A Case Report of a New Emerging Subtype of Rhabdomyosarcoma : Epithelioid and Spindle Cell Variant with Aggressive Behavior

นพพล ชาติอุดมพันธ์, พ.บ.
Noppon Chad-Udompan, M.D.

Abstract

Rhabdomyosarcoma is a rare malignant mesenchymal neoplasm characterized by immature skeletal muscle differentiation. Among its various subtypes, the newly emerging epithelioid and spindle cell rhabdomyosarcoma represents a rare and distinct entity with unique histopathological, immunohistochemical, and molecular features. This case report highlights a 21-year-old male patient diagnosed with this rare subtype, emphasizing the pathological findings, differential diagnosis, prognosis, and potential therapeutic implications.

Introduction

Rhabdomyosarcoma (RMS) is a highly malignant tumor arising from mesenchymal tissues and characterized by skeletal muscle differentiation. RMS subtypes include embryonal, alveolar, pleomorphic, spindle cell/sclerosing rhabdomyosarcoma and ectomesenchymoma.[1] The newly emerging epithelioid and spindle cell variant, first described in 2018 by Watson and colleagues[2,4,] has unique histopathological and molecular characteristics. This subtype exhibits an aggressive prognosis, necessitating precise diagnosis to guide treatment.

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กลุ่มงานพยาธิวิทยากายวิภาค โรงพยาบาลสวรรค์ประชารักษ์
จังหวัดนครสวรรค์
Department of Anatomic pathology, Sawanpracharak Hospital, Nakhonsawan

Corresponding Author: นพพล ชาติอุดมพันธ์
กลุ่มงานพยาธิวิทยากายวิภาค โรงพยาบาลสวรรค์ประชารักษ์
จังหวัดนครสวรรค์
Email: noppon.chad@gmail.com
doi: .....

Case Presentation

A 21-year-old Thai male, weighing 48 kilograms and measuring 161 cm in height, presented with a mass on the left side of the tongue that had persisted for 5 months. A computed tomography (CT) scan revealed an ill-defined border, iso-enhancing lesion with faint rim enhancement involving the left lateral part of the tongue, measuring 1.3 × 2.3 × 2.4 cm. (Fig. 1A) Abnormal regional lymph nodes were also noted.

The mass was excised and sent for histopathological examination, which revealed a soft tissue mass measuring 3 cm. The tumor exhibited poorly cohesive to dyscohesive infiltrative neoplastic cells (Fig. 1B), comprising predominantly epithelioid cells (Fig. 1C) and some spindle cells (Fig 1D). Epithelioid cells demonstrated prominent pleomorphism, nucleoli, and abundant eosinophilic cytoplasm, while spindle cells showed hyperchromatic nuclei and eosinophilic cytoplasm. Eleven mitotic figures were observed in 10 high-power fields (two square millimeters), with no tumor necrosis.

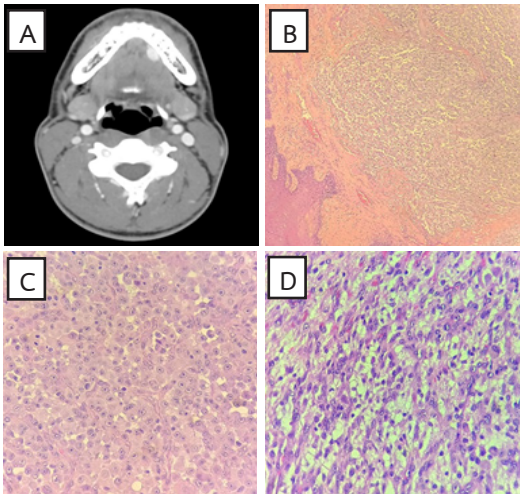

Fig 1. Epithelioid and spindle cell rhabdomyosarcoma. (A) CT shows an iso-enhancing lesion in the left lateral tongue. (B) Infiltrative tumor cells (H&E, 100x). (C) Epithelioid morphology (H&E, 400x). (D) Spindle cell morphology (H&E, 400x).

Immunohistochemistry results showed positivity for vimentin, smooth muscle actin, desmin (Fig. 2A), myogenin (Fig. 2B), myoD1 (Fig. 2C), and ALK protein (Fig. 2D). Focal positivity for EMA was noted, while markers such as caldesmon, CD31, CD34, AE1/AE3, CD45, CD3, CD20, CD30, S100, and HMB45 were negative. Based on these findings, the diagnosis was epithelioid and spindle cell rhabdomyosarcoma.

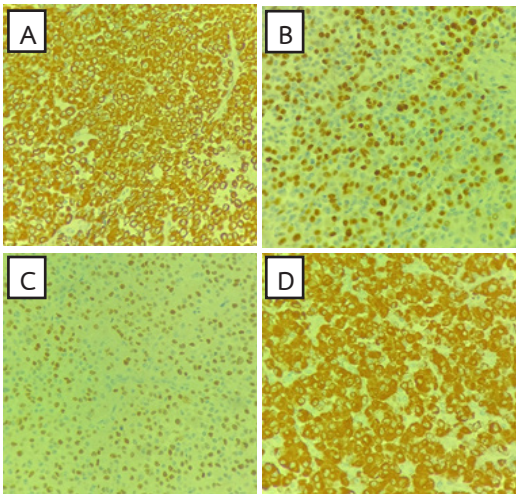

Fig 2. Immunohistochemical findings of epithelioid and spindle cell rhabdomyosarcoma: Tumor cells are positive for desmin (A, 400x), myogenin (B, 400x), myoD1 (C, 400x), and ALK (D, 400x).

Five months after marginal tumor resection, a follow-up magnetic resonance imaging (MRI) scan suggested possible recurrence. The surgeon recommended re-excision, but the patient declined. They consulted an oncologist and initially planned to undergo definitive chemotherapy (vincristine, doxorubicin, cyclophosphamide) and radiotherapy. However, the patient later requested a transfer to a university hospital for continued treatment. He now undergoes CT scans every six months for follow-up.

Discussion

Epithelioid and spindle cell rhabdomyosarcoma, first reported in 2018[2], is characterized by specific histomorphological and molecular features. Unlike the pure epithelioid subtype, which primarily affects older patients (average age 55 years), the epithelioid and spindle cell variant affects younger individuals (average age 27 years). Common tumor locations include the head and neck region, involving both soft tissues and bone.[4,7]

Histopathologically, this subtype demonstrates diffuse infiltration by epithelioid and spindle cells, as seen in our case. The proportion of these two populations can vary. Immunohistochemistry reveals co-expression of skeletal muscle markers (desmin, myogenin, myoD1) and ALK positivity.

By molecular feature, this subtype is associated with TFCP2 rearrangement, often involving gene fusions such as FUS-TFCP2 or FET-TFCP2.[3,4] A 2019 study tested for TFCP2 rearrangement in other RMS subtypes and neoplasms with rhabdomyosarcomatous differentiation yielded negative results. This unique molecular profile highlights the importance of TFCP2 rearrangement as a specific feature of epithelioid and spindle cell rhabdomyosarcoma.[3] Although there is overexpression of ALK protein immunohistochemically, no ALK rearrangement is detected by FISH.[3,4]

Differential Diagnosis

Given the atypical histopathologic features for rhabdomyosarcoma, this disease may be initially approached differently. Differential diagnoses include:

- Inflammatory myofibroblastic tumor: Composed of spindle, stellate, or ganglion-like tumor cells that are positive for ALK but negative for skeletal muscle markers.
- Epithelioid inflammatory myofibroblastic sarcoma: Predominantly composed of large epithelioid cells with vesicular nuclei, prominent nucleoli, and amphophilic cytoplasm. These tumors are positive for ALK with variable desmin positivity but negative for myogenin.
- Proliferative fasciitis and myositis: Characterized by rhabdoid morphology or large ganglion-like cells with round vesicular nuclei, but negative for skeletal muscle markers.
- Proximal-type epithelioid sarcoma: Contains rhabdoid tumor cells and is commonly found in the trunk, hip, and buttock. It is positive for epithelial markers but negative for skeletal muscle markers.
- Malignant melanoma with rhabdomyosarcomatous differentiation: May exhibit similar morphology but is positive for melanoma markers.[4]

The key to accurate diagnosis is incorporating an immunohistochemical panel targeting skeletal muscle differentiation markers.

The prognosis for this subtype is extraordinarily poor, with a median survival time of 17 months, compared to 65 months for pure spindle cell rhabdomyosarcoma.[4,5]

Recent studies on the spindle cell/sclerosing subtype of rhabdomyosarcoma have identified: VGLL2/NCOA2/CITED2 rearrangement[1,8], MYOD1 mutation[1,9] and TFCP2/NCOA2 rearrangement[1,10,11]. The latter is specifically associated with intraosseous spindle cell rhabdomyosarcoma. As more cases of epithelioid and spindle cell rhabdomyosarcoma are reported, further research and potential revisions to the classification of rhabdomyosarcoma—incorporating both epithelioid and spindle cell features—are expected to emerge.

Conclusion

RMS is an aggressive malignant neoplasm. The atypical histopathologic features could mislead diagnoses away from RMS. Recognizing this emerging subtype can enable proper treatment and improve patient survival.

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