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CASE REPORT

Pleural Alveolar Rhabdomyosarcoma

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SUMMARY

Alveolar rhabdomyosarcoma (ARMS) commonly occurring in children and adolescents, is a rare and aggressive soft tissue malignancy. Here, a rare case of pleural ARMS is reported in a boy presenting dyspnea for two weeks. The pathology of a biopsy specimen from pleura showed ARMS. PAX3-FKHR fusion protein is positive and the PAX7-FKHR fusion protein is negative as detected by fluorescence in situ hybridization. The prognosis of this patient was poor and nonresponsive to chemotherapy.
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KEY WORDS

alveolar rhabdomyosarcoma, PAX3-FKHR, PAX7-FKHR

LIST OF ABBREVIATIONS

ARMS - Alveolar rhabdomyosarcoma
ERMS - embryonal rhabdomyosarcoma
CT - computed tomography
FISH - fluorescence in situ hybridization

INTRODUCTION

Rhabdomyosarcoma accounts for about 7 - 8% of childhood cancers. It is the most common soft tissue malignant tumor in children, including embryonal rhabdomyosarcoma (ERMS), alveolar rhabdomyosarcoma (ARMS), and pleomorphic rhabdomyosarcoma (PRMS) [1]. ERMS occurred in children, ARMS in children and adolescents, and PRMS in old people. ARMS is a more malignant form of rhabdomyosarcoma than ERMS and often occurs in limbs [2,3]. Here, we report a case of pleural ARMS.

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Table 1. Sequence of anti-cancer treatments.

Date	Treatment
September 30, 2015	Commenced chemotherapy with gemcitabine combined with cisplatin
December 06, 2015	Completed four cycles of chemotherapy with gemcitabine combined with cisplatin
January 07, 2016	Commenced second-line chemotherapy
April 24, 2016	Completed two cycles of chemotherapy with ifosfamide, mesna, epirubicin, dacarbazine, and another two cycles of chemotherapy with epirubicin combined with dacarbazine

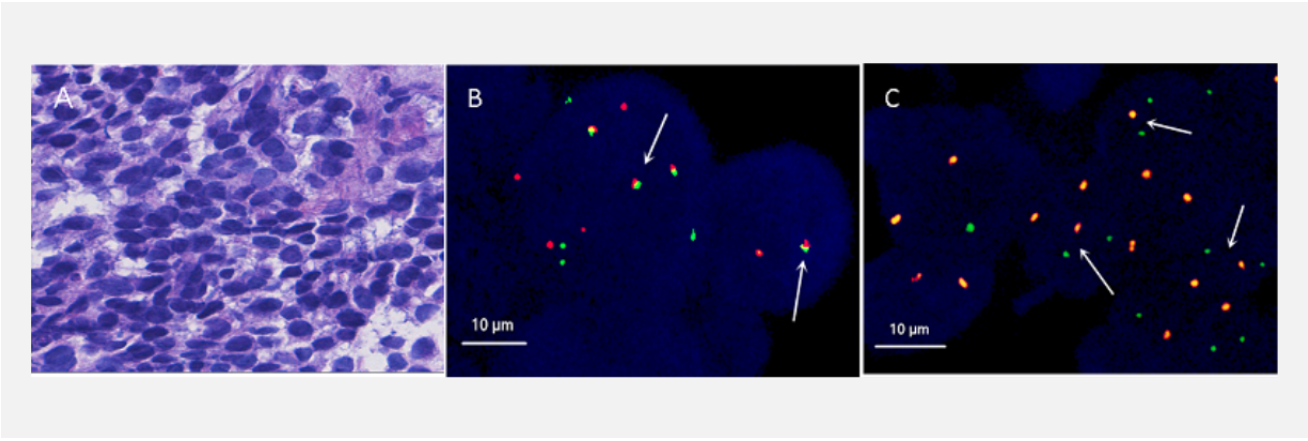


Figure 1. The results of pathology and FISH detection of the patient.

A. Hematoxylin and eosin staining for biopsy specimen from pleura. B. PAX3-FKHR positive. C PAX7-FKHR negative.

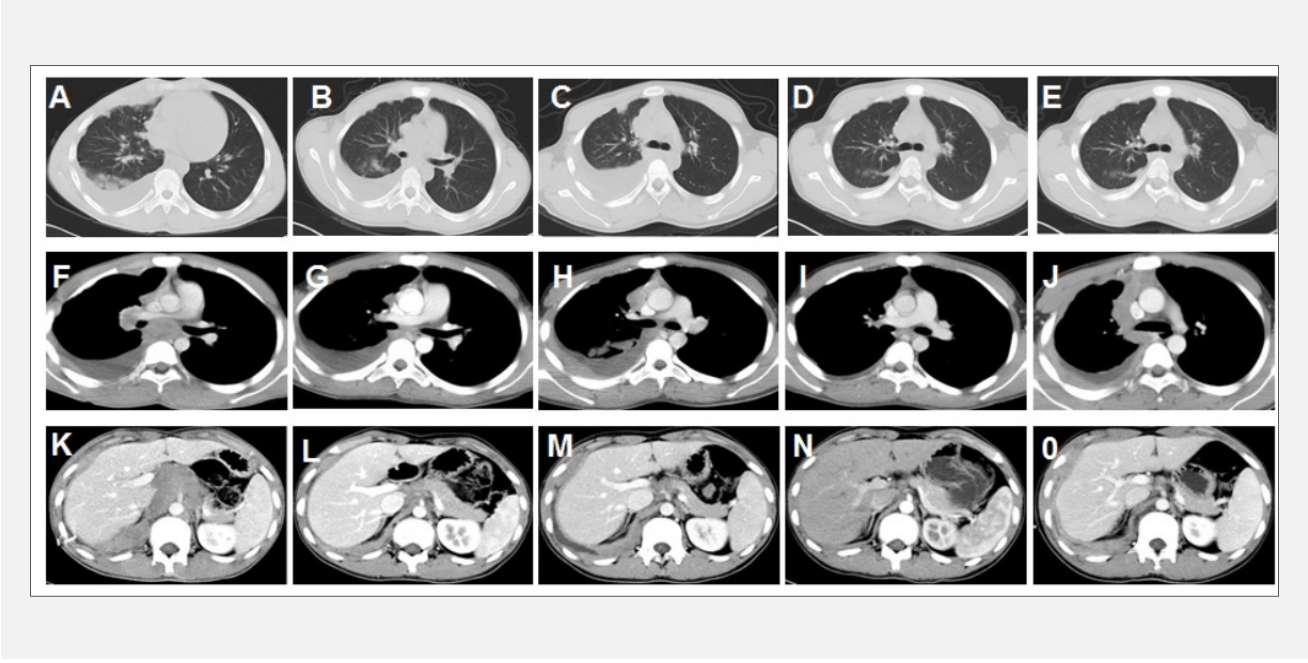


Figure 2. Chest and upper abdominal CT scan of the patient.

A, F, K, before chemotherapy (September 19, 2015). B, G, L, after two cycles of first-line chemotherapy (November 10, 2015). C, H, M, after four cycles of first-line chemotherapy (January 04, 2016). D, I, N, after four cycles of second-line chemotherapy (May 11, 2016). E, J, O, before third-line chemotherapy (June 07, 2016).

CASE PRESENTATION

We report a rare case of pleural ARMS in a seventeen-year-old boy, referred with dyspnea for two weeks. Chest computed tomography (CT) revealed a right-sided pleural effusion and extensive thickening of the pleura accompanied by nodular changes. Thoracic effusion was drained, and formalin-fixed cell block was prepared for pathological diagnosis that revealed a malignant tumor. The biopsy specimen from the pleura showed ARMS (Figure 1) and IHC markers as follows: CK5/6 (-), CK7 (-), EMA (-), TTF-1(-), P63 (-), HBME-1 (-), HMB45 (-), Melan-A (-), MG (-), MyoD1 (-), Myogenin (+), S-100 (-), Syn (-),CHG-A/CGA (-), NF (-), NSE (-), WT-1 (+), Vim (+), Des (+), D2-40 (-), CR/Calretinin (-), CD34 (-), CD99 (-), and FLI-1 (-). PAX3-FKHR fusion protein is positive and the PAX7-FKHR fusion protein is negative (Figure 1, Figure S1) as detected by fluorescence in situ hybridization (FISH) in the biopsy specimen from pleura. The chest and upper abdominal CT after drainage of thoracic effusion revealed that right-sided thoracic effusion was accompanied by extensive thickening of the pleura. This phenomenon was observed in combination with nodular changes, enlarged right hilar and mediastinal lymph nodes, right lower pulmonary nodule, and retroperitoneal lymph nodes (Figure 2A). The whole-body bone scintigraphy revealed no bone metastasis; also, brain magnetic resonance showed no brain metastasis. The patient received two cycles of Gemcitabine coupled with Cisplatin, and the disease was stabilized (Figure 2B). Subsequently, another two cycles of Gemcitabine with Cisplatin were administered, followed by Bevacizumab two times through thoracic perfusion. After completing four cycles of chemotherapy, the disease progressed (Figure 2C). Two cycles chemotherapy using Ifosfamide, Mesna, Epirubicin, and Dacarbazine were administered, after which, grade IV leucopenia and thrombocytopenia appeared. The chemotherapy regimen was adjusted to Epirubicin combined with Dacarbazine for another two cycles, and partial response was achieved (Figure 2D). After one month, the disease progressed again (Figure 2E). The patient died 17 months after pathological diagnosis. The sequence of anti-cancer treatments is summarized in Table 1. This case report was approved by the Medical Ethical Committee of Zhejiang Cancer Hospital. The patient and his father as legally authorized representative signed the informed consent for publication of this case report and accompanying images.

DISCUSSION

ARMS is an aggressive malignant soft tissue tumor that arises from primitive striated muscle cells known as rhabdomyoblasts. ARMS shows poor prognosis and has limited therapeutic options. Primary pulmonary ARMS is very rare. Noda et al. reported a 22-month-old boy with ARMS of the lung responding to chemotherapy and radiotherapy [4]. Almberger et al. report a primary thoracic ARMS in a girl. It is difficult to confirm ARMS, and molecular examination is helpful [5]. Histologic examination of a needle biopsy specimen from a mass above the diaphragm confirmed the diagnosis of rhabdomyosarcoma, and molecular examination revealed a PAX3-FKHR fusion transcript specific to the ARMS [6]. We report a very rare case of pleural ARMS. Myogenin, an extremely reliable and specific marker for rhabdomyoblast differentiation and a useful marker in the differential diagnosis of rhabdomyosarcomas from other malignant small round cell tumors, belongs to a group of myogenic regulatory proteins whose expression determines commitment and differentiation of primitive mesenchymal cells into skeletal muscle. In ARMS, the majority of tumor cells (75 - 100%) were positive for myogenin, while those positive for ERMS ranged from rare to 25% [7]. Myogenin expression was found to be positive in our patient. FKHR-disrupting translocations are specific for ARMS. PAX3-FKHR and PAX7-FKHR fusion transcripts were detected in 55% and 22% of ARMS patients, respectively [8]. In our patient, the PAX3-FKHR fusion protein was positive and PAX7-FKHR fusion protein negative. The fusion status was not associated with outcome differences in patients with locoregional ARMS while there was a striking difference in the outcome between PAX7-FKHR and PAX3-FKHR in patients with metastatic ARMS [9]. PAX7-FKHR ARMS is associated with a remarkable long event-free survival. An extensive cell cycle dysregulation may contribute to poorer prognosis in patients with ARMS that exhibit PAX3-FKHR fusion [9]. In this patient, the tumor was not sensitive to chemotherapy and the patient only lived for 17 months.

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Declaration of Interest:
All authors declare that they have no conflicts of interest.

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Supplementary Figure.

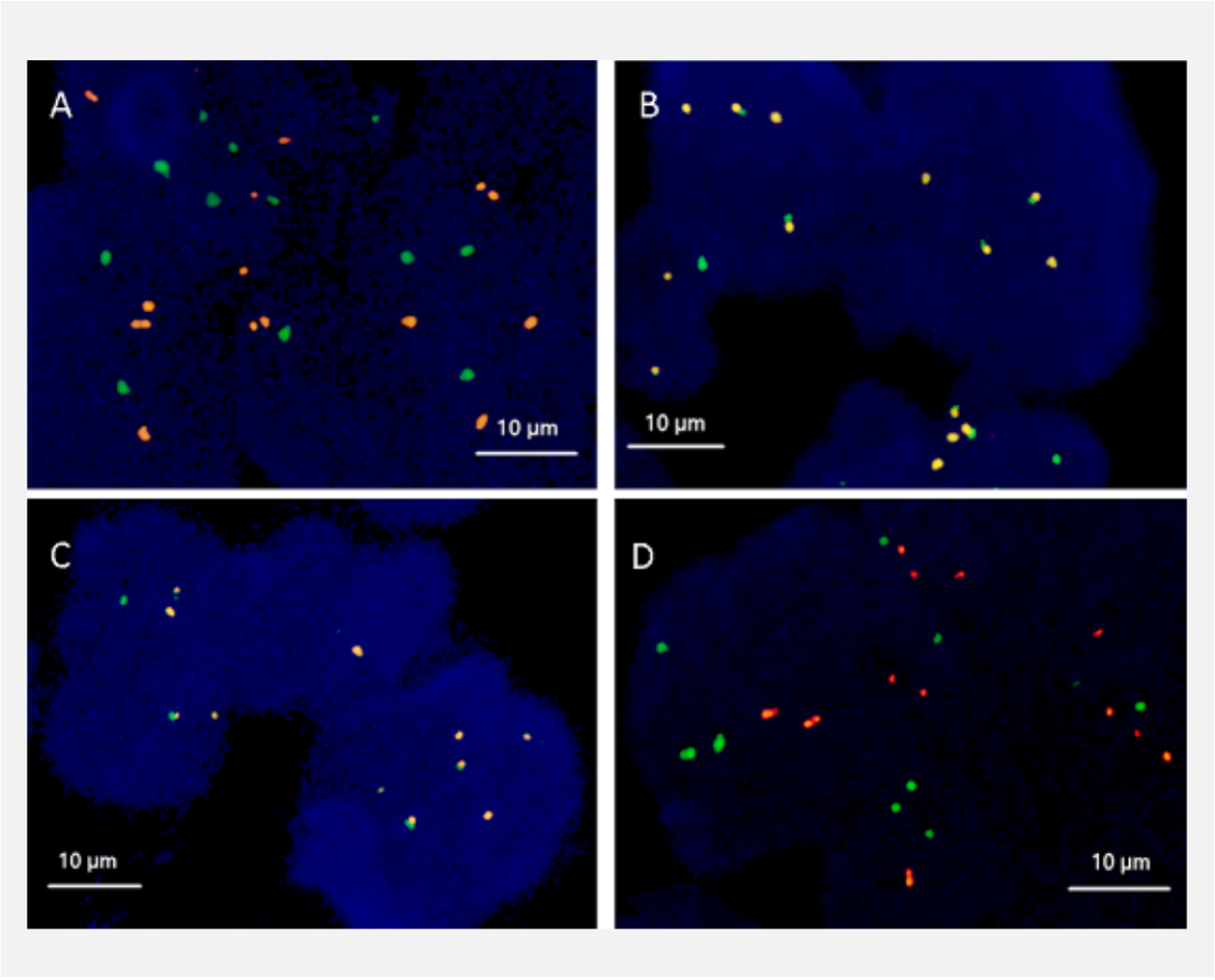


Figure 1. Control of PAX3 and PAX7 by FISH detection.

The SPEC FKHR/PAX3 Dual Color Single Fusion Probe is a mixture of two direct labeled probes hybridizing to the 2q36.1 and 13q14.11 band. The green fluorochrome direct labeled probe hybridizes distal to the PAX3 gene at 2q36.1, the orange fluorochrome direct labeled probe hybridizes proximal to the FKHR gene at 13q14.11. The SPEC FKHR/PAX7 Dual Color Single Fusion Probe is a mixture of two direct labeled probes hybridizing to the 1p36.13 and 13q14.11 band. The green fluorochrome direct labeled probe hybridizes distal to the PAX7 gene at 1p36.13, the orange fluorochrome direct labeled probe hybridizes proximal to the FKHR gene at 13q14.11. Tumor samples were considered positive for FKHR/PAX3 or FKHR/PAX7 fusion results if more than 30% of 100 nuclei showed fusion of orange signals and green signals. A total of 100 tumor nuclei were submitted for analysis. (A) PAX3 negative control; (B) PAX3 positive control; (C) PAX7 positive control; (D) PAX7 negative control.