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Embryonal Rhabdomyosarcoma of The Lung: A Common Tumor with Atypical Primary Site

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ABSTRACT

Introduction: Embryonal rhabdomyosarcoma is the commonest type of rhabdomyosarcoma in children. Its common primary sites include but not limited to head and neck, genitourinary, and extremities. However, embryonal primary pulmonary rhabdomyosarcoma is extremely rare.

Case presentation: Our patient, 5 years old male presented with a four-week history of progressive worsening shortness of breath. The patient also had previous history of recurrent pneumonitis. On imaging, contrast enhanced chest CT demonstrated 16.1 x 13.1 x 13.3cm predominantly cystic mass with solid component on the right hemithorax. Metastatic workup was none revealing. Hence, open thoracotomy was done to cut out the mass, and sample was sent for histopathologic and immunohistochemistry assessment. Microscopy revealed pleomorphic round to oval to spindle blue cells in myxoid stroma along with anaplastic cells. Furthermore, the cells immunohistochemically reacted positively for smooth muscle actin, myogenin, and vimentin. Hence, the mass was confirmed to be embryonic type rhabdomyosarcoma of the lung. Accordingly, chemotherapy commenced, and he was given three cycles. Unfortunately, the patient died after three months. This case underscores the importance of suspecting primary pulmonary rhabdomyosarcoma in patients with recurrent bouts of pneumonic symptoms. Moreover, primary pulmonary rhabdomyosarcoma should be part of the differential diagnosis for lung mass with mixed components (cystic and solid).

Conclusion: Finally, embryonic rhabdomyosarcoma showing anaplastic cells tends to have unfavorable prognosis.

Keywords: *Embryonal, Rhabdomyosarcoma, Recurrent Pneumonitis, Cystic-Solid, Case Report*

Introduction

Rhabdomyosarcoma (RMS) is a cancer of mesenchymal origin with striated muscle differentiation. It is the most prevalent soft tissue cancer in children, contributing to more than half of childhood soft tissue sarcomas. The usual primary sites of this tumor include head and neck region, genitourinary, extremities, and chest wall (Türkkan *et al*., 2010; Xiaoxia *et al*., 2023; Ladra *et al*., 2019). However, rhabdomyosarcomas primarily originating from lung are extremely rare, only accounting for 0.5 % of childhood rhabdomyosarcomas (Nunes *et al*., 2023). According to the 2020 World Health Organization classification of soft tissue tumors, there are four histology types of RMS: embryonal, alveolar, pleomorphic, and spindle cell/sclerosing. In children, embryonal RMS is the commonest type; furthermore, it has better prognosis when compared with the other histology types. Alveolar type is known for its notorious metastatic tendency with poor prognosis (Hafiz and Bamefleh, 2022). In this case report, we present a case of embryonal primary pulmonary rhabdomyosarcoma in a 5-year-old child.

Case Presentation

Our patient, 5 years old male presented with worsening of shortness of breath of one month duration. Initially, the dyspnea was occurring during strenuous activities such as running, but later, it became apparent during minimal activities such as walking. In association to that, he had cough and low-grade intermittent fever. Moreover, the patient was admitted to the local primary hospital in his hometown multiple times over the last 10 months with the impression of severe recurrent pneumonitis. Otherwise, family history was no revealing, and the patient was fully vaccinated. Vital signs were stable except for respiratory rate which was slightly elevated for age (42 breaths per minute). Physical examination showed absent air entry in the right lung, and SpaO2 was 90%.

Up on laboratory investigation, complete blood count, erythrocyte sedimentation rate, and renal function test were all normal. Tuberculosis screening was negative. In addition, contrast enhanced chest CT demonstrated 16.1 x 13.1 x 13.3cm cystic mass with solid component in the right hemithorax (Fig. 1). The mass has peripheral curvilinear type pleural based calcifications, and has mass effect on the mediastinum and vascular structures (Fig. 1-2). Moreover, the mass is predominantly cystic, and obscures branches of right pulmonary artery as well as branches of right main bronchus (Fig. 3-4). Lastly, metastatic workup was negative.

Consequently, open thoracotomy was done to remove the mass (Fig. 5), and sample was sent for histopathological and immunohistochemical evaluation. Microscope revealed hyper and hypo cellular

areas composed of fascicles and dis-cohesive sheets of moderately to highly pleomorphic round to oval to spindle blue cells with coarse chromatin and clear to basophilic cytoplasm, embedded within myxoid tissue. In addition, areas of anaplasia were noted, and mitotic activity was brisk (Fig. 6-8). Immunohistochemically, tumor cells were positive for smooth muscle actin, myogenin, and vimentin (Fig. 9-11). Therefore, the final diagnosis became embryonal type primary pulmonary rhabdomyosarcoma.

The patient was then started with chemotherapy (Vincristine, Adriamycin, Cyclophosphamide) and took three cycles. Regrettably, he passed away three months after the diagnosis.

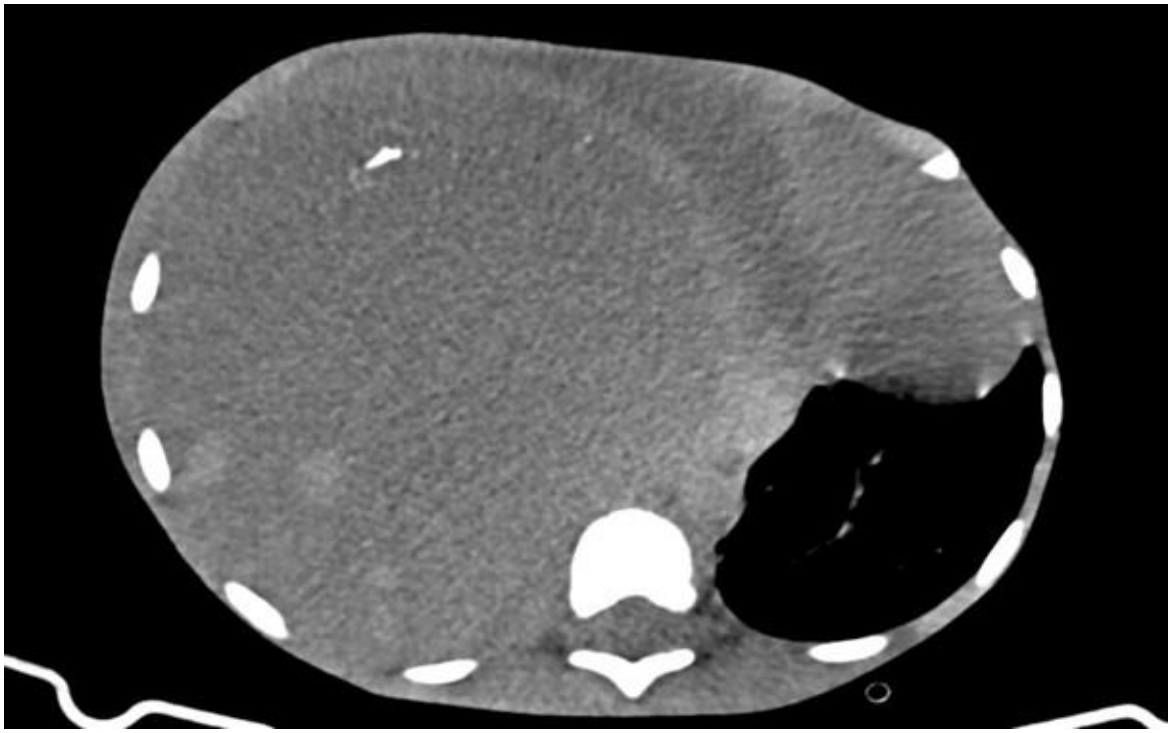

Figure 1: Axial section of pre-contrast CT scan of the chest on soft tissue window at the level of T6 vertebra:-there is non-visualized right lung parenchyma with right hemi-chest completely filled by large mixed cystic and solid density mass with cystic component density ranging from 13-19HU and solid component ranging 41 to 55HU. The lesion fills and replaces the right hemi-chest extending from anterior to posterior chest wall having peripheral curvilinear type of pleural based calcifications and mass effect with shifting of the mediastinum and heart to the contralateral side.

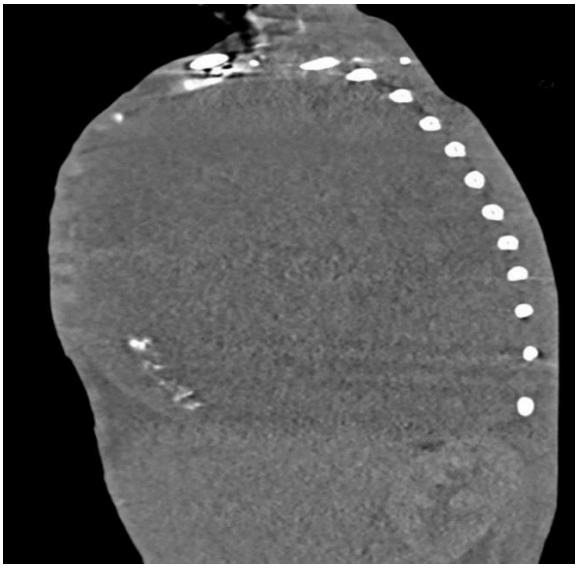

Figure 2: Right para-sagittal section of pre-contrast CT scan of the chest on soft tissue window showing similar lesion completely filling the right pleural cavity with non-visualized normal lung tissue and the lesion has no gross extension to the chest wall as well as to neck and diaphragmatic outlines.

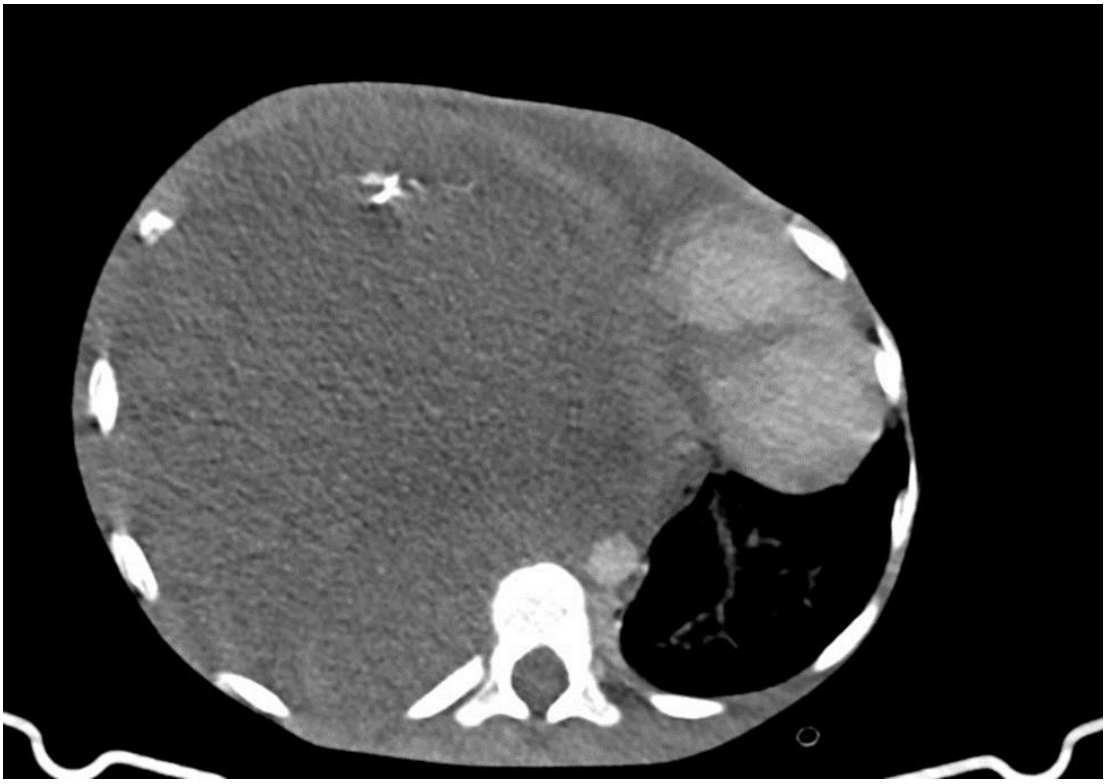

Figure 3: Axial section of post-contrast CT scan of the chest on soft tissue window:- The soft tissue component of the mass has post contrast enhancement while the cystic component is not enhancing, , there is visualized right pulmonary artery and main bronchus with non-visualized lobar & segmental bronchus and pulmonary arterial branches with the respective anatomic position is occupied by the tumor. There is no normal lung tissue seen on the right while the contralateral lung has compressed from mass effect but has normal lobar and segmental differentiations.

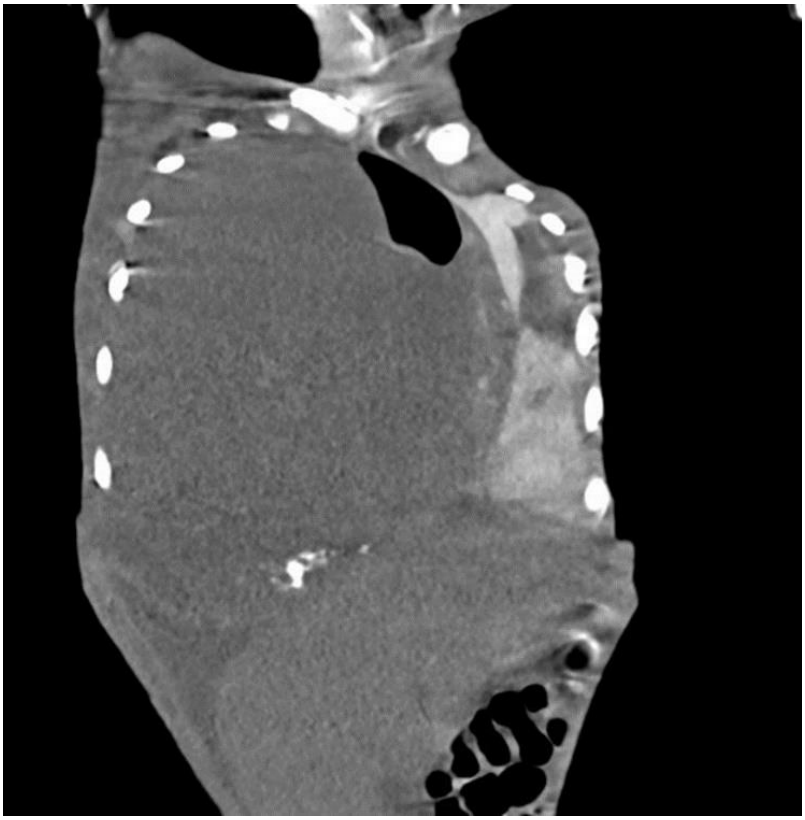

Figure 4: Coronal section of post-contrast CT scan of the chest on soft tissue window: - The tumor is well delineated inside the right plural cavity with no gross extension to the chest wall as well as to the neck above and diaphragm bellow.

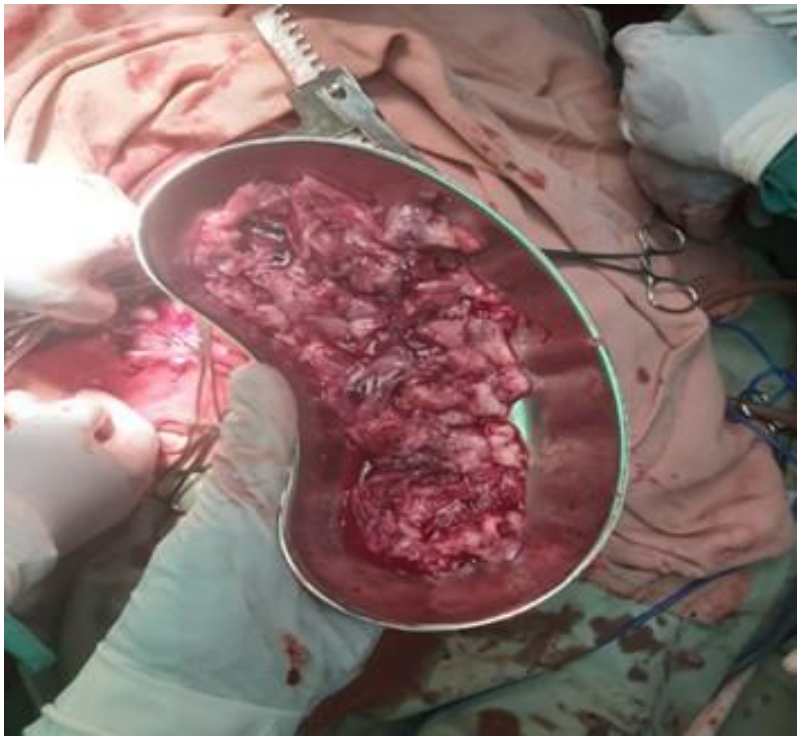

Figure 5: Grey white to hemorrhagic resected lung tissue.

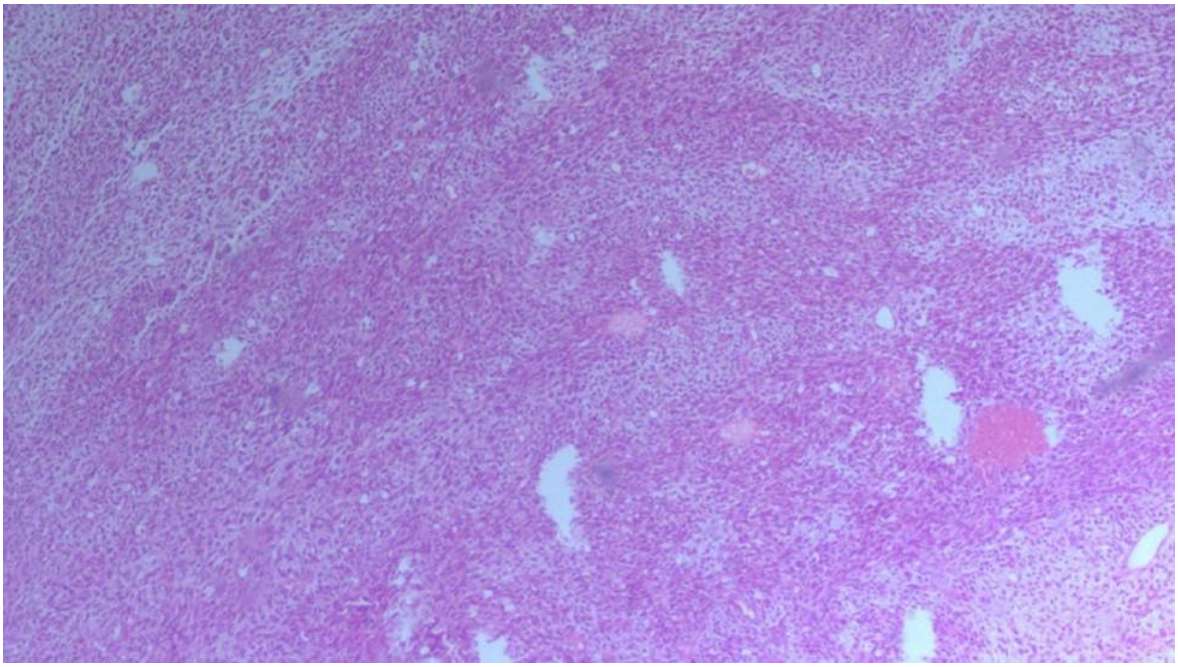

Figure 6: 4x: Microscopy revealed hyper and hypocellular areas composed of fascicles and dis-cohesive sheets of moderately to highly pleomorphic round to oval to spindle blue cells with coarse chromatin and clear to basophilic cytoplasm, embedded within myxoid tissue.

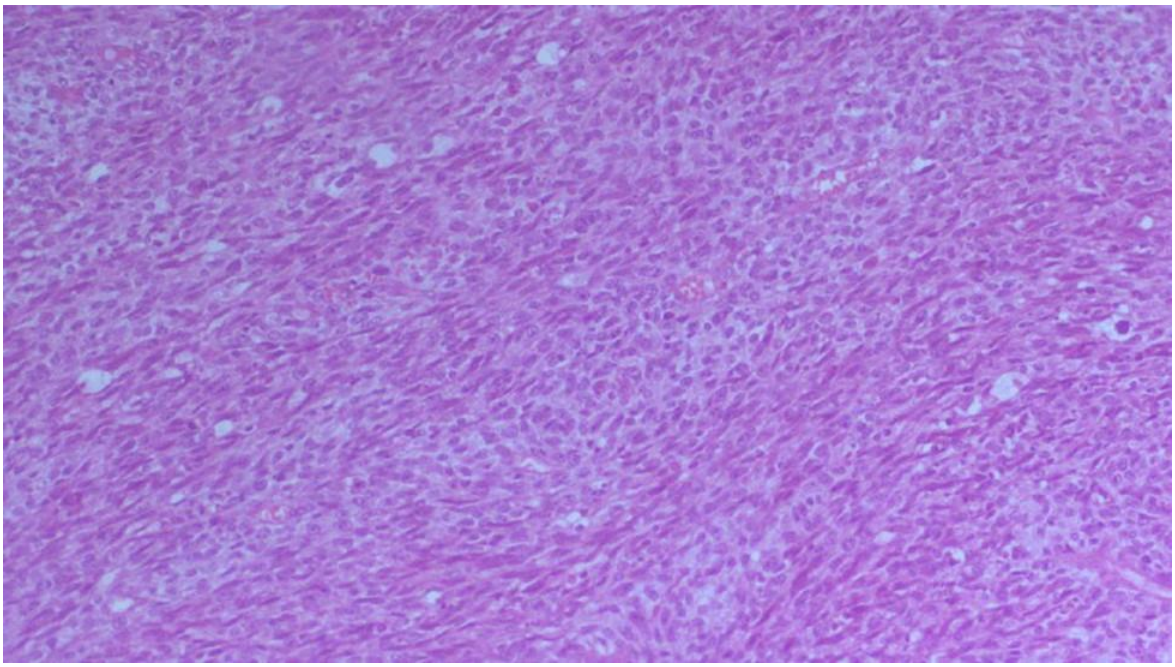

Figure 7: 10x: magnification showing sheets of moderately to highly pleomorphic round to oval to spindle blue cells embedded within myxoid tissue.

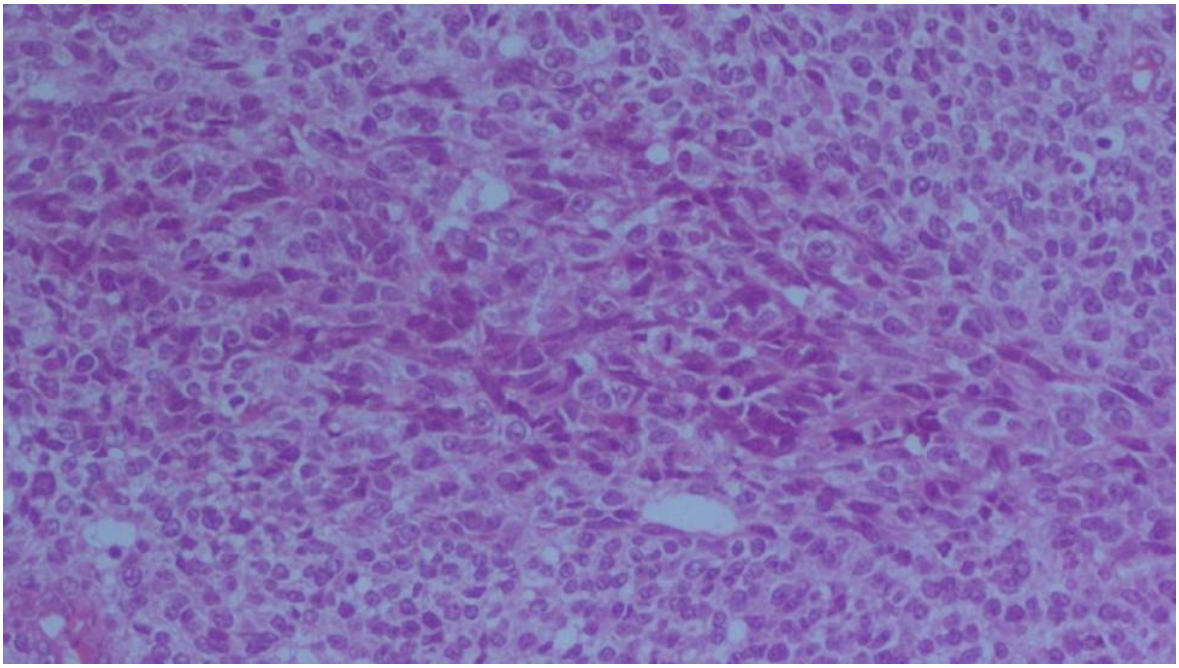

Figure 8: Higher magnification (40x) showing areas of anaplasia with brisk mitotic activity.

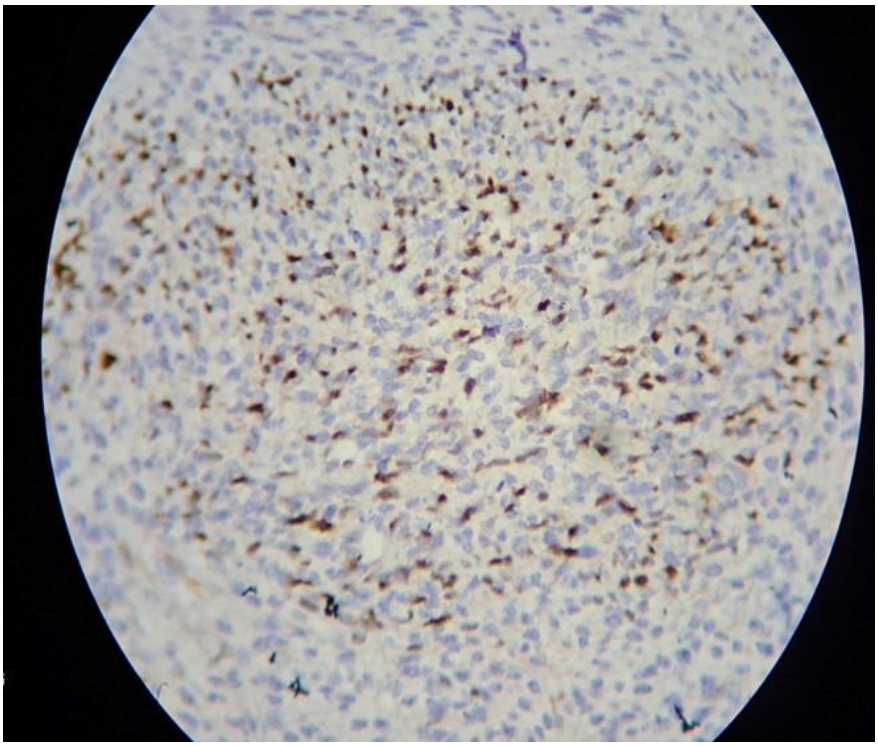

Figure 9: 40x: Diffuse positivity for myogenin.

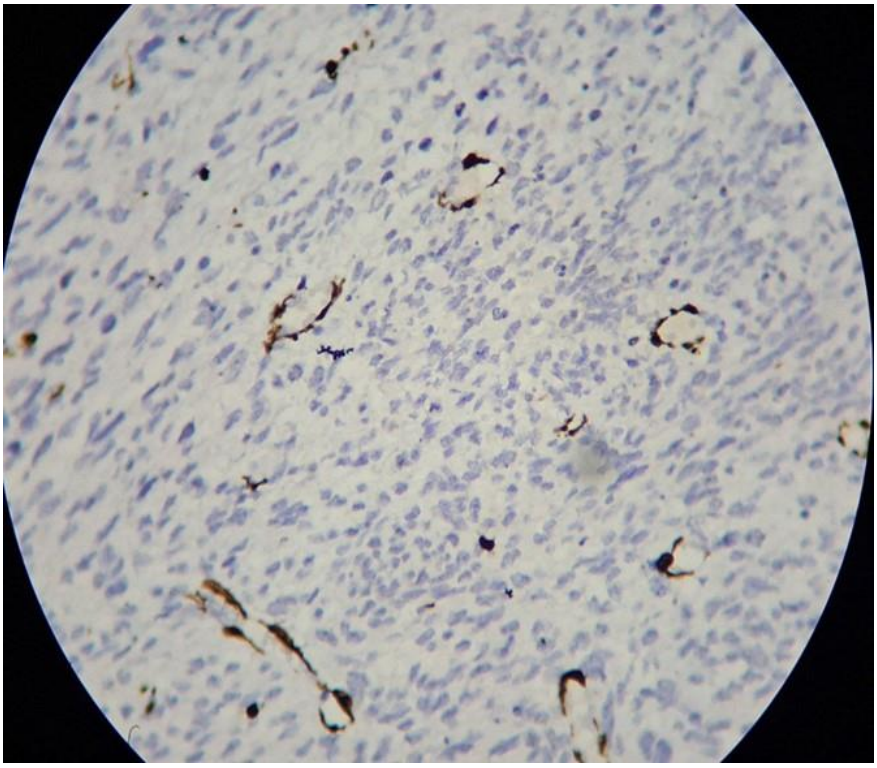

Figure 10: 40x: Scattered positivity for smooth muscle actin.

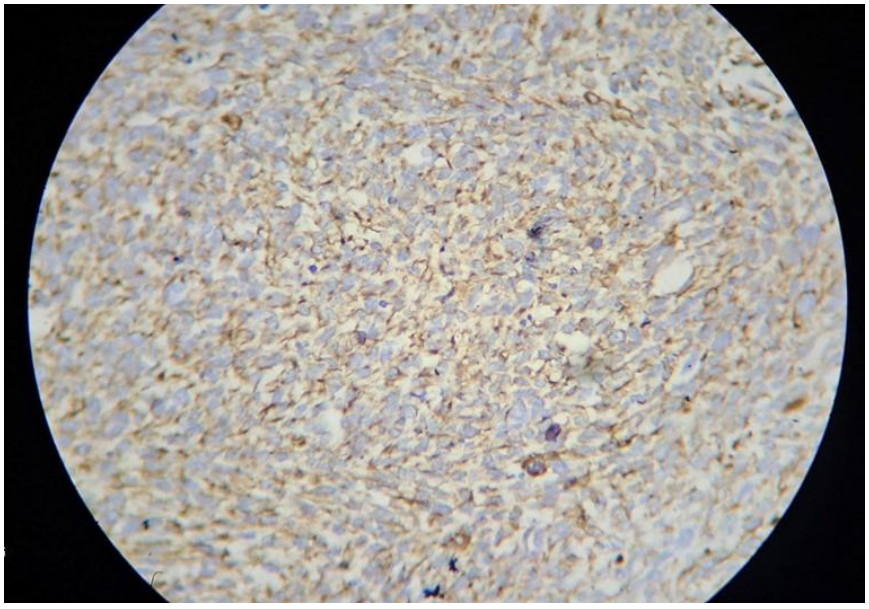

Figure 11: 40x: Diffuse positivity for vimentin.

Discussion

Primary lung tumors generally are extremely rare in the pediatric population. Among these tumors, the commonest in children are bronchial adenoma, bronchogenic carcinoma, and plasma cell granuloma. On the other hand, primary RMS of the lung is uncommon, contributing to 4.4 % of all pulmonary tumors occurring in children (Mostafa, 2022).

Depending on the background tissue it arises from, primary pulmonary rhabdomyosarcoma (PPRMS) can be divided in to two: PPRMS developing in a previously existing congenital cystic anomaly and PPRMS occurring in the background of normal lung tissue. There are two schools of thoughts regarding the pathogenesis of PPRMS. The first one elaborates that PPRMS originates from ectopic islets of striated muscle. Since these islets of striated muscles are frequently present in congenital cystic lesions, this theory provides plausible explain for the occurrence of PPRMS in the background of congenital cystic lung lesions. The second theory suggests that malignant transformation of primitive mesenchymal cells leads to the formation PPRMS. The background in which PPRMS develops has both clinical and prognostic implications. In fact, PPRMS developing in the background of congenital cystic malformation commonly presents with spontaneous pneumothorax (Lokesh *et al*., 2013; Hassan, 2013; Iqbal *et al*., 2002).

Clinical sign/symptoms include shortness of breath with sudden or progressive onset, cough, fever, wheeze, and spontaneous pneumothorax. Patients may also present with chest pain, loss appetite, hemoptysis, and recurrent pneumonitis (Lokesh *et al*., 2013; Hassan, 2013; Iqbal *et al*., 2002; Allan *et al*., 1987; McDermott *et al*., 1993; Amirikar *et al*., 2022). Given the fact that 20% of rhabdomyosarcomas already have metastasized upon presentation, it is possible for patients to manifest with features of metastases, beside respiratory symptoms. Supporting this, there were reported PPRMS cases in which patients presented with abdominal complaints, due to small bowel metastases (Sun and Shen, 2019; Xi and Tong, 2018). Our patient presented with progressive dyspnea, low grade intermittent fever, and cough, and had history of recurrent pneumonitis.

Among the histological types, embryonal RMS and alveolar RMS are the commonest in children and adolescents. In comparison, pleomorphic and embryonal types are the commonest in adults (Xiaoxia *et al*., 2023; Hafiz and Bamefleh, 2022; de Vries ISA *et al*., 2023). Embryonal type often shows dispersed spindle cells with in myxoid stromal tissue, commonly expresses actin, myosin, desmin, and myoD1, and has comparatively better prognosis. Anaplastic cells can be seen in 3 to 13 % of embryonal RMS, and their presence indicates unfavorable prognosis (Hafiz and Bamefleh, 2022; Balaji *et al*., 2017; Łomiak *et al*., 2023). Histologically, alveolar type demonstrates loss of cohesion with thin fibrous septa that resembles

the morphological structure of alveolus of the lung. Furthermore, alveolar type more intensely expresses myogenin than myoD1, and associated with poorer prognosis (Kandola *et al*., 2018; Van Rijn *et al*., 2008). Pleomorphic type, on the other hand, shows cells ranging from small epithelial to large cells with segmented nucleus and distinct nucleoli. Moreover, pleomorphic RMS poorly expresses myogenin (Sun and Shen, 2019; Łomiak *et al*., 2023).

Common radiological findings include but not limited to cystic or solid or cystic-solid (mixed components) lung mass with associated atelectasis (lobar or segmental), and pleural effusion (unilateral or bilateral). In addition, nodular growths and calcifications on the peripheral aspect of lung lesion can be seen. Although not specific, PPRMS arising from congenital cystic lesion usually involves single lobe or segment. In our case, the mass involved the entire right lung, which indicated that the mass most likely occurred in the back ground of a normal lung tissue. Due to easy accessibility, ultrasound can be used as initial imaging modality to evaluate RMS and to take ultrasound guided core needle biopsies. Nonetheless, in the case of PPRMS, contrast enhanced computed tomography or magnetic resonant imaging is mandatory for accurate visualization and characterization (de Vries ISA *et al*., 2023; Van Rijn *et al*., 2008; Almberger *et al*., 2001; Saboo *et al*., 2012).

It is worthy considering pleuropulmonary blastoma (PPB), lymphoma, primitive neuroectodermal tumors (PNET), and malignant peripheral nerve sheath tumors (MPNST) as differential diagnosis. PPB has various subtypes: type 1 is cystic, type 2 is mixed (both cystic and solid components), and type 3 is solid lesion. In addition, PPB is commonly seen before 6 years of age, can also occur in the back ground of congenital cystic lung lesion, and strongly expresses vimentin and pan ck. PPRMS and PPB are very difficult to differentiate, except only the last one shows blastema. Apart from that, anaplastic cells and epithelial components are absent in PPB (Xiaoxia *et al*., 2023; Lokesh *et al*., 2013; Amirikar *et al*., 2022; Balaji *et al*., 2017). In our case, taking in to account age of the patient, and the radiologic features, we strongly suspected the possibility of type 2 PPB in this particular patient. However, microscopic examination revealed embryonal histology with anaplastic cells. Moreover, the tumors cells reacted positively for myogenin, which is specific for RMS.

Factors associated with poor prognosis include advanced age at presentation, alveolar and pleomorphic histology, size > 5 cm, and presence of metastasis at presentation. Moreover, primary tumor locations such as para-meninges, chest, abdomen, and extremities have unfavorable prognosis. Majority of intrathoracic rhabdomyosarcomas including PPRMS manifest late with substantial tumor burden, which makes their prognosis poor (Türkkan *et al*., 2010; Türkkan *et al*., 2010; Türkkan *et al*., 2010; de Vries ISA *et al*., 2023). On the contrary, PPRMS developing in the background of cystic lesion tend to show better

prognosis in comparison with those developing in a normal lung tissue. This could be due to the higher chance of being detected early enabling complete surgical resection (Lokesh *et al*., 2013). In our case, we were unable to uncover any evidence regarding the presence of underlying congenital cystic lesion, the tumor size was > 5 cm at presentation, and anaplastic areas were seen microscopically. These were the identified poor prognostic factors in our patient.

Conclusion

Lung is uncommon primary site of rhabdomyosarcoma. The possibility of primary pulmonary rhabdomyosarcoma should be entertained in any patient having recurrent pneumonia, since with early diagnosis both complete resection and cure could be achieved. Furthermore, primary pulmonary rhabdomyosarcoma should be considered as top differential diagnosis for cystic-solid (mixed) lung masses. Lastly, the presence of anaplastic cells in the back ground of embryonal histology harbors unfavorable prognosis.

Abbreviation

RMS : Rhabdomyosarcoma
PPRMS : Primary Pulmonary Rhabdomyosarcoma
PPB : Pleuropulmonary Blastoma
Chest CT : Computed tomography of the chest

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Disclosure: The authors report no conflicts of interest in this work.

Informed Consent Statement: Written consent was received from the patient's parents for publication

Data Availability Statement: Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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