Med & Health Jun 2019; 14(1): 228-233 https://doi.org/10.17576/MH.2019.1401.22

CASE REPORT

Alveolar Rhabdomyosarcoma of the Neck in a Two-Months-Old Baby: Diagnostic Challenges

NORDASHIMA AS[1], AZYANI Y[1], AMIZATUL AINI S[1], BOEKHREN KB[2], PATHMANATHAN R[3], HAMIDAH A[2]

[1]Department of Pathology, [2]Department of Paediatrics , Faculty of Medicine, Universiti Kebangsaan Malaysia Medical Centre, Jalan Yaacob Latif, Bandar Tun Razak, 56000 Cheras, Kuala Lumpur, Malaysia.
[3]Subang Jaya Medical Centre, 1, Jalan SS 12/1A Subang Jaya 47500 Selangor Darul Ehsan Malaysia.

ABSTRAK

Rabdomiosarkoma (RMS) adalah sejenis sarkoma yang biasa terdapat pada kanak-kanak dan remaja. Penyakit ini jarang berlaku pada bayi dan menimbulkan kesukaran dari segi diagnosis dan perawatan selanjutnya. Di sini, kami ingin membentangkan kes seorang bayi yang didiagnosa sebagai rabdomiosarkoma alveolar yang agresif. Bayi tersebut mengalami kebengkakkan di leher yang melibatkan tulang belakang dan saraf neurogenik. Pemeriksaan tisu histopatologi mendedahkan tumor sel berbentuk bulat dan primitif tanpa pembezaan rabdoid. Berdasarkan simptom klinikal dan neurologi, lokasi tumor dan histopatologi mencadangkan penyakit neuroblastoma pada awalnya. Walau bagaimanapun, pemeriksaan lanjut menunjukkan sel tumor adalah positif kepada desmin dan mempamerkan nuklear immunoreaktiviti kepada MyoD1 dan miogenin, yang menyokong diagnosis rhabdomyosarkoma. Fluorescent in situ hibridisasi mengesahkan terdapat translokasi t(2;13)(q35;q14) dan mengesahkan diagnosis rabdomiosarkoma alveolar. Pesakit menjalani kemoterapi tetapi meninggal dunia selepas dua bulan kerana kejutan septik. Rabdomiosarkoma adalah tumor yang amat agresif dan boleh membawa kesukaran dari segi diagnostik. Kes ini menunjukkan kajian molekular adalah amat penting dalam membuat diagnosis yang tepat agar kemoterapi yang sesuai dapat dimulakan.

Kata kunci: alveolar, bayi, FISH, rabdomiosarkoma

ABSTRACT

Address for correspondence and reprint requests: Dr. Nordashima Abd Shukor. Department of Pathology, Faculty of Medicine, Universiti Kebangsaan Malaysia Medical Centre, Jalan Yaacob Latif, Bandar Tun Razak, 56000 Cheras, Kuala Lumpur, Malaysia. Tel: +603-9145 5365 Email: nordashima@ppukm.ukm.edu.my

Rhabdomyosarcoma (RMS) is the most common soft tissue malignancy in children and adolescents. The rarity of its occurrence in infant poses a great difficulty in terms of diagnosis and management. Here, we report an aggressive case of alveolar rhabdomyosarcoma in an infant who presented with neck swelling and neurological complications. The Magnetic Resonance Imaging (MRI) revealed a soft tissue swelling of the neck with intraspinal extension and spinal cord compression, raising the possibility of a neurogenic or malignant nerve sheath tumour. Histopathological examination revealed a primitive, small round cell tumour with no rhabdoid differentiation. The clinical presentation, neurological symptoms, tumor location and the histopathologic features were highly suggestive of neuroblastoma. However, the tumour cells were positive for desmin with focal and weak nuclear positivity for myogenin and MyoD1; immunoexpressions which were in favour of rhabdomyosarcoma. Fluorescent in situ hybridization (FISH) confirmed the presence of a translocation t(2;13)(q35;q14), supporting the diagnosis of alveolar rhabdomyosarcoma. Despite chemotherapy, patient succumbed to death after two months due to septic shock. Rhabdomyosarcoma is highly aggressive mesenchymal neoplasm which may present with diagnostic difficulty. This case highlights the importance of molecular studies in making an accurate diagnosis so that appropriate chemotherapy may be instituted.

Keywords: alveolar, FISH, infant, rhabdomyosarcoma

INTRODUCTION

Rhabdomyosarcoma (RMS), constitute a distinctive group of malignant tumours that share a tendency to undergo myogenesis (Parham et al. 2006). It is recognized as childhood and young adolescent malignancy. RMS is most frequently encountered soft tissue sarcoma in infant and children (Vankalakunti et al. 2006). It occurs in any sites of anatomical location where there is skeletal muscle differentiation present (Chu 2013). The vast majority of RMS occurs in head and neck region, extremities, genitourinary system and trunk. RMS bears variable histological pattern including poorly differentiated tumours that are very difficult to diagnose without the help of immunohistochemical or molecular study. RMS have distinct clinical, pathologic and molecular differences which varies in clinical outcome and approach to therapy. The most prevalent subtype is embryonal rhabdomyosarcoma (ERMS) accounting for about 60% of RMS cases. It occurs mainly in children younger than 10 years associated with a favourable prognosis (Marshall et al. 2012). The alveolar subtype (ARMS) constitutes another 20% of RMS cases and occurs predominantly in adolescents (Marshall et al. 2012). ARMS are more aggressive with poorer prognosis.

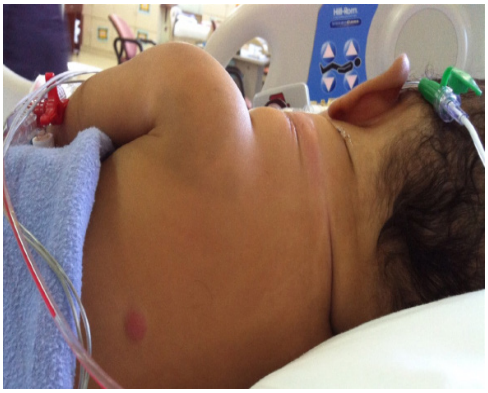

Figure 1: Hard and lobulated mass at the left neck measuring 10 x 5 cm

CASE REPORT

A 2-month-old girl presented with history of reduced left hand movement and progressive swelling of left neck region for two weeks associated with partial ptosis of the left eye. Physical examination revealed a hard and lobulated mass at the left neck measuring 10 x 5 cm (Figure 1). There was presence of left Horner syndrome and lower motor neuron symptoms of the left upper limb. An urgent magnetic resonance image (MRI) of the neck and thorax showed a soft tissue mass at the left neck which was homogenous and multilobulated, extending from C2 to T5 vertebral body. Multiple enlarged lymph nodes at the left axillary region were detected. The mass showed intraspinal extension and spinal cord compression, thus raising the possibility of a neurogenic or malignant nerve sheath tumour.

Histopathological examination of the biopsy of the mass revealed a primitive, small round cell tumour with no rhabdoid differentiation (Figure 2A). Based on the tumour morphology, the differential diagnoses include rhabdomyosarcoma, lymphoma, neuroblastoma and epithelial tumour. The tumour cells were positive for desmin with focal and weak nuclear

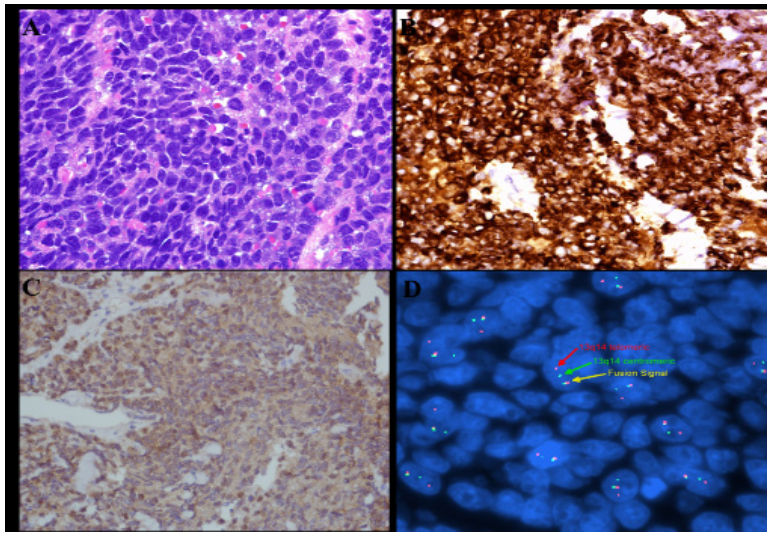

Figure 2: (A) Sheets of poorly differentiated tumour cells (H&Ex400) showing positive immunostaining for (B) desmin; x400; (C) MyoD1 expression of weak nuclear positivity with cytoplasmic,non-specific background staining; (D) FISH analysis shows abnormal cells with one green, one orange and one fusion signal pattern.

positivity for myogenin and MyoD1 (Figure 2B & 2C). S100, chromogranin, neuron-specific enolase (NSE), synaptophysin, vimentin, pan-cytokeratin and leucocyte common antigen (LCA) were negative. Ki67 proliferative index was high (90%). The immunohistochemical studies were in favour of rhabdomyosarcoma. Further confirmation by fluorescent in situ hybridization (FISH) showed presence of translocation t(2;13) (q35;q14), thus supporting the diagnosis of alveolar rhabdomyosarcoma (Figure 2D).

The patient's condition rapidly deteriorated and had to be ventilated. Chemotherapy MT95 protocol (Strategy 953 (ARM B)) was commenced consisting of intravenous fosfamide, vincristine and actinomycin D. Unfortunately, the patient developed severe neutropenic sepsis and succumbed from septic shock.

DISCUSSION

The presenting signs and symptoms of RMS are variable and depending on the sites of origin of the primary tumour (Dagher & Helman 1999). The common sites include the head and neck, gastrointestinal, urinary tracts and the extremities (Parham et al. 2006). Head and neck RMS can arise from the orbit, parameningeal sites, scalp, parotid glands, oral cavity, pharynx, thyroid, parathyroid glands and neck region. There are two distinct types of RMS, namely the embryonal and the alveolar subtypes. The diagnosis of ARMS is considered when the histopathologic examination of the tumor tissue shows undifferentiated small round blue tumor cells lining up the spaces reminiscent of pulmonary alveoli. RMS may display cross-striation which is characteristic of skeletal or rhabdomyoblast differentiation (Dagher & Helman 1999). Ancillary studies that include a panel of immunohistochemical staining need to be carried out in diagnosing RMS (Parham et al. 2006). Muscle specific protein markers such as alpha-actin, myogenin, myosin, desmin, myoglobin, Z-band protein and Myo-D are very useful (Dagher & Helman 1999). In difficult cases, additional molecular study is important to confirm the diagnosis and subtypes of RMS. The majority of ARMS tumours carry a characteristic chromosomal translocations of t(2;13) (q35;q14) (Marshall et al. 2012). This chromosomal translocations produce an oncogenic (PAX3-FOX01) fusion protein and can be detected in 55% of ARMS cases. Another 22% of ARMS cases exhibit translocation of t(1;13) (p36;q14) with characteristic (PAX7-FOX01) fusion oncogene proteins (Marshall et al. 2012).

In cases of small round blue cell tumors of the head and neck, several differential diagnoses need to be considered, which include Ewing sarcoma/PNET, neuroblastoma and lymphoma (Reshma et al. 2013). Ewing sarcoma is group of highly malignant small round cells characterized by monotonous round blue cell tumour. It is common in children and young adult. Immunohistochemistry studies will show tumour cells positivity for CD99 and FLI-1expression.

Cytogenetic studies exhibit *EWSR-ETS* fusions. It involves the *EWS* gene which also known as *EWSR1* located on chromosome 22 and a member of ETS family including *FLI1* and *ERG* (Pinto et al. 2011).

Neuroblastoma of head and neck is the second most common tumour after rhabdomyosarcoma. It can manifest as extracranial soft tissue tumour in infant less than 12 months (Sameer et al. 2017). The tumor originates from primitive neuroectodermal cells derived from neural crest cells. Histologically, it exhibits small round cells with features of neural or ganglionic cells depending on maturation and differentiation. Immunohistochemical studies show positivity for neuron specific enolase, synaptophysin and chromogranin (Reshma et al. 2013). Common lymphoma in paediatric patients include lymphoblastic lymphoma and Burkitt lymphoma and the immunohistochemistry studies performed, shows positivity for lymphoid markers. Thus, immunohistochemistry is very crucial in diagnosis of small round blue cell tumors to help reach to the specific diagnosis. Failure to give a specific diagnosis leads to different treatment modalities.

As seen in the current case, alveolar rhabdomyosarcoma behaves aggressively. It is prone to metastasis and carries poor prognosis. Management of RMS requires multimodality therapeutic approach including surgery, chemotherapy and radiotherapy (El Nadi et al. 2013). Many authors agree that management of infant less than one year should be a tailored therapeutic approach. The prognosis of RMS depends on the grade of the tumour, age, type of resection, histology, translocation and number of sites with metastases (Eguía-Aguilar et al. 2016). The prognosis is less favourable due to the physiologic immaturity of many organ systems in infants (Pinto et al. 2003).

CONCLUSION

Rhabdomyosarcoma is a highly aggressive mesenchymal neoplasm which may present with diagnostic difficulty. Correlation with clinical, radiological and histopathological examination along with immunohistochemical and molecular study are crucial for accurate diagnosis and appropriate chemotherapy.

REFERENCES

Chu, W.P. 2013. Anterior mediastinal alveolar rhabdomyosarcoma in an infant: rare site for a common paediatric tumour. *Hong Kong Med J* **19**(5): 458-9.

Dagher, R., Helman, L. 1999. Rhabdomyosarcoma: An overview. *Oncologist* **4**(1): 34-44.

Eguía-Aguilar, P., López-Martínez, B., Retana-Contreras, C., Perezpena-Diazconti, M. 2016. Alveolar rhabdomyosarcoma: origin and prognostic implications from molecular findings. *Bol Med Hosp Infant Mex* **73**(6): 405-10.

El Nadi, E., Moussa, E. A., Zekri, W., Taha, H., Yones, A., Zaghloul, M. S., El Wakeel, M., Labib, R. M. 2013. Outcome of rhabdomyosarcoma in first year of life: children's cancer hospital 57357 Egypt. *Sarcoma* 2013: 439213.

Marshall, A.D., Grosveld, G.C. 2012. Alveolar rhabdomyosarcoma-the molecular drivers of PAX3/7-FOXO1-induced tumorigenesis. *Skelet Muscle* **2**(1): 25.

Parham, D.M., Ellison, D. 2006. Rhabdomyosarcomas in adults and children: an update. *Arch Pathol Lab Med* **130**(1): 1454-65.

Pinto, A., Dickman, P., Parham, D. 2011. Pathobiologic markers of the ewing sarcoma

family of tumors: state of the art and prediction of behaviour. *Sarcoma* **2011**: 856190.

Reshma, V., Kavita, R., Priya, N.S., Umadevi, H.S., Mohsin, G., Sreelatha, H. 2013. Small round cell tumor of the head and neck region: a review. *Int J Oral Maxillofac Pathol* **4**(2): 24-33.

Sameer, A., Omar, K., Manalang, M., Weatherly, R. 2017. Clinical manisfestations of neuroblastoma with head and neck involving in children. *Int J Pediatr Otorhinolaryngol* **97**(2017): 157-62.

Vankalakunti, M., Das, A., Rao, N.K. 2006. Postauricular congenital alveolar rhabdomyosarcoma - a case report of an unusual entity. *Diagn Pathol* **1:** 37.

Received: 30 Jul 2018
Accepted: 7 Mar 2019