Case Report

Infantile rhabdomyofibrosarcoma: A distinct variant or a missing link between fibrosarcoma and rhabdomyosarcoma?

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Abstract

Infantile rhabdomyofibrosarcoma (IRMFS) is a rare soft tissue tumour affecting infants and young children. It occupies an intermediate position between infantile fibrosarcoma and spindle cell rhabdomyosarcoma in its clinical presentation, behaviour, morphology, immunohistochemical and ultrastructural features. This case is reported here to reiterate its occurence as tumour with distinct morphological immunohistochemical and clinical behavioral patterns.

Key Words: Infantile rhabdomyofibrosarcoma, infantile fibrosarcoma, spindle cell rhabdomysarcoma.

Introduction

Childhood fibrous tumours continue to be enigmas especially those which do not have any adult counterpart. Accurate prediction of biological behaviour based on morphological features may be difficult leading to inappropriate therapy. We present such a case of infantile rhabdomyofibrosarcoma (IRMFS), the reports of which are scant in the literature.

Case Report

Clinical summary

One and half year old male child developed a swelling in the right fore arm region of six months duration. He underwent excision in another institution and the specimen was submitted in multiple pieces measuring together 4 x 3.5 x 2.5 cm. The cut sections were grey white in appearance with out any areas of hemorrhage or necrosis. Multiple sections from the specimen submitted showed a lesion composed of long fascicles of spindle cells with elongated nuclei and dispersed chromatin. These areas are interspersed with numerous rhabdomyoblasts which are polygonal in shape with abundant eosinophilic cytoplasm and eccentrically placed oval nuclei [Figures 1 and 2]. Necrosis, pleomorphism and mitotic figures were not seen in any of the sections examined. Immunohistochemistry with vimentin, smooth muscle actin and desmin were all strongly positive in both the population of the cells [Figure 3]. The features were consistent with IRMFS.

The patient received chemotherapy with six cycles of vincristine, cyclophosphamide and adriamycin at three weekly intervals. Post-chemotherapy MRI scan showed a recurrent tumor which was completely excised with wide resection margins. The sections from the same

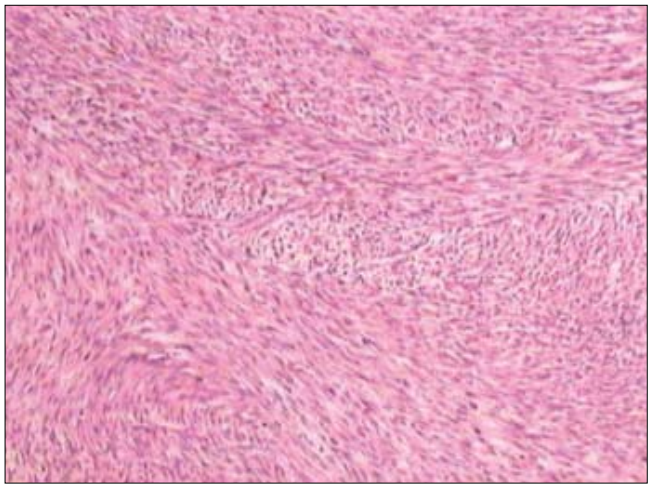

Figure 1: Morphology of tumor. Lower magnification showing predominantly spindle cells in long fasicles (H/E, 40x)

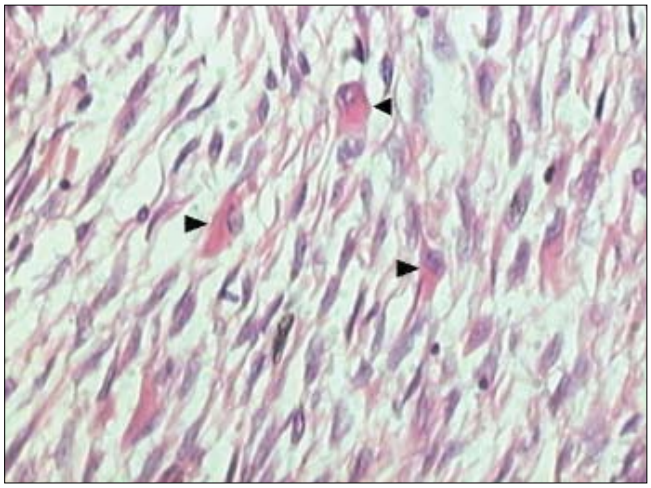

Figure 2: Higher magnification showing predominantly spindle cells with scattered (black arrow heads) rabdomyoblastic cells (H/E, 400x)

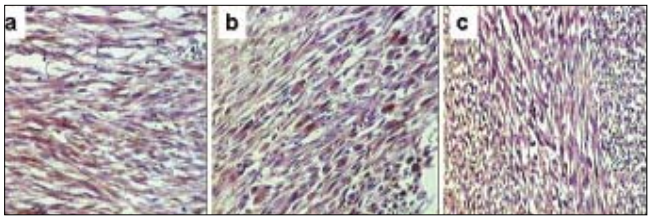

Figure 3: Immunohistochemistry. Both spindle cells and rabdomyoblastic cells showing positivity for a. Vimentin, b. Desmin, c. SMA

showed similar morphology as the original tumor with relative predominance of rhabdomyoblastic cells over the spindle cells [Figures 4 and 5]. There was no associated necrosis, pleomorphism or any mitoses in these sections also. The resected margins were grossly and microscopically free of tumor. Undifferentiated round to oval cells resembling the immature rhabdomyoblasts were not seen in either of two specimens.

The patient is on follow up without any evidence of any further recurrence or metastasis since last two years.

Discussion

Infantile fibrosarcoma is a relatively rare tumour initially described by Stout in 1962. Which presents as a non-tender, pain less swelling with variable rate of growth.[1] This tumour mainly involves the extremities and head neck region with rare occurrence in retroperitoneum, mesentery and orbit.[2-5] Microscopically it is composed of spindle cells arranged in long fascicles with minimal pleomorphism and mitoses. Spindle cell rhabdomyosarcoma occurs more commonly in paratesticular region and rarely affects head and neck.[6] Histologically it is composed of an exclusive population of elongated fusiform cells with cigar shaped nuclei and

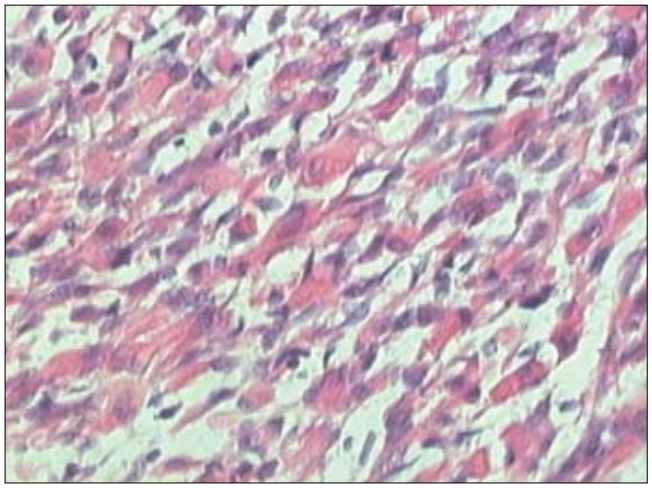

Figure 4: Morphology of recurrent tumor. Predominance of rhabdomyoblastic cells over spindle cells (H/E, 200x)

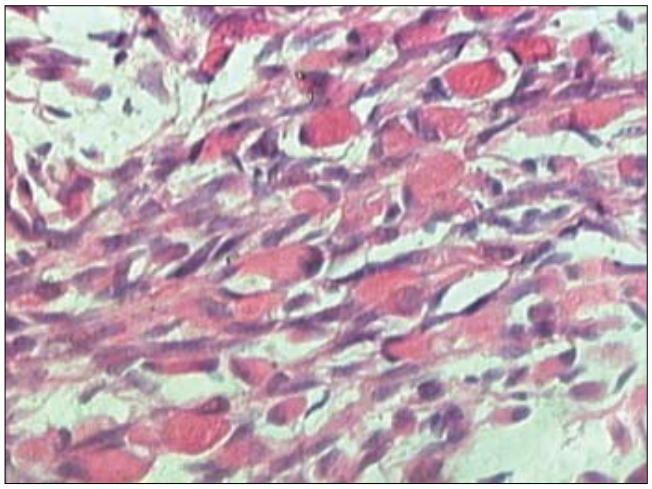

Figure 5: Recurrent tumor morphology at higher magnification (H/E, 400x)

prominent nucleoli. Cytoplasmic cross striations may be seen.

Lundgren *et al* (1993) identified for the first time IRMFS in three children. These were initially diagnosed as infantile fibrosarcoma, but two of the patients developed metastasis and died within two years of primary operation whereas the third patient was alive with local recurrence. This behaviour was contrary to the favourable course of infantile fibrosarcoma. An extensive comparitive immunohistochemical, ultrastructural and cytogenetic studies were done on these cases along with other cases of infantile fibrosarcoma.[7] Two more cases of IRMFS were subsequently reported.[8,9]

[Tables 1 and 2] highlight the various observations on all the cases of infantile rhabomyofibosarcoma reported in the literature. The present case is similar in many

Table 1: Clinical profiles of the cases of infantile rhabdomyofibrosarcomas reported

Author	No. of cases	Age/Sex	Site	Treatment	Clinical course
		2 yr/F	Intramuscular, thigh	WLE, CT	Pulmonary & liver metastases,
					death 1 yr
Lundgren et al;1993	3	13 mon/F	Intramuscular, back	WLE, CT	Recurrence & pulmonary metastases,death 2 yr
		3 yr/M	Minor pelvis, prostate	PE, CT	Local recurrence,alive, 6 mon
Mentzel	1	4 yr/M	Intrathoracic, extrapleural	Surgery, CT, RT	Local recurrence, metastases in
et al;1996					lung & thymus, death 3 yr
Miki et al;1999	1	15 mon	Buttock	CT,surgical resection,	No recurrence OR metasasis for
				Intraoperative RT	25 mon
Present study	1	18 mon	Fore arm	Excision,CT,WLE	Local recurrence after 6 mon, alive

Abbreviations: WLE, wide local excision; CT, chemotherapy; PE, partial excision; RT, radiotherapy

aspects that the patient is below 2 years with involvement of extremity and showing biphasic population of spindle cells admixed with polygonal rhabdomyoblastic cells. Both of these cells showed positivity for vimentin, desmin and focally for SMA in concordance with the previous studies. There was distinct absence of any undifferentiated small round to oval cells, any pleomorphism, necrosis or mitosis. The tumour recurred within six months of first surgery however the patient did not develop any metastasis.

One notable feature in our case is that there was an overt increase of rhabdomyoblastic cells over the spindle cell population in recurrent tumour after chemotherapy. This feature has been observed in one case of IRMFS and some of childhood rhabdomyosarcomas following chemotherapy.[9,10]

Current molecular genetic studies report a characteristic translocation of t(12;15) (p13;q25) and the fusion transcript ETV6-NTRK3 detected by Reverse transcriptase polymerase chain reaction as diagnostic feature of infantile fibrosarcoma but specific cytogenetic abnormalities have not been reported in cases of spindle cell rhabdomyosarcoma.[11] In the above mentioned cases of IRMFS, monosomies of chromosomes 19 and 22 and der(2) t(2;11)(q37;13) were observed in three cases.[7,9] These cytogenetic variations need to be supported studies on larger number of cases. The confirmatory categorization of the present case as IRMFS is limited by lack of cytogenetic and molecular studies.

Conclusion

Infantile rhabomyofibosarcoma occupies an intermediate position between an indolent behaving infantile fibrosarcoma and an aggressively behaving rhabdomyosarcoma. The number of cases of IRMFS reported in the literature are too small to arrive at a definite cytogenetic conclusion. The inadequacy of cases also hinders the correct categorization of this tumour. Hence these kind of cases need more diligent work up and close follow up.

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Table 2: **Immunohistochemical, ultrastructural and cytogenetic features in IRMFS**

Author	No. of cases	Immunohistochemistry	Electron microscopy	Cytogenetics
Lundgren	3	Vimentin - positive	Fibroblastic & myofibroblastic	Case 1: 45XX, Monosomy 19
et al;1993		Desmin - positive	differentiation Sarcomere like	Case 2: Monosomy 22
		Muscle specific actin - positive	structures	Case 3: 45XY, Monosomy 19
		α-SMA 1 - positive		
Mentzel	1	Vimentin - positive	Not done	Not done
et al;1996		Desmin - positive		
		Muscle specific actin - positive		
		Myo D1 - Focal positive		
		α-SMA - negative		
		Neuroepithelial markers - negative		
		CD34, CD31- negative		
Miki	1	Vimentin - positive	Fibroblastic features	46XY, der(2) t(2;11)(q37;13)
et al;1999		(most tumor cells)	Occassional cells with	
		Desmin - positive	thick & thin filaments	
		(Round cells & some spindle cells)		
		Myo D1 - positive		
		(most rhabdomyblastic cells &		
		some spindle cells)		
		Myoglobin - weakly positive		
		(Round cells)		
		S-100 - negative		
		NSE - negative		
		α-SMA - negative		
		Factor VIII - negative		
		CD34 - negative		
Present study	1	Vimentin - positive	Not done	Not done
		Desmin - positive		
		SMA - positive		

Abbreviations: SMA, smooth muscle actin; NSE, neuron specific enolase.

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