CASE REPORT

Atypical Teratoid/Rhabdoid Tumour of Brain

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Abstract

Primitive neuroectodermal tumor (PNET) / medulloblastoma (MB) are the most common malignant central nervous tumors of the first decade of life. Atypical teratoid / rhabdoid tumor (ATT / RT) is a tumor of infancy and childhood although occasional cases have also been described in adults. ATT/RT has a characteristic histopathological, immunocytochemical and ultrastructural features. ATT /RT is a rare tumor, incidence of which remains to be defined with only hundred published cases. The present report documents the clinical features, histological and immunohistochemical findings of a case of ATT / RT.

Key Words

Neuroectodermal, Rhabdoid tumour

Introduction

Primitive neuroectodermal tumor/medulloblastoma are the most common malignant central nervous tumors of the first decade of life. Within past decade, a number of reports have been published of an aggressive central nervous system tumor which is grossly and radiologically indistinguishable from PNET - MB and histologically resembles rhabdoid tumor of kidney and other extrarenal sites. These tumors have been called atypical teratoid / rhabdoid tumors (ATT /RT) (1-3). Atypical teratoid / rhabdoid tumor (ATT / RT) is a tumor of infancy and childhood (4,5) although occasional cases have also been described in adults (6,7). Prognosis of ATT / RT is poor with most of the patients dying shortly after the diagnosis (8). ATT / RT has a characteristic histopathological, immunocytochemical and ultra-structural features. ATT / RT is a rare tumor, incidence of which remains to be defined with only hundred published cases.

In children it is very important to recognize these tumors and differentiate them from PNETs because of their worse prognosis. The present report documents the clinical features, histological and immunohistochemical findings of a case of ATT / RT.

Case Report

A five and a half months old female child was admitted in the neurosurgery ward of G.B. Pant hospital New Delhi with complaints of repeated vomiting for seven days, deformity of the face to the left side while crying and unable to close her left eye for seven days.On general physical examination patient was conscious, afebrile, with stable vital signs and good hydration. There was no pallor / cyanosis / icterus. Examination of cardiovascular system, respiratory system and abdomen was within normal limit .On CNS examination there was seventh nerve palsy. No other neurological deficit was found. Routine investigations were within normal limits. CT- scan showed a left cerebellar mass extending to the brainstem with hydrocephalus, MRI revealed a large irregular mass in the infratentorial compartment involving major portion of left vermis, left cerebellar hemisphere and extending to brainstem. Mass effect on fourth ventricle was seen.

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The mass was encasing basilar artery. Right VP Shunt (Chabara NDR) was put on the day of admission. After one week left paramedian suboccipital craniotomy was done. Fresh tissue was fixed in 4 percent buffered formalin and processed routinely for paraffin embedding for light microscopy and immunohistochemistry. Sections of 3-4 mm thickness were stained with Haematoxylin and Eosin, Reticulin and AS stains. Immunohisto-chemistry was done on paraffin embedded sections by immunoperoxidase method by using antibodies to GFAP, S-100, desmin and cytokeratin. Light microscopy section showed a cellular tumor composed of cells present in sheets with fibrovascular septa in between. Cells were round to polygonal with well-defined cell membrane, granular eosinophilic cytoplasm; vesicular eccentrically placed nucleus and prominent nucleoli. No inclusion bodies were seen in the cytoplasm. Many cells showed vacuolated cytoplasm. These cells showed mild degree of pleomorphism. Nodules of small-undifferentiated cells with deeply basophilic nuclei and scant cytoplasm (PNET like area) were also present. Thin strands of fibrovascular tissue were also present in the tumor. Perivascular arrangement of tumor cells was noted. Numerous mitotic figures were seen. Areas of necrosis were present. (Fig 1). No vascular endothelial cell proliferation was seen. Immuno-histochemistry depicted that tumor cells were positive for GFAP, cytokeratin, smooth muscle actin, neuron specific enolase, and S-100 and negative for synaptophysin.

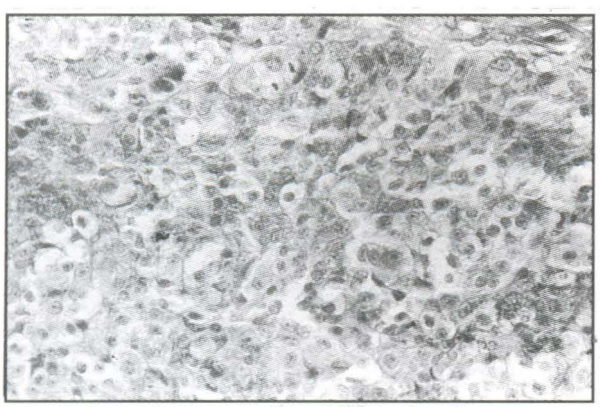

Fig. 1. Cells with clear and granular abundant cytoplasm nucleus eccentric placed prominent nucleoli. Mitosis is also seen 200XH&E.

Discussion

Malignant rhabdoid tumors represent embryonal neoplasms originally described in kidney as rhabdomyosarcomatoid subtype of Wilms' tumor, but later identified as a tumor distinct from Wilms' tumor (9). Haas *et. al.* (10) proposed this term to emphasize its teratomatous character. Atypical teratoid /rhaboid tumor is a distinct clinicopathologic neoplasm defined by characteristic histological features and cytogenetics (11). Roorke *et. al.* (3,4) described this entity in 52 infants and with mean age of diagnosis 29 months with slight male predominance. Half of their patients had posterior fossa mass similar to our case. In their series, one third of the ATT/ RT had evidence of leptomeningeal spread at the time of diagnosis. The longest survival was five and half years in a three-year-old child who already had subarachnoid spread at the time of presentation. ATT can be distinguished from PNET on meticulous examination of histological sections. Light microscopy shows presence of characteristics rhabdoid cells in most of the areas. Cells are round to polygonal with dense eosinophilic cytoplasm and eccentrically placed nucleus with prominent nucleoli, PAS positive paranuclear inclusion are also seen, but were not observed in our case. Along with these rhabdoid cells also seen are PNET like areas, mesenchymal differentiation, and epithelial features like adenomatous or papillary pattern, Homer and Flexner/ Winterskeiner rosettes. Such disparate element suggests teratoma. However, it does not resemble teratoma in any other way including location, gross, or microscopic appearance. Immunohistochemical markers for embryonal tumors are consistently negative except for AFP where it show occasional positivity (1,3,4,9,11).

Immunohistochemistry in our case showed positivity for GFAP, S-100, smooth muscle actin and vimentin, which is consistent with the results of other authors (Table 1). A review of literature (3,11-13) shows that vimentin positivity is the most consistent immuno-histochemical finding, while variable positivity for S-100 is seen .EMA was positive in 93 percent cases. GFAP was positive in all the 55 cases and SMA showed

reactivity in 50 percent cases (11). Therefore a combination of GFAP, vimentin and EMA appears to be essential for diagnosis in histological characteristic lesion.

Table I

Immunohistochemical profile of atypical teratoid tumors

	VIM	NF	NSE	SYN	GFAP	ACT	CK	EMA	S-100
Roorke *et. al.* 4	++	++	nd	++	+++	++	nd	++	nd
Behring *et. al.* 13	++	++	+	—	+/–	—	+	+/–	+
Present case	nd	nd	++	—	++	++	+	Nd	+

Note : VIM = vimentin, NF = neurofilament protein, NSE = Neuron specific enolase, SYN = synaptophysin, GFAP = glial fibrillary acidic protein, ACT = actin, CK = cytokeratin, EMA = epithelial membrane antigen.

Ultrastructurally (8,14) rhabdoid cells showed presence of whorled bundles of intermediate filaments in cytoplasm of perikaryon which are positive for vimentin. Some cells have basal lamina on one aspect. Cells with interdigitating cytoplasmic borders and rare cell with microtubules may be seen.

Cytogenetics or FISH studies (3,4,11) have shown abnormalities in chromosome 22; most commonly monosomy. Translocation and deletion are also found implicating presence of tumor suppressor gene involved in development and progression of these tumors. Light microscopy and immunohistochemistry indicate that rhabdoid cell is a highly transformed malignant cell with a capacity for multipotent differentiation.

In conclusion, separation of ATT / RT from PNET based on histology and immunohistochemistry is important because ATT /RT are aggressive tumor with poor prognosis and currently there is no effective therapy. Prognosis of ATT / RT is grim and are generally radioresistant and ineffective to chemotherapy. However, Hilden *et. al.* (5) advocate high dose chemotherpy with autologous bone marrow transplant with promising results.

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