Primary Pulmonary Alveolar Rhabdomyosarcoma in a Pediatric Patient: A Case Report With Literature Review

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Abstract

Rhabdomyosarcoma (RMS) is a rare soft tissue tumor originating from skeletal muscle that is mostly reported in children. The most common sites of involvement are the head, neck, and extremities. The 2020 WHO classification divide RMS into four types: embryonal, alveolar, pleomorphic, and spindle cell/sclerosing. Reports of RMS with primary lung origin are rare. We present a case of RMS in a 16-month-old boy who presented with a lung mass and microscopic examination with fluorescence in situ hybridization confirmed the diagnosis of alveolar RMS. In conclusion, RMS should be considered in the differential diagnosis of any lung mass with small round blue cell morphology in the microscopic evaluation and should be distinguished from metastatic RMS of other sites, pleuropulmonary blastoma, lymphoma, neuroblastoma, primitive neuroectodermal tumor (PNET)/EWING, and malignant peripheral nerve sheath tumors (MPNST).

Introduction

Rhabdomyosarcoma (RMS) is a malignant soft tissue neoplasm having skeletal muscle differentiation [1]. It is the most commonly occurring tumor in the pediatric age group and has a higher prevalence in males [1,2]. RMS is most frequently found in the head and neck area, followed by the genitourinary tract and extremities [3]. The World Health Organization (WHO) of soft tissue tumors has identified four subtypes: embryonal, alveolar, pleomorphic, and spindle cell/sclerosing [4]. The embryonal type is the most common type in children, with a favorable prognosis compared with other types [5]. Alveolar RMS has a high rate of metastasis and unfavorable prognosis; it is characterized by a chromosomal alteration - a fusion between the FKHR (also known as FOXO1) gene and either the PAX3 or PAX7 gene [6]. RMS rarely originates in the lung and only 32 such cases have been reported in the literature [7].

We report a case of a 16-month-old baby boy who presented clinically with shortness of breath and radiologically with a lung mass. The clinical presentation, radiological findings with pathology report, and fluorescence in situ hybridization (FISH) are compatible with primary alveolar RMS.

Case Presentation

A 16-month-old baby boy with known G6PD deficiency and club foot presented with progressive shortness of breath. His mother reported that the shortness of breath was associated with fever and decreased appetite. The baby had been delivered normally at full-term.

Physical examination revealed that the patient appeared ill and distressed. The vital signs were as follows: blood pressure, 100/70 mmHg; heart rate, 108 bpm; respiratory rate, 45 breaths/min; and O₂ saturation, 89%. The chest examination revealed decreased breath sounds in the right chest. The remainder of the systemic review was unremarkable.

Radiological studies, including computed tomography (CT) and magnetic resonance imaging (MRI), were performed. The studies revealed a lobulated mass (7.3 x 6.4 x 4.4 cm) in the base of the right lung that involved the diaphragm, mediastinal pleura, and right pericardial space; the mass encased the esophagus and extended to the interlobular fissure. Three other pleural-based nodules were identified in the right upper lobe (Figures 1A, 1B). Based on the clinical and radiological findings, CT-guided core needle biopsies were obtained and sent for histopathology study.

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A pathological examination revealed six cores of lesioned tissue composed of nests of small round blue cell tumors, with some cells having little cytoplasm. The nuclei were round with euchromatin and focal cytoplasmic striation was noted. Necrosis was rare (Figures 2A, 2B). An immunohistochemistry panel was performed to label the following markers: desmin, pan-cytokeratin (CKpan), myogenin, synaptophysin, MyoD1, chromogranin, CD99, and CD45 S100. The tumor cells showed diffuse positivity for desmin, myogenin, MyoD1, and focal positivity for S100. The cells were negative for CD99, CKpan, CD45, chromogranin, and synaptophysin (Figures 2C, 2D). FISH revealed rearrangement of the FOXO1 gene at 13q14 (FOXO1 [13q14]), which is characteristic of alveolar RMS.
FIGURE 2: Histopathology examination with hematoxylin and eosin (H&E) stains and immunohistochemistry studies. Examination revealed neoplastic growth in the form of nests of small round blue cell tumors with some cells having a little amount of cytoplasm. (A) The nuclei were round with euchromatin. (B) Focal cytoplasmic striation was noted. Necrosis was rare (10x & 40x). (C) The desmin stain was diffuse positive with a membranous pattern. (D) MyoD1 showed nuclear positivity.

Based on the clinical history of no other primary in other sites of body and radiology in addition to microscopic features, immunohistochemistry, and the FISH study, the final diagnosis was primary pulmonary RMS, alveolar type. The patient received chemotherapy and radiotherapy for 10 months, demonstrating improvement at a follow-up imaging study. The patient showed complete remission at one-year post-treatment follow-up.

Discussion

RMS is a primitive mesenchymal tumor with skeletal muscle differentiation. RMS is common in children and has a poor prognosis. Alveolar RMS has the worst prognosis due to its unique PAX3-FOXO1 fusion gene molecular phenotype [4].

RMS is associated with a congenital cystic adenomatoid malformation (CCAM) but may also occur in a healthy lung. The etiology of primary pulmonary RMS is still unknown, but there are two main hypotheses for its origin: first, the tumor may arise from heterotopic islets of striated muscle, which could explain the frequent association of RMS with pulmonary malformations such as cystic adenomatosis; and second, the tumor may arise from metaplastic changes in uncommitted mesenchymal cells in the absence of congenital abnormalities [3]. Like other lung neoplasms, RMS can present as a cough, respiratory distress, hemoptysis, chest pain, and/or recurrent pneumonitis [7]. Spontaneous pneumothorax has also been reported, especially in RMS cases that grow in the background of CCAM [8].

The main differential diagnosis is pleuropulmonary blastoma, lymphoma, neuroblastoma, primitive neuroectodermal tumor (PNET)/EWING, and malignant peripheral nerve sheet tumors (MPNST). Pleuropulmonary blastoma has blastema, anaplastic and epithelial components that are not present in RMS. The nuclear positivity for MyoD1 and myogenin is specific for RMS among other differential diagnoses.

An extensive search of English research literature (including PubMed, Google Scholar, and OVID) identified 32 cases reported as primary pulmonary RMS in the pediatric age group (Table I) [8-32]. Fallon et al. diagnosed the first pediatric case of primary RMS in 1970 in a six-year-old girl [8]. Among the other cases, the ages of the patients ranged from five months to 16 years old. Nine of the cases developed in a background of CCAM, while the others—including our case—developed in a normal lung. Twenty-five of the cases were embryonal, two were pleomorphic, two were undifferentiated, and one had alveolar morphology. Our case represents the second reported case of alveolar RMS. Most patients received a chemotherapy
regimen (vincristine, actinomycin, ifosfamide, and doxorubicin, in combination) according to the Intergroup Rhabdomyosarcoma Study (IRS) V protocol. Chemotherapy was combined with radiotherapy in several cases.

| Study | Age | Site | RMS Type | Treatment | Follow up |
|-------|-----|------|----------|-----------|----------|
| Fallan et al., 1970 [8] | 6 years | Right bronchus | Embryonal | Chemotherapy and radiotherapy | Disease free to age 33 |
| Udea et al., 1977 [9] | 1-1/2 years | Left upper lobe, CCAM | Embryonal | Chemotherapy | Disease free to age 17 |
| Krous and Sexauer, 1981 [10] | 2-1/2 years | Left lower lobe | Embryonal | Chemotherapy and radiotherapy | Metastasis of brain and lymph node and death six months after diagnosis |
| Thomas et al., 1981 [11] | 1 year and 9 months | Right-middle and lower lung | Embryonal | Chemotherapy | Disease free to age 5 |
| Hartman and Shochat, 1983 [12] | 11 years | Left main bronchus | Undifferentiated | Chemotherapy and radiotherapy | Free of disease 24 months after resection |
| Hartman and Shochat, 1983 [12] | 13 years | Right side | Undifferentiated | Chemotherapy and radiotherapy | Disease free 5 years after the diagnosis and 1 year developed brain metastasis |
| Allan et al., 1986 [13] | 2-1/2 years | Right lower lobe | Embryonal | Surgery and chemotherapy | Recurrent disease on the ipsilateral side 11 months after diagnosis |
| Allan et al., 1986 [13] | 1 year and 9 months | Left lower lobe | Embryonal | Surgery and chemotherapy | Disease free after 4 years |
| Williams, 1986 [14] | 1 year and 9 months | Right lower lobe, CCAM | Embryonal | Surgery and chemotherapy | Disease free to age 24 |
| Shariff et al., 1988 [15] | 1 year and 3 months | Left lower lobe, CCAM | Embryonal | Surgery only | Disease free to age 3 |
| Hedlund et al., 1989 [16] | 1 year and 10 months | Right side | Not recorded | chemotherapy | Disease free after 9 months. |
| Hedlund et al., 1989 [16] | 1-1/2 years | Left upper lobe | Embryonal | chemotherapy | Disease free after 12 years |
| Murphy et al., 1992 [17] | 3 years | Right middle lobe and right lower lobe, CCAM | Embryonal | Surgery and chemotherapy | Disease free to age 3 |
| Murphy et al., 1992 [17] | 3-1/2 years | Left lower lobe, CCAM | Embryonal | Surgery and chemotherapy | Disease free to age 6 |
| McDermott et al., 1993 [18] | 3 years | Right lower lung | Embryonal | Surgery and chemotherapy | Brain metastases and death |
| McDermott et al., 1993 [18] | 2 years | Left side | Embryonal | Surgery and chemotherapy with radiotherapy | Died 5 months after intracerebral metastasis |
| Bogers et al., 1993 [19] | 1-1/2 years | No information | No information | Chemotherapy | No information |
| Doval et al., 1994 [20] | 10 years | Left main bronchus | Embryonal | Bronchoscopy with chemotherapy and radiotherapy | Disease Free |
| | 1 year | Surgery with | Recurrence with brain metastasis after 6,
TABLE 1: Cases of primary pulmonary RMS

| Case | Age and Duration | Location | Histology | Treatment | Outcome |
|------|------------------|----------|-----------|-----------|---------|
| 19   | Noda et al., 1995 [21] and 10 months | Right upper lung | Alveolar | chemotherapy and radiotherapy | 11, and 24 months and then complete remission till 5 years of age |
| 20   | d'Agostino et al., 1997 [22] | Right lower lobe, CCAM | Embryonal | Surgery and chemotherapy | Disease Free to age 72 |
| 21   | Ozcan et al., 2001 [23] | Left upper lobe, CCAM | Embryonal | Surgery and chemotherapy | Disease free to age 15 |
| 22   | Iqbal et al., 2002 [24] | Left lower lobe, CCAM | Embryonal | Surgery and chemotherapy | Disease free 13 months after surgery |
| 23   | Doladzas et al., 2005 [25] | Left lower lobe, CCAM | Pleomorphic | No information | Disease free 10 years after diagnosis |
| 24   | Pia et al., 2005 [26] | Right lower lobe, CCAM | Embryonal | Chemotherapy pre- and post-surgery | Disease free to age 24 |
| 25   | Chang et al., 2008 [27] | Right upper and middle lobes | Embryonal | Surgery and chemotherapy with proton beam radiation | Local recurrence after 24 weeks of treatment |
| 26   | Türkkan et al., 2010 [28] | Left lower zone | Embryonal | Chemotherapy followed by radiation | Died 9 months after the diagnosis |
| 27   | Lokesh et al., 2011 [29] | Right side | Embryonal | Chemotherapy | Disease free for 160 months |
| 28   | Lokesh et al., 2011 [29] | Right lower lobe | Embryonal | Chemotherapy | Disease free for 19 months |
| 29   | Lokesh et al., 2011 [29] | Right lower lobe | Embryonal | No chemotherapy or radiotherapy | Disease free for 7 months |
| 30   | Hassan et al., 2013 [30] | Left lower lobe | Embryonal | No information | No information |
| 31   | Balaji et al., 2016 [31] | Right lower lobe | Not determined | Chemotherapy | Disease free after 6 years |
| 32   | Mallapa et al., 2019 [32] | Left middle and lower zones | Embryonal | Chemotherapy | No information |
| 33   | Present case | Right lower lung | Alveolar | Chemotherapy and radiotherapy | Disease free |

Conclusions

Primary pulmonary RMS is a rare disease that exhibits aggressive behavior. RMS should be included in the differential diagnosis of any lung mass with small round blue cell morphology. Clinical and radiological assessment is necessary to exclude metastatic RMS from other sites. In addition to RMS, other differential diagnoses that should be considered for a lung mass are pleuropulmonary blastoma, lymphoma, neuroblastoma, PNET/EWING, and MPNST.

Additional Information

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