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Rhabdomyosarcoma: Review

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ABSTRACT

Rhabdomyosarcoma (RMS) is a malignant soft tissue tumour of muscle tissue. The alveolar rhabdomyosarcoma in the head and neck has poor prognosis. The solid variant of the alveolar rhabdomyosarcoma can be histopathologically misdiagnosed into other small round cell tumours occurring in childhood. The prognosis depends on timely, apt diagnosis and specific treatment. We discuss the diagnostic difficulties histopathologically and other adjunctive diagnostic techniques for this neoplasm.

Keywords: Rhabdomyosarcoma, small round cell tumours, adjunctive diagnostic techniques

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INTRODUCTION

Rhabdomyosarcoma (RMS) is a malignant soft tissue tumour of myogenic lineage. It is the most common soft tissue sarcoma in children and adolescents representing 6% to 7% of childhood malignancies. WHO has defined rhabdomyosarcoma as a highly malignant tumor of rhabdomyoblasts in varying stages of differentiation with or without cross-striations. Rhabdomyosarcoma was first described by Weber in 1854 [1].

ETIOPATHOGENESIS

They are considered to originate from malignant change of primitive mesenchymal cells rather than differentiated muscle [2]. No specific etiology exists but cytogenetic and molecular studies have identified chromosomal translocations and mutations in oncogenes [1]. MyoD1 and myogenin are considered useful markers for diagnosing rhabdomyosarcomas and also differentiating them from other soft tissue tumors [3]. Alveolar rhabdomyosarcoma has shown a characteristic translocation (2;13)(q35;q14)) fusing the PAX3 gene with the FKHR gene. Treatment accounts for multidisciplinary approach with surgical intervention, multiagent chemotherapy with or without radiotherapy since they can metastasize to bone marrow and bone marrow aspiration should be a part of the staging procedure [4-6].

REVIEW

Rhabdomyosarcoma is a malignant tumor of mesenchymal origin which arises from cells of skeletal muscle lineage**.** It is the most common soft –tissue sarcoma of children with an annual incidence of 4 to 7 per million. Males demonstrate a higher predilection. ARMS accounts for about 15% of all rhabdomyosarcomas. Head and neck RMS clinically presents itself as non-specific or minimal symptoms that of swelling, trismus and parasthesia ultimately leading to delay in diagnosis. Striking clinical features are cranial nerve palsies in parameningeal locations which indicate skull involvement.

Cytology of solid variant of ARMS is almost similar to that of classic. ARMS is a cellular, compact, round cell tumour, high nuclear-cytoplasmic except for occasional spindle cell rhabdomyoblasts. The nuclei are round or oval with distinct smooth, rarely irregular nuclear membrane. The nuclei are larger than that of embryonal RMS and exhibit a coarse chromatin with either several nucleoli or unidentifiable nucleoli**,** the ERMS shows loosely arranged cells tend have oblong shapes, the nuclei are smooth and oval with fine chromatin and inconspicuous nucleoli [7].

TYPES: There are 3 variants of rhabdomyosarcomas:

- **Embryonal variant:** Almost 49% of all rhabdomyosarcomas, seen in children before the age of 10 years. Rarely seen in patients older than 40 years.
- **Alveolar variant:** Accounts for 30% of all rhabdomyosarcomas and is seen in age group between 10-25 years. Preferred site is deep soft tissues of extremities.
- **Pleomorphic variant:** Rare variant arising in adults older than 45 years [4].

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HISTOLOGY

They are mainly composed of small, round densely packed cells, which are arranged around spaces resembling pulmonary alveoli. The solid variant of alveolar rhabdomyosarcoma exhibits small, round densely packed cells without alveolar spaces. It does not have any prognostic value. Alveolar tumors show a distinguished chromosomal translocation marker t(2;13) (q35;q14) [8].

DIAGNOSIS

Intra-oral rhabdomyosarcoma can be detected by antenatal ultrasound which requires an extensive perinatal multidisciplinary team approach. Initially, it is ideal to completely resect the primary tumor with negative gross and microscopic margin. Radiation modality preferred is fractionated high-dose-rate (F–HDR) brachytherapy which achieves excellent local control and disease free survival, in properly selected children with soft tissue sarcomas and preserves the normal bones and organ development [9]. Computed tomography and magnetic resonance imaging are useful in exhibiting the differential diagnosis of cystic lesion of head and neck region occurring in children. They provide additional information about any bony and soft tissue extension of the lesion [10]. The definitive diagnosis is based upon the myogenesis of the tumor which includes giant or multinucleated myoblasts strap or tadpole cells, individual tumor cells and densely eosinophilic cytoplasm. However, rhabdomyosarcoma is mostly poorly differentiated hence its diagnosis is hard to obtain [3]. Histological classification provides a great platform for the prognosis outcome for the patients because botyroid and spindle cell variant projects a fair prognosis while embryonal variant has a better prognosis when compared to alveolar rhabdomyosarcoma. Therefore classification is of utmost importance [11].

TREATMENT

The treatment modalities include surgical intervention, chemo-radiation therapy. Radiation therapy controls the local microscopic or gross residual disease. Systemic radiotherapy plays a vital role in in primary cytoreduction as well as eradication of gross and micrometastatic disease. Recently, evidence suggests that efficacy of etoposide and ifosfamide in rhabdomyosarcoma has been included in its treatment protocol [12]. Despite of an aggressive therapy patients with metastatic disease possess worse prognosis. Topotecan, a camptothecin analog act as an inhibitor of topoisomerase I, are examined worldwide for its effectiveness in rhabdomyosarcoma [13]. The complications caused by these drugs are devastating as they may lead to development of secondary malignant neoplasm. Etoposide are found to be associated with secondary leukemias and bone marrow sarcomas in sites of previous radiation treatment [14].

FUTURE CHALLENGES

Various investigational approaches are continuing worldwide for setting up the standard therapy for the newly diagnosed patients with metastatic disease but there is a doubt whether these additional agents in combination with same mechanism of action will ultimately improve the prognosis.

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CONCLUSION

Till today, various factors contribute to ARMS tumor development and its aggressiveness. So, it is critical for us to draft a resounding clinico-diagnostic approach for the better understanding and treatment options. These new opportunities will render to develop specifically targeted therapies for these round cell tumors.

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