

Rhabdomyosarcoma with Bone Marrow Infiltration: A Diagnostic Dilemma

R Khanna, D M, S Belurkar, C Manohar, S Ray, P Srilatha, N Suvarna

Citation

R Khanna, D M, S Belurkar, C Manohar, S Ray, P Srilatha, N Suvarna. *Rhabdomyosarcoma with Bone Marrow Infiltration: A Diagnostic Dilemma*. The Internet Journal of Oncology. 2012 Volume 8 Number 2.

Abstract

Rhabdomyosarcoma is the most common soft tissue sarcoma in children and adolescents. In adults, the prevalence is much lower. Most patients present with a mass in the head and neck region, urogenital region or even with distal extremity involvement. A bone marrow infiltration at the time of clinical presentation has also been documented in literature. But a simultaneous marrow infiltration can simulate a hematopoietic neoplasm, leading to diagnostic errors. We document one such challenging case of a 47 year old male patient presenting with bicytopenia. Patient was hospitalized following a referral due to a mass in the left cheek, diagnosed earlier as clear cell sarcoma. Bone marrow aspirates yielded a dry tap, with sinusoidal blood and both the aspirate as well as the imprint smear showed pleomorphic cells with vacuolated cytoplasm. The corresponding trephine biopsy showed diffuse and interstitial infiltrates of rhabdoid cells with focal areas of infarct. Considering the morphological details, a diagnosis of rhabdomyosarcoma was rendered after ruling out other possibilities. A review of the lesional biopsy with ancillary techniques eventually corroborated the bone marrow diagnosis.

INTRODUCTION

Rhabdomyosarcoma (RMS) stands as the most common soft tissue sarcoma in children younger than 15 years¹. In adults, the incidence is much lower after the age of 45 with various studies showing an average prevalence of 2-5%¹. It is presumed to arise from a primitive mesenteric cell rest committed to the skeletal muscle differentiation². According to the World Health Organization³ classification, there are three subtypes in order of prevalence: embryonal, alveolar and pleomorphic. While the embryonal RMS is most often seen in the head and neck region, the other two are reported in the distal extremities. Regardless of the subtype, the tumor is notorious to disseminate widely at the time of clinical presentation. The most common sites of metastases include lungs, lymph nodes and bone marrow¹. The bone marrow involvement is seen in about 30% of cases of metastasis⁴. Etcubanas et al⁵ reported a series of 10 cases of metastatic rhabdomyosarcoma, in which an extensive search for the primary was futile. They explained the cytological details and the difficulties in making a diagnosis in such cases, without assessing the involvement of bone marrow. More recently, Reid and colleagues⁶ in their paper shed light on the histological features of RMS infiltrating the bone marrow. Since then, frequent case reports have followed. Although ancillary techniques have certainly enhanced the

diagnostic precision, the morphological overlap with other hematopoietic neoplasms has puzzled many pathologists.

We report a case of alveolar rhabdomyosarcoma infiltrating the bone marrow at the time of clinical presentation.

CASE REPORT

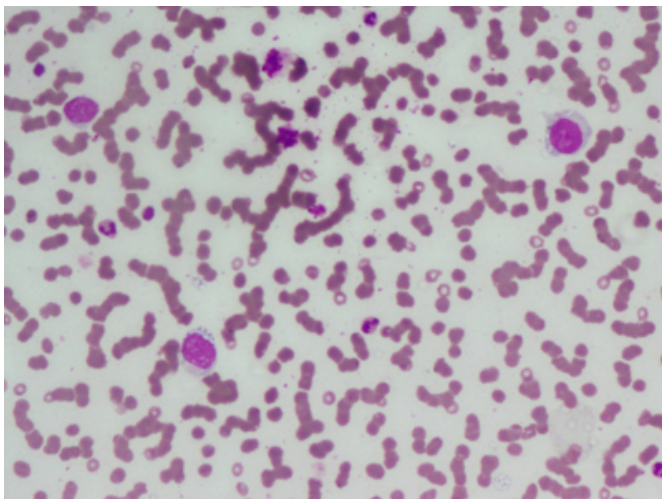
A 47 year old male patient, laborer by occupation was referred to our hospital with a diagnosis of clear cell sarcoma of the oral cavity, which was diagnosed elsewhere. He complained of generalized body ache, loss of appetite and significant weight loss. He also provided history of pain during chewing and a disturbing cough. Per oral examination revealed a 2x1 cm swelling in the left buccal mucosa with overlying ulceration. Further examination showed multiple level 1 lymph nodes in the left side. Following hospitalization, the hematological investigations comprising of complete hemogram and a peripheral smear examination revealed a bicytopenic profile with anemia and thrombocytopenia. Occasional nucleated red blood cells were also seen in the smear. A bone marrow study was requested to elucidate the reason for bicytopenia and a possible infiltration.

Meanwhile, radiological investigations (CT scan) revealed few ill defined nodules in both lungs with minimal pleural

effusion, suggesting either a neoplastic or an infective aetiology. Further, CECT scans also revealed multiple homogeneously enhancing paravertebral soft tissue masses extending into the spinal canal. A possibility of neurofibroma was also suggested. The bone marrow aspirates studied, yielded a dry tap. However, an analysis of the sinusoidal blood and the accompanying imprint smear revealed several abnormal cells dispersed singly. Higher magnification demonstrated pleomorphic features comprising of moderate to abundant vacuolated cytoplasm, round to oval hyperchromatic nucleus with prominent nucleoli (Fig.1). Binucleate and multinucleated forms were also noted. Interspersed areas showed normal marrow elements with scattered lymphoid cells. The tumor cells were negative for routine cytochemical stains. A diagnosis of marrow infiltration by a sarcoma was suggested with an advice to await the ensuing biopsy.

Figure 1

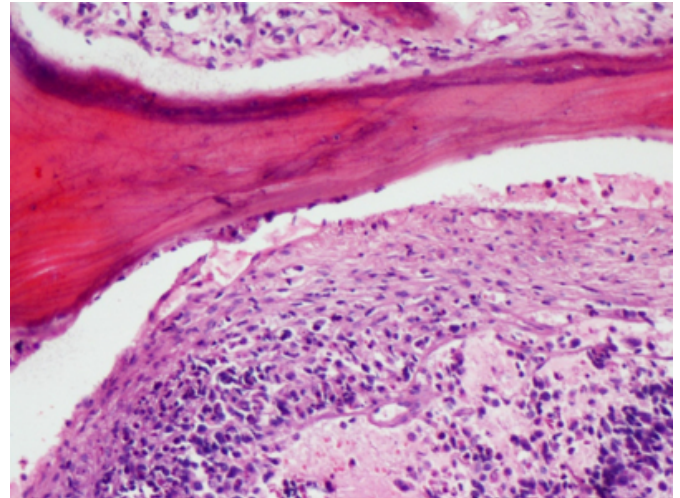
Figure 1: Bone marrow aspirate showing singly dispersed tumor cells



The trephine biopsy showed bony trabeculae enclosing partly cellular and partly fibrosed cellular marrow spaces showing both interstitial and diffuse infiltration by pleomorphic malignant cells (Fig.2). The cells were medium to large, with high N/C ratio, immature nuclear chromatin and prominent nucleoli. Focal areas of infarct were also noted.

Figure 2

Figure 2: Trephine biopsy showing diffuse infiltration by rhabdomyosarcoma



The histopathology slides from the outside laboratory were reviewed and a diagnosis of alveolar rhabdomyosarcoma (solid variant) was rendered. The immunohistochemistry profile done on the blocks from the lesional biopsy showed strong positivity for Desmin while S100 was negative (Fig.3 and Fig.4).

Figure 3

Figure 3: Tumor cells showing positivity for Desmin

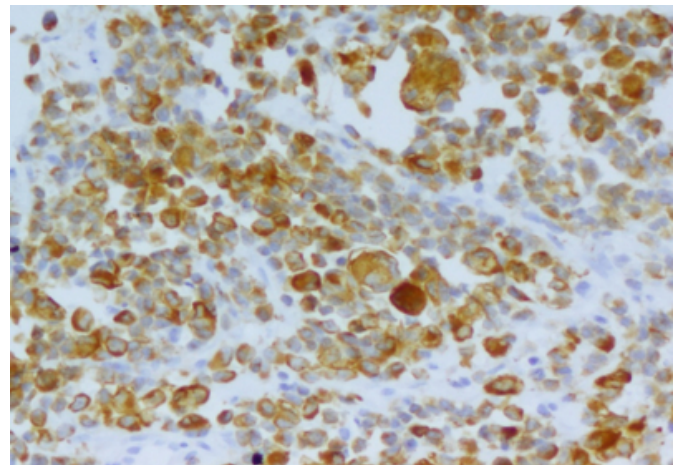
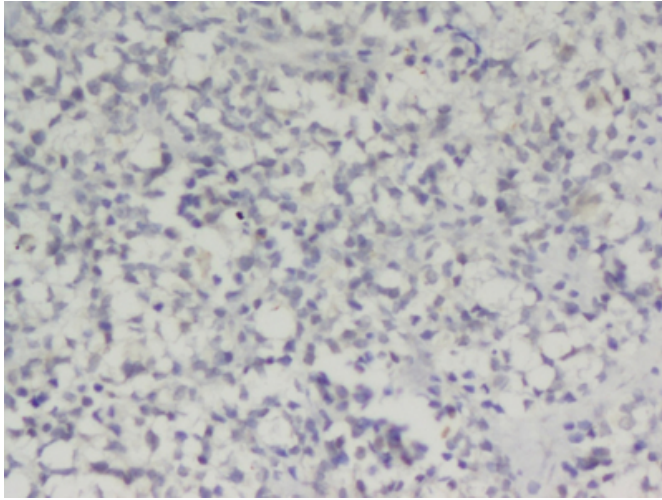


Figure 4

Figure 4: Tumor cells are negative for S100



Considering the above findings, a final diagnosis of marrow infiltration by rhabdomyosarcoma was given. The patient was started on Ifosfamide and Etoposide and was advised follow up. The chemotherapy was complicated with grade III anemia and grade IV thrombocytopenia. Additional packed cell transfusion and GM-CSF support was also provided to tide over the complications. At the time of submitting this article, the patient's progress has been unremarkable.

DISCUSSION

Rhabdomyosarcoma is an aggressive soft tissue malignancy, not uncommonly seen in adults. Its prevalence though, is much lesser after the fifth decade of life. According to the Intergroup Rhabdomyosarcoma Study report, bone marrow involvement is found in about 29% of RMS patients in clinical stage IV (disease dissemination with metastasis)⁴. Our case is unusual in the sense that it was a middle aged patient with simultaneous marrow involvement which led to a diagnostic challenge. Microscopic examination of the bone marrow aspirate in such cases reveals a diffuse infiltrate of blast-like cells with moderate agranular cytoplasm, large round nuclei and prominent nucleoli. The chromatin has often been described as fine, reticulated or slightly clumped, with cytoplasmic vacuolations being consistently found. Other relevant features described include multinucleated cells and tumor cells with hemophagocytic activity⁷. This cytological spectrum has been described in both alveolar and embryonal variants. Alveolar rhabdomyosarcoma has a higher tendency to disseminate than embryonal⁴, which is seen in our case too. Few cases of RMS presenting with only signs and symptoms associated with marrow infiltration

have also been documented, thus simulating a clinical picture of hemoblastosis⁸.

The differential diagnosis includes hematolymphoid neoplasms such as acute leukemia (both myeloid and lymphoblastic) and Non Hodgkin lymphoma. The other cases that have to be ruled out include neuroblastoma, Ewing sarcoma, peripheral neuroectodermal tumor and Wilm's tumor in the pediatric age group. Other rare tumors reported include small cell hepatoblastoma, pancreatoblastoma, small cell desmoplastic tumor and even seminoma⁸.

Additional cytochemistry and immunohistochemical analysis is imperative to reach a conclusive diagnosis of rhabdomyosarcoma. The tumor cells in RMS are negative for myeloid markers (myeloperoxidase and alpha-naphthyl acetate esterase) but positive for PAS⁸. The PAS positivity fails to distinguish RMS from other small round cell neoplasms such as lymphomas and leukemias, which demonstrate a similar reaction. On immunohistochemistry, the RMS phenotype depends on the degree of differentiation with the most primitive tumor cells being positive to vimentin, to be rendered positive for desmin and muscle-specific actin by further differentiation⁸. The best differentiated cells are also positive for myoglobin and myosin³. In the present case, immunohistochemistry was not performed on the bone marrow biopsy as it was done on the blocks available from the lesional biopsy which showed a strong positivity for Desmin and negativity for S-100.

Few reported cases of alveolar rhabdomyosarcoma (solid variant) infiltrating the bone marrow have been documented^{9,10} but the histologic examination of the primary tumor was not demonstrated in these cases. As mentioned earlier, bone marrow involvement by alveolar rhabdomyosarcoma is more common than embryonal. These cases demonstrate t(2;13) translocation as opposed to the more conventional t(1;13) chromosomal translocation¹¹.

CONCLUSION

We report a rare case of bone marrow infiltration by alveolar rhabdomyosarcoma with a primary in the left buccal mucosa. The case is unusual for a couple of reasons: infrequent incidence in this age group and a simultaneous marrow involvement, which is a rare phenomenon. Morphologically also, such cases pose serious diagnostic challenges as one considers a possibility of other small round malignant tumors of the bone marrow. A multidisciplinary approach comprising of histology, immunohistochemistry and electron microscopic studies on

the bone marrow are crucial to achieve the diagnosis of RMS.

References

1. Weiss SW, Goldblum JR. Rhabdomyosarcoma. Enzinger and Weiss's Soft Tissue Tumors, fifth ed. Weiss SW and Goldblum JR (editors), Elsevier, China 2008:595-632.
2. Pappo AS, Shapiro DN, Crist WM et al. Biology and therapy of pediatric rhabdomyosarcoma. *J Clin Oncol* 1995; 13:2123-2139.
3. Parham DM, Barr FG. Alveolar Rhabdomyosarcoma. In: World Health Organization (WHO) Classification of Tumors. Pathology and Genetics of tumors of Soft Tissues and Bone. Fletcher CDM, Unni KK, Mertens F (editors). IARC press. Lyon 2002:150-152.
4. Breneman JC, Lyden E, Pappo AS et al. Prognostic factors and clinical outcomes in children and adolescents with metastatic rhabdomyosarcoma- a report from the Intergroup Rhabdomyosarcoma Study IV. *J Clin Oncol* 2003; 21:78-84.
5. Etcubanas E, Peiper S, Stass S, Green A. Rhabdomyosarcoma, presenting as disseminated malignancy from an unknown primary site: a retrospective study of 10 pediatric cases. *Med Pediatr Oncol* 1989; 17:39-44.
6. Reid MM, Saunders PWG, Bown N, Bradford CR, Maung ZT, Craft AW, Malcolm AJ. Alveolar rhabdomyosarcoma infiltrating bone marrow at presentation: the value to diagnosis of bone marrow trephine biopsy specimen. *J Clin Pathol* 1992; 45:759-762.
7. Huntrakoon M, Callaway LA, Vergara GG. Systemic rhabdomyosarcoma presenting as leukemia: case report with ultrastructural study and reviews. *J Surg Oncol* 1987; 35:259-265.
8. B.Jelic-Puskaric et al. Rhabdomyosarcoma with bone marrow infiltration mimicking hematologic neoplasia. *Coll. Anthropol* 2010; 34(2):635-639.
9. Boman F, Champigneulle J, Schmitt C et al. Clear cell rhabdomyosarcoma. *Pediatr Pathol Lab Med* 1996; 16:951-959.
10. Jani P, Charles C. Ye. Massive bone marrow involvement by clear cell variant of rhabdomyosarcoma. *Indian journal of Pediatrics* 2009; 76:224-228.
11. Barr FG. Molecular genetics and pathogenesis of rhabdomyosarcoma. *J Pediatr Hematol Oncol* 1997; 19:483-491.

Author Information

Ruchee Khanna, MD (Pathology)

Dept. of Pathology, Kasturba Medical College, Manipal University

Deepak Nayak M, MD (Pathology)

Dept. of Pathology, Kasturba Medical College, Manipal University

Sushama V. Belurkar, MD (Pathology)

Dept. of Pathology, Kasturba Medical College, Manipal University

Chethan Manohar, MD (Pathology)

Dept. of Pathology, Kasturba Medical College, Manipal University

Satadru Ray, M.Ch (Surgical Oncology)

Dept. of Surgical Oncology, Kasturba Medical College, Manipal University

P.S. Srilatha, MD (Pathology)

Dept. of Pathology, Melaka Manipal Medical College, Manipal University

Niveditha Suvarna, MD (Pathology)

Dept. of Pathology, Melaka Manipal Medical College, Manipal University