RHABDOMYOSARCOMA IN CHILDHOOD A 13 YEAR REVIEW FROM THE UNIVERSITY HOSPITAL KUALA LUMPUR 1967 - 1980

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SYNOPSIS

A review of rhabdomyosarcoma in childhood reveals that the pattern and results of treatment have changed with the introduction of multimodal therapy. Outcome in our series have been poor due to advanced disease, poor compliance to follow up resulting from poor socio-economics and educational levels of our patients and their faith in traditional medicine. Improvement in the prognosis can only be anticipated with earlier diagnosis and reduction in defaulter rate.

INTRODUCTION

Rhabdomyosarcoma is the most common soft tissue sarcoma in children admitted to the University Hospital, Kuala Lumpur (1) as in other countries (2, 3). Major advances in the classification and management of this tumour have been witnessed in recent years. In the past, the outlook was poor, but with the introduction of multimodal therapy, a survival rate of 70% is now possible (4).

We review here, our experience of all cases of rhabdomyosarcoma in childhood admitted to the Paediatric Unit, University Hospital over a 13 year period, and compare their epidemiological features, clinical presentation, histological typing, clinical grouping and outcome of treatment with other centres.

MATERIALS AND METHODS

During the period 1967 to August 1980, 11 children with rhabdomyosarcoma were admitted to the University Hospital, Kuala Lumpur. Diagnosis was based on histological examination of biopsy specimens and/or the surgically excised tumour mass, and subclassified into embryonal (including botyroides type), alveolar, pleomorphic and mixed types. (WHO, International Histological Classification of Tumour, 1978). Details of the patients' presenting complaint, physical findings and results of investigations were recorded. The extent of disease at diagnosis was clinically evaluated in each patient and clinical grouping was carried out based on the system adopted by the Intergroup Rhabdomyosarcoma Study (5) (Table III).

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RESULTS

EPIDEMIOLOGY

The eleven cases of rhabdomyosarcoma comprise 3.1% of all childhood malignancies and 50% of all soft tissue sarcoma seen at the University Hospital. Seven were male and four female; their mean age was 3 years and ranged from 4 months to 8 years.

CLINICAL FEATURES

The main presenting features are seen in Table I. All the patients presented with progressive swelling in the respective primary sites, except 2 patients; one presented with rhinorrhoea and nasal obstruction, and the other with haematuria. Two complained of pain over site of the swelling. Systemic symptoms like anorexia, weight loss or fever were uncommon. Other than swelling due to the primary tumour, few physical signs were present and generally included either regional or distant lymphadenopathy, hepatosplenomegaly, proptosis or palpation of a mass per rectal examination. The site of the primary tumour in our 11 cases is shown in Table II. The more common locations were the orbit, head and neck, extremities, groin and introitus respectively. The duration of symptoms prior to diagnosis ranged from 1 week to 4 years. It was generally short for tumours arising from the head and neck and genito-urinary region, and long where the extremities or trunk were involved.

Table I Clinical features of 11 cases of rhabdomyosarcoma

Symptoms	No. of cases	Signs	No. of cases
Progressive swelling of primary sites	9	Regional lympha-denopathy of primary site	3
Anorexia	3	Proptosis	3
Weight loss	3	Hepatosplenomegaly	2
Pain over swelling	2	Distant lympha-denopathy	1
Eye discharge	2	Mass per rectal examination	1
Loss of vision	1	Pallor	1
Rhinorrhoea and nasal obstruction	1		
Haematuria	1		

Table II Site of primary tumour and duration of symptoms prior to diagnosis

Primary Site	No. of cases	Duration of symptoms prior to diagnosis
Head & neck (Total 5)		
Orbit	3	2 mos., 3 mos., 14 mos.
Extra-orbit	2	1 mo., 3 mos.
Extremities (Total 3)		
Elbow	1	3 yrs.
Thigh	1	3 mos.
Calf	1	4 yrs.
Genitourinary (Total 2)		
Introitus	1	3 mos.
Bladder neck	1	1 wk.
Trunk (Total 1)		
Groin	1	4 mos.
Total	11	

INVESTIGATIONS

Routine haematological investigations were not very helpful. Diagnosis was established by examination of tumour tissue obtained either by biopsy or at operation. Radiological investigations including skeletal survey were undertaken in appropriate cases to localise the site of tumour and to evaluate the extent of the disease. Other tests included intravenous pyelogram, bone marrow examination, liver scan and carotid angiogram.

X-ray examination revealed bony destruction at the site of the primary tumour in 4 patients - (case Nos. 1, 4, 7 and 8 as seen in Table V) who also had metastases either in the thoracic cavity, spine, long bones or distant lymph nodes as seen in figure 1. Brain metastases were diagnosed in 2 patients (case Nos. 4 and 7) from electroencephalographic and carotid angiogram studies.

Bone marrow examination in all patients and liver scan in the two patients studied were normal.

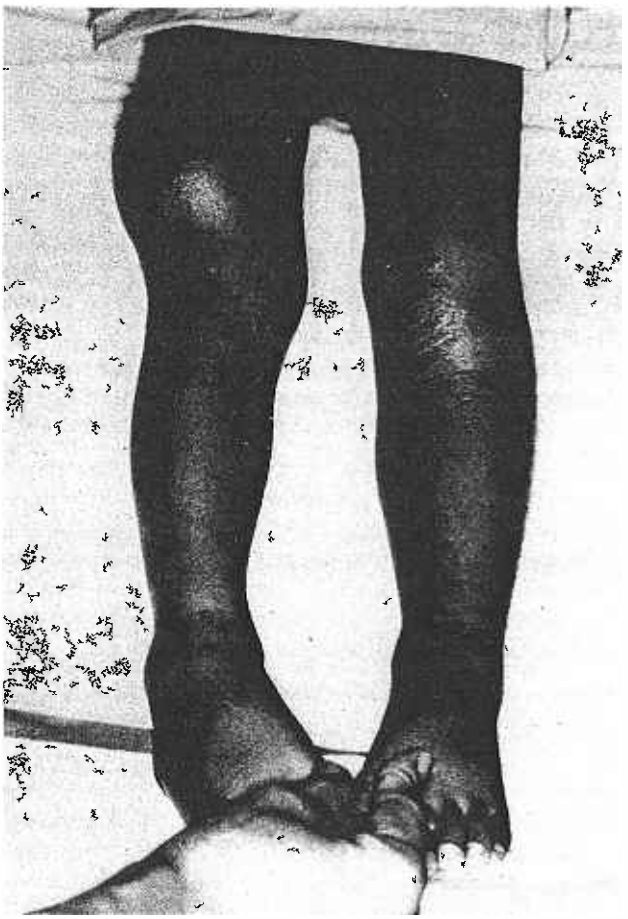

Figure 1 (a) Primary tumor in right lower thigh with metastasis to left upper tibia

HISTOLOGY AND CLINICAL GROUPING CLASSIFICATION

Histological classification was based on International Histological Classification of Tumour, WHO (1978). The tumours were classified as (1) predominantly embryonal, (2) predominantly alveolar, (3) predominantly pleomorphic and (4) mixed type (combining the features of (1), (2) or (3) as seen in figures 2-6 respectively. Extent of disease was classified according to the Intergroup Rhabdomyosarcoma study (5) as

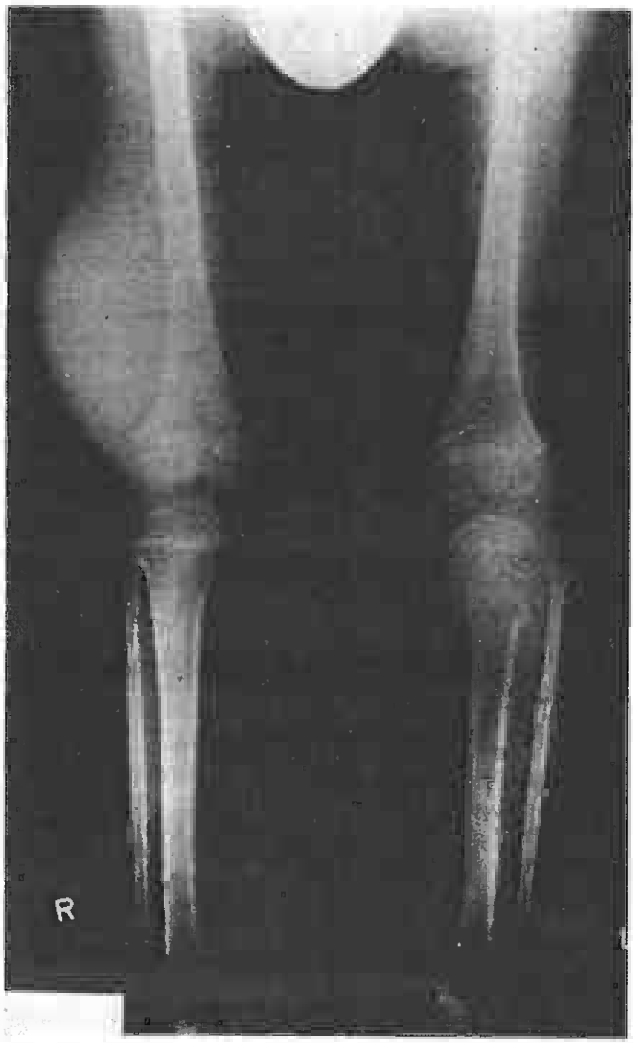

Figure 1 (b) Primary tumour in right lower thigh with metastasis to left upper tibia.

shown in Table III. Group I refers to localised disease, group II and III to regional disease and group IV to generalised disease.

Table IV shows that most of our tumours are of the predominantly embryonal type, and more than 75% of patients belong to clinical groups III and IV.

Table III Clinical Grouping Classification of Rhabdomyosarcoma (Intergroup Rhabdomyosarcoma Study, 1977)

Group	Features
I	Localised disease, completely resected, regional nodes not involved. a) Confined to muscle or organ of origin. b) Contiguous involvement - infiltration outside the muscle or organ of origin, as through fascial planes. Inclusion in this group includes both the gross impression of complete resection and the microscopic confirmation of complete resection.
II	a) Grossly resected tumour with microscopic residual disease. No evidence of gross residual tumour. No clinical or microscopic evidence of regional node involvement b) Regional disease, completely resected (regional nodes involved completely resected with no microscopic residual) c) Regional disease with involved nodes, grossly resected, but with evidence of microscopic residual.
III	Incomplete resection or biopsy with gross residual disease.
IV	Metastatic disease present at onset.

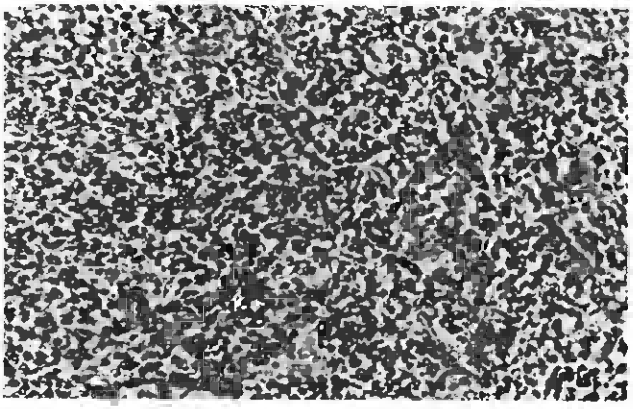

Figure 2 Embryonal rhabdomyosarcoma (H & E x 330). The malignant cells occur in sheets and contain oval to slightly elongated nuclei.

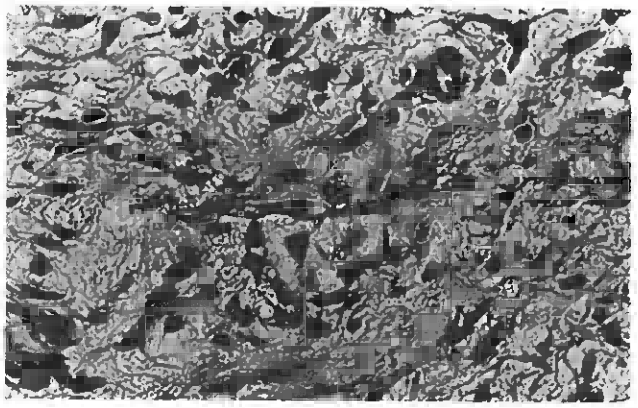

Figure 3 Embryonal rhabdomyosarcoma (PTAH x 650). An elongated rhabdomyoblast with cytoplasmic cross-striations is seen in mid-field.

TREATMENT AND OUTCOME

The treatment of our patients with rhabdomyosarcoma has varied over the years (see Table V). Before 1975, treatment was inconsistent and only one patient (case No. 3) received surgery, radiotherapy and combination chemotherapy (methotrexate, vincristine and actinomycin-D). Four other patients received either surgery or radiotherapy while one patient received both. Since 1975, multimodal therapy comprising surgery + radiotherapy + combination chemotherapy (vincristine, actinomycin-D, adriamycin and cyclophosphamide) has been instituted in 6 cases.

The outcome has been poor, six of the eleven patients were lost to follow up within 6 months; two died within 8 months, one has just completed treatment and two are still on therapy. The 3 most recent patients have shown better response than the previous cases. One patient (case No. 9, Table V) presented with orbital tumour (Fig. 7) (Embryonal, Clinical Group I) and following multimodal therapy has remained tumour free after stopping treatment. The other 2 patients presented with tumour in the bladder neck (Embryonal, Clinical Group III) and back of neck (Fig. 8) (Alveolar, Clinical Group III) respectively. Surgical excision of the tumours was not possible in both patients. Combination chemotherapy and radiotherapy were given and remarkable response was achieved (Fig. 9).

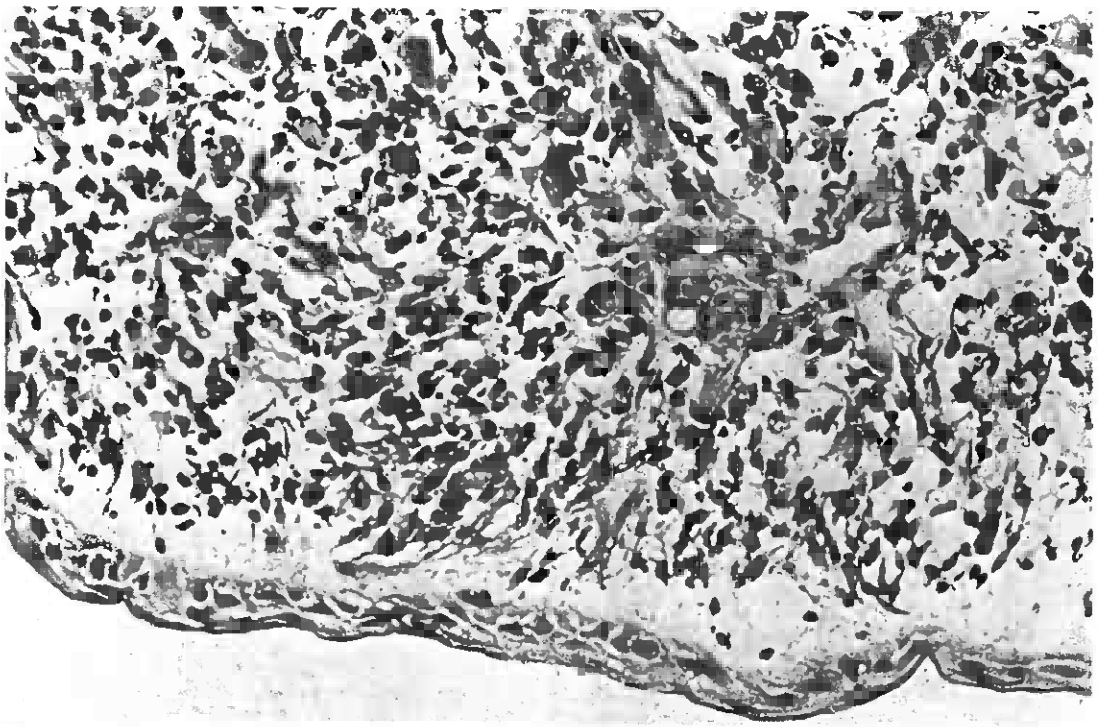

Figure 4 Sarcoma botyroides (H & E x 330). A polypoidal mass with loose, myxomatous stroma. Scattered in the stroma are rhabdomyoblastic cells of varying maturity and morphology, including long fusiform cells, globular cells and undifferentiated small round cells.

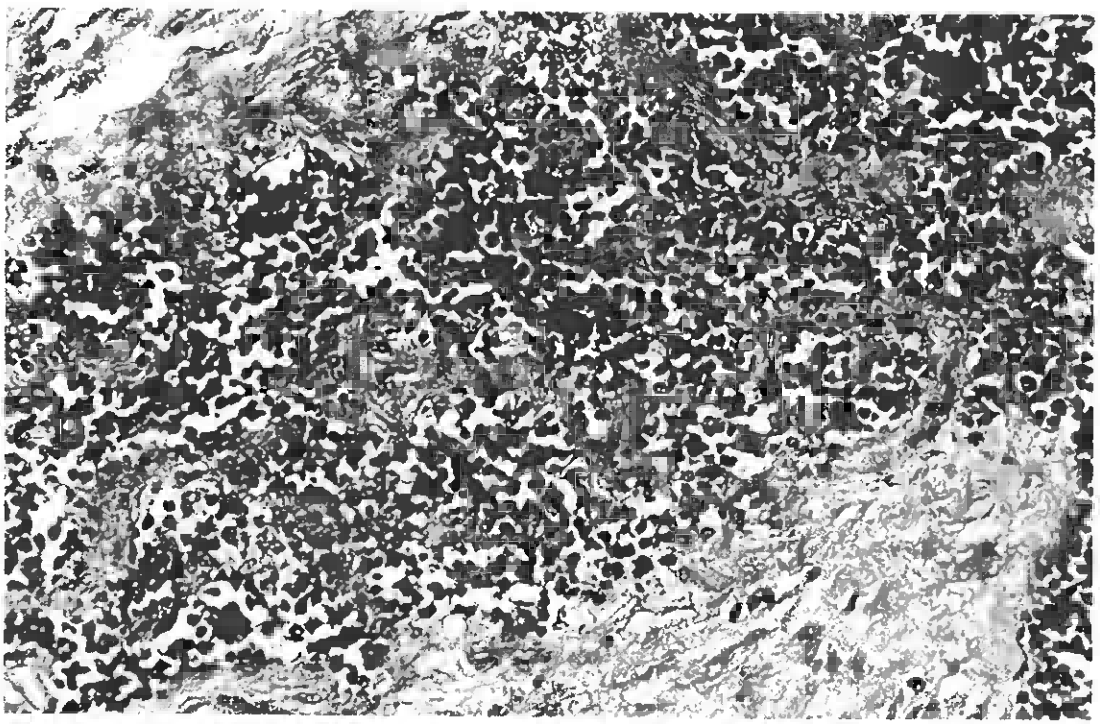

Figure 5 Alveolar rhabdomyosarcoma (H & E x 250). The tumour cells are dark and uniform in size and show a tendency to line irregular clefts, giving an 'alveolar' pattern.

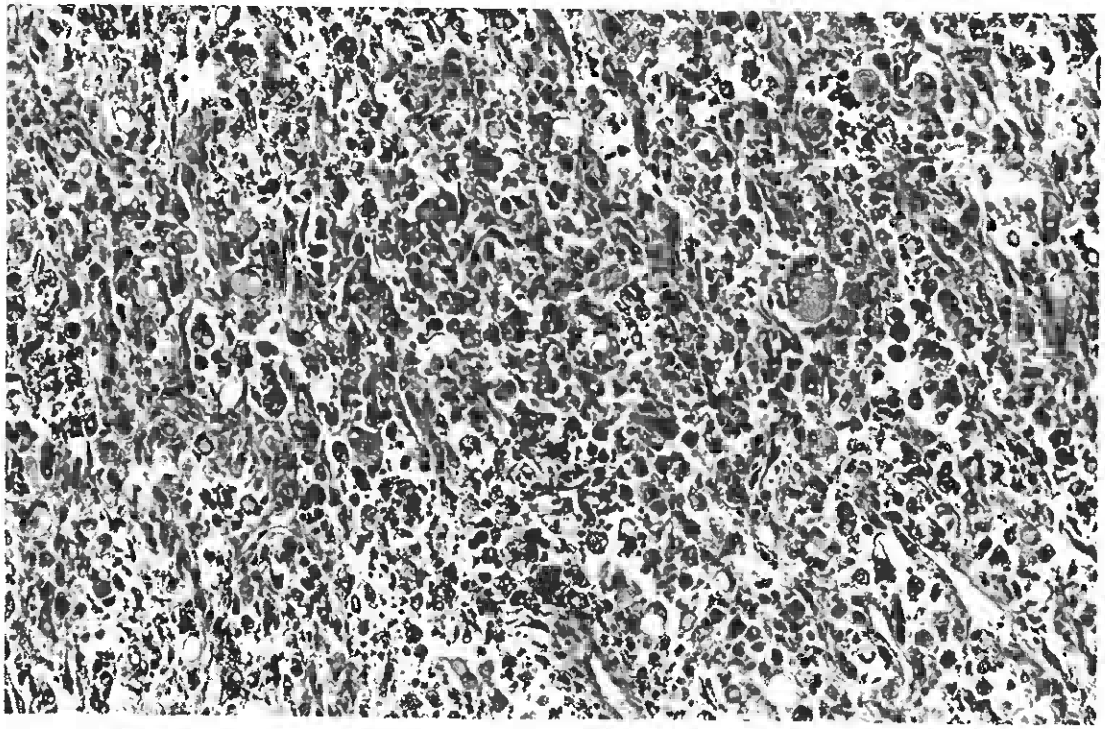

Figure 6 Pleomorphic rhabdomyosarcoma (H & E x 200). The tumour shows marked cellular pleomorphism, globular cells, tadpole cells and giant mononuclear cells are arranged haphazardly without pattern.

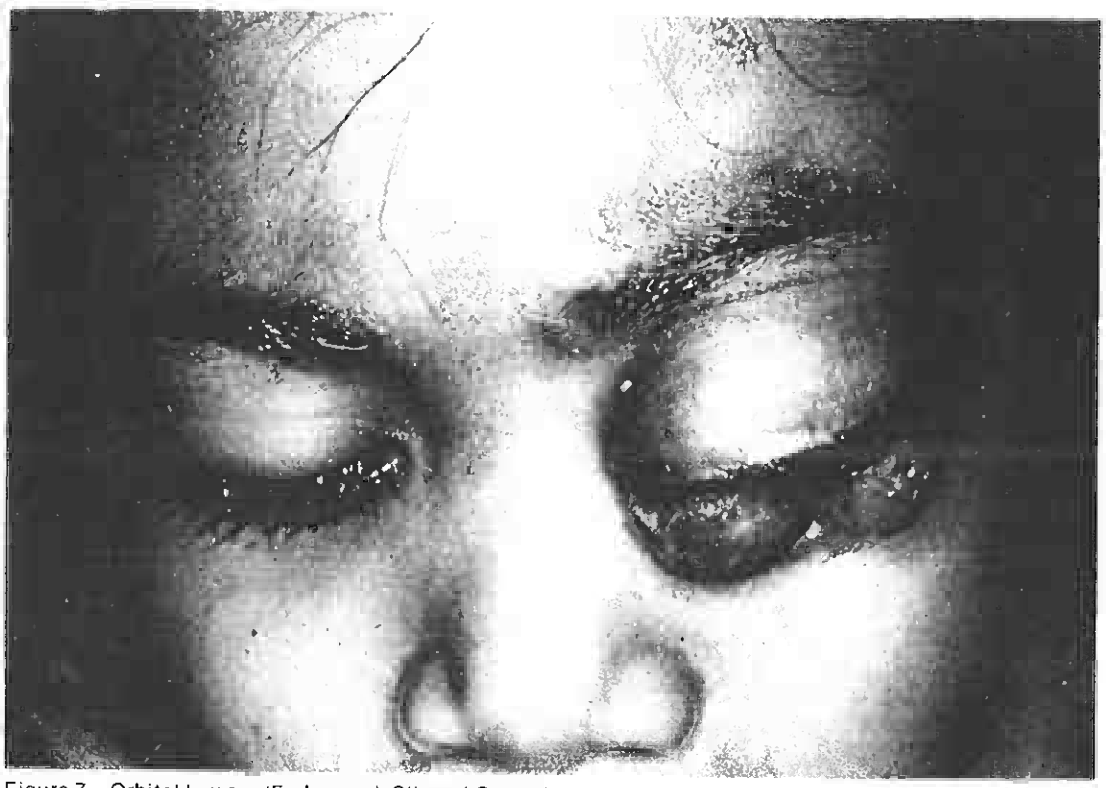

Figure 7 Orbital tumour (Embryonal, Clinical Group I)

Table IV Distribution of 11 cases of Rhabdomyosarcoma by Histological Classification and Clinical Grouping Classification

Clinical Grouping Classification	Histological Classification				Total No. of cases
	Embryonal (including Botyroides	Alveolar	Pleomorphic	Mixed	
I	2				2
II	1				1
III	3	1			4
IV		2	2		4
Total No. of cases	6	3	2		11

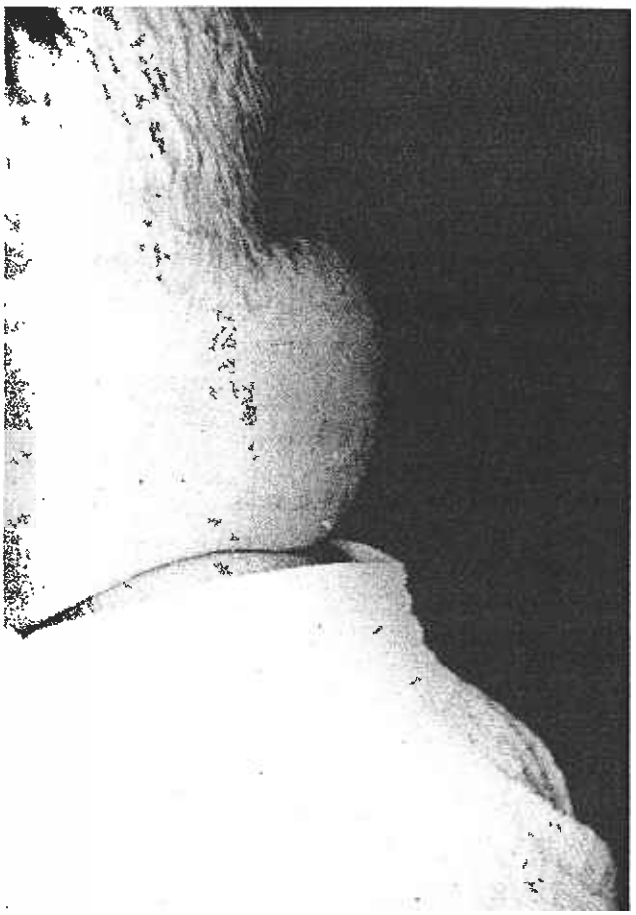

Figure 8 Tumour at back of neck (Alveolar, Clinical Group III)

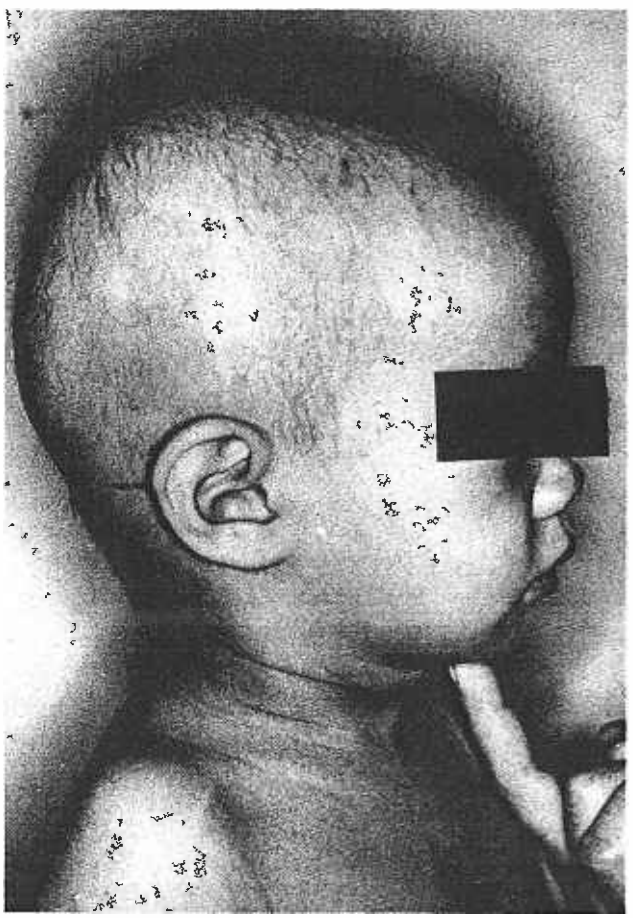

Figure 9 Tumour at back of neck after treatment using multimodal therapy.

Table V Clinical features and outcome of treatment in 11 cases of rhabdomyosarcoma

No.	Year of admission	Age/Sex/Race (yrs)	Primary Site	Metastases	Histological and clinical grouping classification	Treatment			Outcome
						Surg.	RT	CT	
1	1970	6/F/M	(L) calf	(L) groin and popliteal mass, Supraclavicular node	Pleomorphic IV	–	+	–	LTFU after 2½ mos.
2	1970	5½/M/C	Nasopharynx	–	Embryonal I	Complete excision	–	–	LTFU
3	1973	2/F/M	Introitus	LI	Embryonal III	Total Hysterectomy	+	+	Died after 20 days.
4	1974	8/M/C	Orbit	LI; T_{12} & L_4; Paravertebral, paratracheal, superior mediastinum metastases	Embryonal IV	–	*	–	LTFU after 2 mos.
5	1974	4 mos/F/C	Orbit	LI	Embryonal III	Partial removal	*	–	Agreed to treatment 20 mos. after diagnosis. LTFU after 1 week.
6	1975	5 mos/M/M	Groin	LI and destruction of iliac crest	Embryonal II	Complete excision	+	+	LTFU after 1 month.
7	1975	2/M/M	Elbow	LI of bone. Pulmonary and parietal metastases	Pleomorphic IV	Amputation	–	+	Died after 8 mos.
8	1978	9 mos/M/M	Thigh	LI; Posterior mediastinum Vertebral T_3; (L) upper tibia; (L) parotid region.	Embryonal IV	–	+	+	Responded well. LTFU after 6/12.
9	1979	7/F/M	Orbit	–	Embryonal I	Complete excision	+	+	Off treatment after 1 yr. No evidence of disease.
10	1980	8 mos/M/C	Bladder Neck	LI	Embryonal (Botyroides) III	–	+	+	Responding to treatment.
11	1980	1½/M/C	Neck	LI	Alveolar III	–	+	+	Responding to treatment.

Race : M = Malay; C = Chinese; LI = Local infiltration; LTFU = Loss to follow up; mos = months

DISCUSSION

The epidemiology and clinical presentation of our patients appear similar to those reported in other countries (2, 6). The most common primary sites are the head and neck, both orbital and extra-orbital (40%), genito-urinary and intra-abdominal sites (35%), and trunk and extremities (25%) (4, 3, 7) almost similar to that observed in our series. The single most important determinant of prognosis is the extent of the disease at the time of presentation (2, 8). Other features like age, sex and histological subtype were found to be not of statistical significance (2). The outcome of treatment has been poor as most of our patients had advanced disease and failed to come for follow up treatment. Even in established centres, the results of treatment of such cases have been poor and range from 6 to 22% disease free survival in Clinical Group IV as compared with 85% for Clinical Groups I and II. The high defaulter rate in our series can be attributed to the low socioeconomic and educational status of our patients, who generally consider cancer to be incurable. The strong cultural inclination towards traditional medicine may also contribute to the delay in seeking treatment and poor compliance to modern therapy.

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