

# Research Journal of Pharmaceutical, Biological and Chemical Sciences

## Multimodality Approach in Paratesticular Rhabdomyosarcoma: A Brief Review.

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### ABSTRACT

Paratesticular rhabdomyosarcoma is a rare tumor arising from the mesenchymal tissues of the spermatic cord, epididymis, testis and testicular tunics. It represents only 7% of all patients entered in the Intergroup Rhabdomyosarcoma Study (IRS) and 17% of all malignant intrascrotal tumors in children less than 15 yrs old. It is an aggressive tumor with both hematogeneous and lymphatic spread. Multimodality approach has resulted in improved outcomes.

**Keywords:** paratesticular, rhabdomyosarcoma, chemotherapy

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## INTRODUCTION

Rhabdomyosarcoma is one of the most frequent soft tissue sarcomas in children constituting 50% of soft tissue sarcoma in children and adolescence [1]. Rhabdomyosarcoma arises from immature mesenchymal cells and can develop anywhere in the body. Paratesticular rhabdomyosarcoma (RMS) is rare and consists 7% of all rhabdomyosarcomas [1]. Paratesticular rhabdomyosarcoma represents the most common non-germinal malignant tumor in this site [2]. The peak incidence is between 1 to 5 years of age [3].

### Clinical presentation

The clinical presentation includes a short history of painless swelling of the scrotum or mass above testis in a child or a young adult.

### Histopathology

Embryonal rhabdomyosarcoma is the predominant histological subtype in 90% of paratesticular rhabdomyosarcomas and has a good prognosis. Ferrari et al reviewed 216 patients of paratesticular RMS [4]. The histological subtype was embryonal RMS in 181 (84%), alveolar RMS in 18 (8%), spindle cells in 10 (5%), and “not otherwise specified” in 7 (3%) of cases.

### Pattern of Spread

Rhabdomyosarcoma is regarded as a highly malignant tumor with frequent recurrence. Spread of the tumor is mostly by lymphatics to the iliac and para-aortic nodes, but hematogeneous spread does occur, most commonly to the lungs and liver [2,5]. This influences the therapeutic approach in which surgery, chemotherapy and, in selected cases, radiation therapy plays an essential role [6].

### Investigations

Staging work-up includes chest X-ray, CECT of chest, abdomen and pelvis, bone scan and bone marrow examination. Baseline blood investigations include hemogram, renal function tests and liver function tests. Staging is done as per TNM staging and Clinical groups are divided as per IRS guidelines.

### Management

Treatment strategies reviewed in the literature include radical high inguinal orchidectomy, chemotherapy (CCT), radiotherapy (RT) and retroperitoneal lymph node dissection (RPLND) [6-8]. The initial treatment is high inguinal orchidectomy. Trans-scrotal biopsy or trans-scrotal orchidectomy is avoided.

The role of RPLND still remains controversial [9]. Hermans and colleagues described 19 paratesticular RMS patients treated with RPLND, and claimed that a combination of RPLND and systemic CCT afforded a high cure rate [10] Ferrari and colleagues reported on 44 patients with paratesticular RMS who did not undergo RPLND [11]. The authors considered that RPLND was unnecessary for localized disease because of the sensitivity afforded by computed tomography, the potential RPLND associated morbidity, the low rate of retroperitoneal recurrence, and the presumed efficacy of CCT in controlling of microscopic disease. An alternative approach toward the treatment of clinically enlarged retroperitoneal lymph nodes involves the use of a more intensive adjuvant chemotherapy regimen. Such an approach is based on results obtained in the IRS - III trial (the Third Intergroup Rhabdomyosarcoma Study), which showed that patients experienced poor outcomes if treated with RPLND followed by CCT [12] The 5-year survival rates were 69% and 96% in patients with clinically negative nodes treated with and without RPLND, respectively. CCT can control micrometastases into retroperitoneal nodes when a primary tumor has been completely resected.

The efficacy of chemotherapy has diminished the role of surgery and radiotherapy following radical excision in early stages. Ferrari and colleagues reported that CCT was effective to treat childhood RMS, in adjuvant setting [4]. Vincristine, dactinomycin, cyclophosphamide, adriamycin, epirubicin, ifosfamide, carboplatin and etoposide were used in different combinations, and with varying dose schedules, in the cited study. A metaanalysis of genitourinary sarcoma treatments used in 14 randomized trials in various centres showed that doxorubicin-based adjuvant CCT prolonged the time to local recurrence and distant failure, but the data was not statistically significant [13]. Also, such treatment was associated with a considerable degree of toxicity. About a third of patients with paratesticular sarcomas die from metastatic disease.

Radiation therapy is used in conjunction with chemotherapy. It improves local and regional control of disease. It is indicated in selected group I and II patients, and in all group III patients. Newer targeted agents are also being tried in trial settings, namely Sunitinib, lexatumumab, temsirolimus and bevacizumab. Long term results of targeted therapies are awaited.

The combined modalities of surgery, chemotherapy and radiation therapy have greatly improved the survival rate in childhood paratesticular rhabdomyosarcomas without significant long-term complications [14,15]. The actual survival without relapse is 83% and the overall survival rate is 90% [16]. Survival rate depends, with statistical significance, on tumor histology, diameter, stage and location, patient age, response to CCT and metastases status [17,18].

## CONCLUSIONS

Paratesticular rhabdomyosarcomas are rare neoplasms in children with aggressive growth patterns. The management is a paradigm of cooperation between clinicians, surgeons and pathologists from establishing diagnosis to organizing the therapeutic strategy. Radical high inguinal orchidectomy is the primary treatment. Systemic CCT is essential in both early and

advanced disease and has resulted in improved survival outcomes. With new techniques and drugs, there is a significant improvement of therapeutic standard and paratesticular RMS represent a model of therapeutic implementation and achievement in oncology.

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