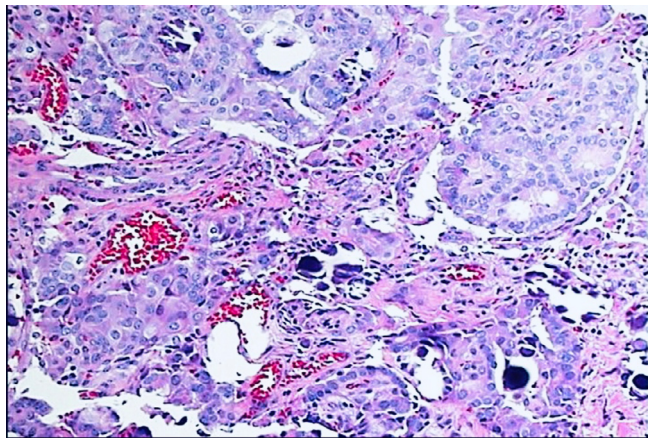

Fig. 4 – Tumor with psammomatous type calcifications (H&E x20) magnification.

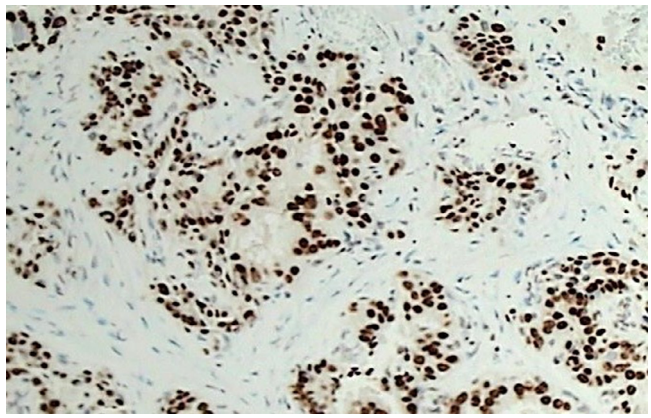

Fig. 5 – TTF-1 immunohistochemistry (IHC) stain x20 magnification.

cells. TROP 2 stain was diffusely positive confirming a diagnosis of metastatic thyroid carcinoma.

Discussion

Lung cancer in the adult population is the most common cancer related death in both men and women worldwide followed by breast and colon cancers. The American Cancer Society in a recent document reports that in 2020 there will be an estimated 228,820 new cases of lung cancer and 135,720 deaths from it in the United States alone [1]. Lung cancers arise from the epithelium in the airways or pulmonary alveolar parenchyma. Two major histologic subtypes have been described which include small cell carcinoma and non–small cell carcinoma, and their distinction is important in assessing prognosis and treatment. Resection can be curative in most early stage non–small cell carcinomas, while chemotherapy is the choice of treatment for small cell carcinomas of the lung. In children, both benign and malignant tumors of the lung are extremely rare and in the malignant category, metas-

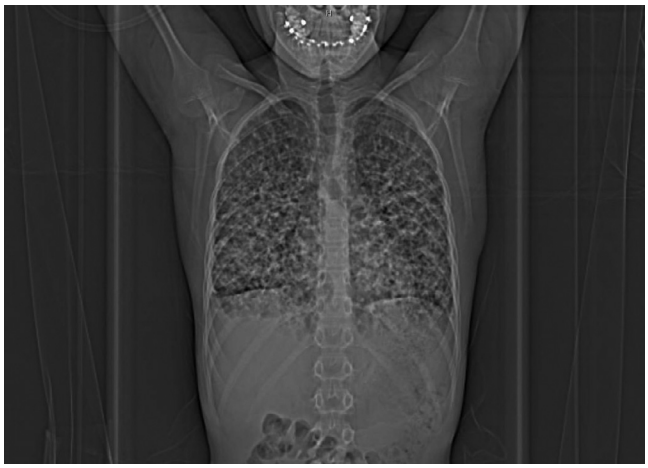

Fig. 6 – AP view of chest (6 months follow-up).

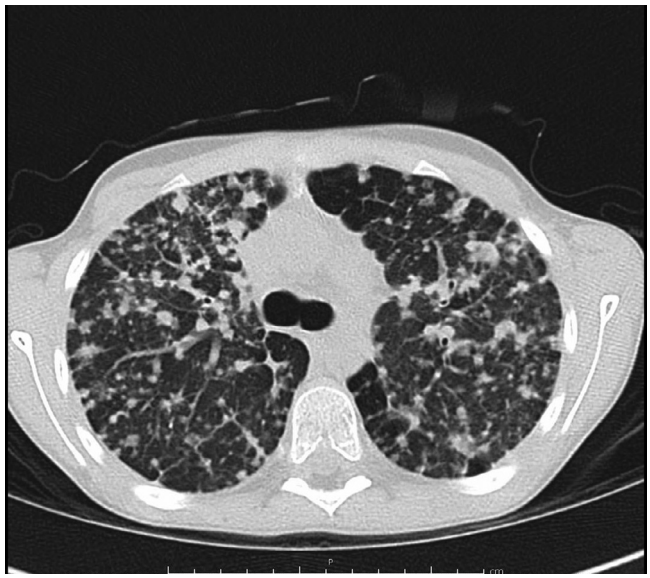

Fig. 7 – CT of chest with contrast (6 month follow-up).

tases outnumber primary tumors. Of all the lung masses in children, a benign development or reactive process is the most common lesion occurring 10 times as frequently as tumors [2]. These include bronchogenic cysts, intra and extra lobar sequestrations, cystic adenomatoid malformations and various infectious etiologies and sarcoidosis. Overall, malignant tumors are more common than benign tumors in a ratio of 3-1. In the benign category of lung tumors, ˜ 55% are myofibroblastic tumors. Neuroendocrine tumors including carcinoid tumors and pleuropulmomary blastomas constitute the most in the malignant category of tumors. In the malignant category, metastases outnumber primary tumors by a ratio of 5-1. The lung is a very common site for metastatic disease and at times can be the only expression of disease and distant spread without any identifiable primary lesion as was observed in our patient. Most metastases are bilateral and multiple presenting as miliary nodules to cannon-ball like lesions. Rarely metastasis can be single and can present with cavitation and pneumothorax mimicking tuberculosis and this type is frequently seen in association with Wilms tumor. Lymphangitic spread may result in severe respiratory distress in the absence of CXR abnormalities. Differential diagnosis between primary and metastatic tumors can be extremely difficult at times and even impossible in few. Multiple lesions with lymphatic spread and presence of a primary site support a diagnosis of metastatic disease.

Due to the rarity of lung tumors in the pediatric population, incidence data and literature is limited to mostly individual—anecdotal case reports and literature on adult patient population with metastatic disease. However, several retrospective studies mostly on adult patient population each spanning over 25 years had shed more insights into understanding pathobiology of pediatric lung tumors. Hoe et al. [3] reported 12% rate of distant metastases in their study of 731 patients with thyroid cancer analyzed between 1956 and 1978. Nemic et al. [4] in 1979 in a series of multiple publications spanning over 20 years reported similar (12%) incidence rate. Massin et al. [5] however, observed a lower incidence rate of 7% in their study population comprising 831 patients. An incidence rate of 20% is reported by Casinelli et al. [6]. This wide range of incidence in these long retrospective studies could be due to varying inclusion criteria for the diagnosis of thyroid cancer both on imaging and histologic evaluation. Data on pediatric pulmonary metastases by thyroid cancer is even sparser and is mostly based on general reviews on the thyroid cancer in Pathology textbooks. Cohen et al. in 1982 [2] in the largest retrospective review to date, published their data on pediatric lung tumors spanning 31 years. In their study of 465 pediatric lung tumors, metastases outnumber primary tumors 35-8 (7.5%-1.7%). Similarly, Dishop et al. in 2008 [7] published the data on and their experience with pediatric primary and metastatic lung tumors based on biopsies and resections. Their study included 294 pediatric lung tumors over a period of 25 years. Approximately 17% of these were primary lung tumors and the rest (83%) were metastatic tumors. Wilms tumor and osteosarcoma were most frequent metastatic tumors accounting up to 30% and 20% in both Cohen et al. and Dishop et al. studies. None of the metastatic tumors in both these large-scale studies was from thyroid tumors. Comprehensive retrospective review (1960-1990) of pediatric thyroid cancer metastases to lungs in patients under 25 years of age was first reported by Vassillipoulu-Sellin et al. in 2008. [8]. In their study of thyroid cancer patients under 25 years of age, 19 of 209 had pulmonary metastases. All the patients had the regional node involvement at the time of diagnosis. CXR was normal in 50% of these patients, however, intense and diffuse radioiodine uptake was observed in 90% of the study population. Micronodular pattern consisting of multiple small nodules was the most common radiologic appearance in their study. Our patient exhibited similar morphologic pattern on CXR and CT scan, however, he had neither thyroid mass nor lymphadenopathy present at the time of his presentation and diagnosis. In their study, Pulmonary metastases was observed most frequently in age groups 4-12 and 13-16 accounting for 15% and 12%, respectively.

Differential diagnosis for thyroid cancer metastases in lung in pediatric patient population includes Langerhans cell

histiocytosis, leukemia-lymphoma, Osteosarcoma, and small blue cell tumors including Wilms tumor, neuroblastoma, rhabdomyosarcoma, and Ewing sarcoma family of tumors. LCH involving lung can mimic metastatic malignancy on CT scan in the form of nodules ranging in size from 1 to 10 mm. Histologically, LCH characteristically presents with interstitial infiltrates of histiocytes with grooved nuclei and these cells are often positive with antibodies against S100 and CD1a. Electron microscopy can be helpful in difficult scenarios. Osteosarcoma metastasis occurs in ˜15% of patients and can often be asymptomatic. Repeated resection of the tumor nodules correlated with overall prolonged survival. Wilms tumor is the most common metastatic tumor and metastatectomy offers survival benefit to these patients (75% 4-year survival rate). In view of often miliary pattern of disease presentation in thyroid cancers in the lung, metastatectomy is not suitable. The primary modality for thyroid cancer metastases in the lung includes radioactive iodine (131 I) treatment which allows complete radiographic resolution and long-term survival benefit to the patients. Our patient underwent total thyroidectomy that showed papillary thyroid carcinoma with no regional node involvement. Radioactive iodine (131 I) was started. On follow-up at 6 months, he continued to have bilateral multiple nodules in the lung (Figs. 6 and 7) and developed nodal metastases in his neck.

In conclusion, we present a rare case of thyroid cancer metastases in a 12-year-old boy with bilateral diffuse miliary type nodules on imaging studies. Our patient neither had a detectable thyroid mass by imaging studies nor lymphadenopathy at the time of diagnosis. Though rare, awareness of this entity with early diagnosis is crucial as radioactive iodine can be curative offering long term survival benefit.

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