

Extremity rhabdomyosarcoma in adolescents and adults A retrospective study of clinical, imaging and treatment findings in four cases

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Abstract: *Extremity rhabdomyosarcoma is rare in adults and requires multidisciplinary management. This retrospective descriptive study evaluated the clinical, imaging, pathological, treatment and outcome characteristics of four patients managed at Hassan II University Hospital, Fez, between January 2016 and December 2020. Data were obtained from clinical records and radiology and pathology reports. The cohort comprised three males and one female, aged 15–45 years, with a mean age of 26.5 years. All primary tumours involved the thigh, with extension to the knee in one case. Tumours were bulky and associated with deterioration in general condition. The reported histological diagnoses were embryonal rhabdomyosarcoma with spindle cell morphology in two patients, alveolar rhabdomyosarcoma in one and pleomorphic rhabdomyosarcoma in one. Two patients were classified as having metastatic disease, although histological confirmation of the suspected sacral lesion was not documented. Management included chemotherapy, radiotherapy in one patient and a subsequent recommendation for amputation in that patient, which was declined. Individual treatment documentation was incomplete. No durable remission was reported, and all four patients died during the documented follow-up. These observations illustrate the diagnostic and treatment challenges of bulky or disseminated disease and support early specialist referral, expert pathological assessment and continuity of care. The small sample precludes conclusions regarding comparative treatment efficacy or population-level prognosis.*

Keywords: rhabdomyosarcoma; extremities; adolescent; adult; magnetic resonance imaging; immunohistochemistry; multidisciplinary treatment.

1. INTRODUCTION

Rhabdomyosarcoma is a malignant mesenchymal neoplasm characterised by skeletal muscle differentiation. Although well recognised in paediatric oncology, it is rare in adults, in whom clinical presentation and histology are heterogeneous. Adult series generally report less favourable outcomes than paediatric cohorts, with differences related to disease stage, tumour subtype and treatment. [1,2]

Extremity tumours present challenges for both oncological control and limb function. A progressively enlarging deep mass may initially cause few symptoms, while increasing tumour bulk can subsequently compromise resectability. Metastatic disease and response to systemic treatment are important determinants of outcome in adult series. [3]

Management requires coordination among radiologists, pathologists, surgeons, medical oncologists and radiation oncologists. Embryonal and alveolar rhabdomyosarcoma should be distinguished from pleomorphic rhabdomyosarcoma, which is addressed within adult-type soft tissue sarcoma guidelines. [4] This study describes four patients with extremity rhabdomyosarcoma and discusses their clinical, imaging, pathological, treatment and outcome findings in the context of published evidence.

2. MATERIALS AND METHODS

2.1. Study design and population

This retrospective descriptive study included four patients managed in the Department of Osteoarticular Surgery B4, Hassan II University Hospital, Fez, Morocco, between January 2016 and December 2020. Case selection required an extremity primary tumour and histological confirmation of rhabdomyosarcoma. The cohort comprised one adolescent and three adults. The originally specified age threshold of >15 years was not applied consistently, as one patient was aged 15 years.

2.2. Data collection and analysis

Clinical records were supplemented by pathology, radiology and oncology-radiotherapy reports. Variables included age, sex, presenting symptoms, primary site, imaging findings, histological diagnosis, disease extent, treatment decisions and outcomes. Analysis was descriptive. Categorical variables were summarised as counts and, where useful, percentages; mean age was calculated from the four individual ages. No comparative tests or prognostic models were used.

Patient-level information was prioritised when aggregate data were inconsistent. Mean tumour size and survival estimates were not calculated because measurements and timelines were insufficiently standardised. Planned treatment was distinguished from documented administration whenever the available information did not establish that treatment had been delivered.

2.3. Diagnostic assessment and management

Assessment included clinical examination, local computed tomography (CT) and/or magnetic resonance imaging (MRI), and pathological examination with immunohistochemistry. Thoracoabdominopelvic CT was documented in all four cases. Treatment strategies were discussed at multidisciplinary tumour board meetings.

2.4. Ethical considerations

Institutional ethics approval or waiver details and applicable consent requirements require confirmation before manuscript submission.

3. RESULTS

3.1. Demographic characteristics

The cohort comprised three males and one female, giving a male-to-female ratio of 3:1. Individual ages were 22, 24, 15 and 45 years, with a mean of 26.5 years. All primary tumours arose in the thigh; the tumour in the 24-year-old woman extended to the knee (Table 1).

Table 1. Demographic and pathological characteristics

Case	Age	Sex	Primary site	Reported histological diagnosis
1	22 years	Male	Left posterior thigh	Embryonal rhabdomyosarcoma with spindle cell morphology
2	24 years	Female	Distal thigh extending to the knee	Embryonal rhabdomyosarcoma, spindle cell variant
3	15 years	Male	Left thigh	Alveolar rhabdomyosarcoma
4	45 years	Male	Left posteromedial thigh	Pleomorphic rhabdomyosarcoma

In case 2, laterality was inconsistent between the clinical assessment (right) and the CT report (left).

3.2. Clinical presentation

All patients had a lower-limb mass and deterioration in general condition. Associated findings included pain, functional impairment and, in some cases, local inflammatory changes. Case 1 presented with local recurrence after excision at another institution. The initial pathological diagnosis had favoured schwannoma; pathology review subsequently supported rhabdomyosarcoma.

Case 2 presented with a bulky mass, functional impairment and severe respiratory compromise associated with thoracic dissemination. Case 3 initially developed febrile polyarthralgia and constitutional deterioration, followed by progressive left thigh swelling; right shoulder swelling was also described. Case 4 had a large, painful mass fixed to deep tissues and restricting joint mobility. Inconsistent chronology precluded calculation of a reliable mean diagnostic interval.

3.3. Imaging and staging

Imaging showed bulky soft tissue masses. MRI characterised their relationship to muscle compartments and adjacent structures, while CT contributed to local assessment and staging (Table 2).

Table 2. Principal imaging and staging findings

Case	Local imaging	Distant disease assessment
1	Mass $>9 \times 4.5$ cm on CT; interaponeurotic lesion adjacent to the sciatic nerve course on MRI	Subcutaneous chest wall lesion considered likely to represent a schwannoma; no other thoracoabdominopelvic abnormality reported
2	Mass approximately 18×10 cm involving the distal thigh and knee	Pulmonary nodules and masses, bilateral pleural disease and a paravertebral lesion involving T12
3	Mass 14.8×11.4 cm on CT; muscle and bone abnormalities on MRI	Suspicious osteolytic sacral lesion; classified as metastatic disease
4	Mass $16 \times 16.5 \times 20.7$ cm on MRI; subtle lesser trochanter osteolysis on CT	No thoracoabdominopelvic metastases reported

Measurements were obtained using different modalities and axes and were not pooled to calculate mean tumour size.

Two patients were classified as having metastatic disease. Pulmonary, pleural and vertebral dissemination was clearly described in case 2. Case 3 included a suspicious sacral lesion, but histological confirmation of a secondary site was not documented.

3.4. Pathological findings

Reported diagnoses comprised two embryonal rhabdomyosarcomas with spindle cell morphology, one alveolar rhabdomyosarcoma and one pleomorphic rhabdomyosarcoma. Immunohistochemistry contributed to diagnosis, with documented desmin expression, focal myogenin staining in an embryonal tumour and diffuse myogenin staining in the alveolar tumour. Histological terminology follows the original pathology reports. No **FOXO1** fusion or **MYOD1** mutation results were available.

3.5. Treatment

Chemotherapy was recorded for all four patients in the aggregate treatment data. However, individual records did not consistently establish the regimen, number of cycles or actual administration. Table 3 distinguishes documented treatment from treatment decisions. Radiotherapy was reported in one patient. No definitive resection at our institution was documented, and the margins of the previous excision in case 1 could not be assessed.

Table 3. Documented management by patient

Case	Treatment or management decision	Relevant circumstances
1	Previous excision elsewhere; radiotherapy and ifosfamide–etoposide chemotherapy reported; amputation subsequently recommended	Local recurrence; amputation declined
2	Hospital admission, oxygen therapy and morphine analgesia	Chemotherapy recorded in aggregate data, without an individual regimen or administration details
3	VAC chemotherapy: vincristine, dactinomycin and cyclophosphamide	Initial response after three cycles, followed by treatment interruptions and progression
4	Initial chemotherapy recommended for a tumour considered unresectable	Regimen and actual administration insufficiently documented

3.6. Outcomes

No durable remission was reported, and all four patients died during the documented follow-up. Reported circumstances were progressive clinical deterioration in case 1, respiratory distress associated with pulmonary and pleural disease in case 2, multiorgan failure in case 3, and clinical deterioration with tumour infection in case 4. Documented care intervals were approximately 4–10 months. Inconsistent dates and the absence of a standardised starting point precluded reliable estimation of median survival.

4. DISCUSSION

4.1. Demographic and clinical profile

The cohort predominantly comprised young adults and showed a male predominance. These findings are compatible with some published series, but four cases cannot establish population-level epidemiological patterns. Comparisons between adult and paediatric rhabdomyosarcoma must account for histological subtype and disease stage. [1,2]

The exclusive thigh location reflects this departmental cohort and should not be interpreted as the anatomical distribution of extremity rhabdomyosarcoma generally. Large tumour size and impaired general condition were prominent, indicating severe disease at specialist assessment. The available data cannot distinguish the contribution of delayed referral from that of rapid tumour growth.

4.2. Role of imaging

Local imaging defined tumour dimensions and relationships to muscle, neurovascular structures and bone. Proximity to the sciatic nerve was particularly relevant in case 1, while bone abnormalities in cases 3 and 4 required specialist interpretation. Soft tissue sarcoma assessment relies on appropriate imaging before biopsy and coordinated planning of tissue sampling and local treatment, especially for deep or bulky lesions. [4] Imaging alone cannot establish rhabdomyosarcoma, and a normal chest radiograph does not constitute adequate systemic staging.

4.3. Pathological confirmation and molecular characterisation

Diagnostic revision in case 1 highlights the importance of expert review of unusual or recurrent spindle cell tumours. Myogenin and MyoD1 support rhabdomyoblastic differentiation, but findings must be interpreted alongside morphology and an appropriate immunohistochemical panel; desmin positivity alone is insufficient. [5,6]

Extensive myogenin expression is associated with alveolar histology. The diffuse staining in case 3 was consistent with this association but did not replace molecular characterisation. Pleomorphic rhabdomyosarcoma also requires demonstration of skeletal muscle differentiation and exclusion of other pleomorphic sarcomas. [7,8]

Studies of **PAX3–FOXO1** and **PAX7–FOXO1** fusions, previously termed PAX3–FKHR and PAX7–FKHR, have refined prognostic assessment. Children's Oncology Group analyses support incorporating FOXO1 fusion status into risk stratification. [9,10] The two tumours labelled embryonal with spindle cell morphology cannot be reclassified without expert review and additional testing. Some spindle cell or sclerosing tumours harbouring **MYOD1** mutations follow an aggressive course. Genomic studies support integrating molecular findings with histology without inferring genotype from morphology alone. [11,12]

4.4. Treatment strategy and local control

Management should consider age, disease extent, histological subtype and opportunities for local control. Cooperative studies support risk-adapted combinations of systemic treatment, surgery and radiotherapy. Paediatric findings cannot be extrapolated uncritically to adults or pleomorphic tumours. [13,14]

Adult series by Ferrari, Esnaola and Little describe multimodal management and emphasise the influence of disease extent and treatment response. Their retrospective design limits causal interpretation of associations between treatment and survival. [1,3,15] Limb preservation is desirable when compatible with satisfactory oncological control. Historical extremity soft tissue sarcoma trials supported limb-sparing surgery with radiotherapy, but do not provide subtype-specific comparisons for every form of rhabdomyosarcoma. [16]

In this cohort, tumour bulk, disease extent and general condition restricted treatment options. Although amputation was declined in case 1, the available data do not establish whether surgery would have altered the outcome.

4.5. Outcomes in the context of published evidence

The four deaths describe this selected cohort and are not a generalisable mortality estimate for extremity rhabdomyosarcoma. Larger adult series provide context but differ substantially in case mix and treatment setting (Table 4).

Table 4. Comparison with major adult series

Study	Patients	Population	Main relevance
Ferrari et al. [1]	171	Adults with rhabdomyosarcoma	Clinical and treatment heterogeneity in adult disease

Study	Patients	Population	Main relevance
Esnaola et al. [3]	39	Adults with rhabdomyosarcoma	Association of metastatic disease and chemotherapy response with survival
Little et al. [15]	82	Adults with locoregional disease	Outcomes following multimodal treatment
Present series	4	One adolescent and three adults with thigh tumours	Bulky disease; four deaths during follow-up

Studies of metastatic rhabdomyosarcoma in children and adolescents identify adverse features related to age, primary site, bone or bone marrow involvement and metastatic burden. These findings inform interpretation of advanced presentations but do not permit reliable retrospective risk scoring in this cohort. [17–19]

Case 3 also illustrates difficulties maintaining treatment continuity. An initial response was followed by interruptions associated with irregular adherence and drug shortages. These events coincided with progression, but their causal contribution cannot be quantified. Early access to specialist care remains important. A large nationwide sarcoma study associated surgery at reference centres with improved survival, supporting specialised care pathways without establishing a specific effect in these four patients. [20]

4.6. Study limitations

The principal limitations were the retrospective, single-centre design and very small sample. Patients differed in age, histology and presentation, including locally advanced, recurrent and metastatic disease. Inconsistencies affected the age criterion, tumour laterality, measurements, chronology and treatment documentation. Molecular results, detailed radiotherapy parameters, chemotherapy dose intensity and standardised functional outcomes were unavailable. These limitations preclude comparative efficacy analyses, identification of independent prognostic factors or robust survival estimation. The study is descriptive and illustrates diagnostic and care-delivery challenges.

5. CONCLUSION

Extremity rhabdomyosarcoma in adolescents and adults is a rare, heterogeneous malignancy requiring specialist management. This four-patient series was characterised by bulky thigh tumours, impaired general condition and unfavourable outcomes. The findings support early referral, expert pathological confirmation, molecular characterisation when indicated, multidisciplinary planning and continuity of treatment. Prospective multicentre studies with standardised data collection are needed to better characterise outcomes in this population.

6. ACKNOWLEDGMENTS AND DECLARATIONS

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