Pediatric Parameningeal Rhabdomyosarcoma in a Developing Country: Treatment Outcomes With Chemotherapy and VMAT-Based Radiotherapy.

Introduction

Rhabdomyosarcoma is the most common soft-tissue sarcoma in children and adolescents. It is a malignant mesenchymal tumor with skeletal muscle differentiation that can arise in almost any anatomical site, although head and neck, genitourinary, and extremity locations are among the most frequently described sites [1,2]. Among head and neck rhabdomyosarcomas, parameningeal tumors represent a particularly complex subgroup because of their proximity to the skull base, meninges, cranial nerves, orbit, nasopharynx, paranasal sinuses, infratemporal fossa, and central nervous system [3,4].

Parameningeal rhabdomyosarcoma is clinically challenging for several reasons. First, the initial symptoms may be nonspecific and may mimic benign ear, nose, throat, or orbital conditions, leading to diagnostic delay. Second, complete surgical resection is rarely feasible because of the deep anatomical location and the risk of major functional or cosmetic morbidity. Third, local progression may result in skull-base invasion, cranial nerve palsy, meningeal extension, visual impairment, airway compromise, and severe treatment-related toxicity [3,5].

For these reasons, treatment is based on a multimodal approach combining systemic chemotherapy and local therapy, most often radiotherapy. Surgery is usually limited to biopsy or selected conservative procedures. Radiotherapy plays a central role in local control, particularly in unresectable or incompletely resected tumors, and the choice of technique is essential in children because of the proximity of several critical organs and the risk of long-term sequelae [6,7].

During the last decades, improvements in chemotherapy protocols, risk stratification, imaging, radiotherapy planning, anesthesia, and supportive care have improved outcomes in pediatric rhabdomyosarcoma [1,8]. However, in low- and middle-income countries, several barriers continue to compromise treatment results, including delayed diagnosis, limited access to specialized imaging, treatment interruptions, lack of pediatric anesthesia support, nutritional difficulties, and socioeconomic constraints.

Modern radiotherapy techniques, particularly intensity-modulated radiotherapy and volumetric modulated arc therapy, allow more conformal dose delivery to complex target volumes while reducing irradiation of adjacent organs at risk. In pediatric parameningeal rhabdomyosarcoma, this is particularly important

because the target volume is close to the optic nerves, optic chiasm, brainstem, cochleae, pituitary region, salivary glands, oral cavity, and developing craniofacial bones [6,9].

The aim of this study was to describe the clinical characteristics, treatment modalities, acute toxicity, early response, and survival outcomes of children treated for parameningeal rhabdomyosarcoma in a single radiation oncology center in Morocco between 2020 and 2024, and to discuss perspectives for improving care in developing countries.

Materials and Methods

Study design and setting

We conducted a retrospective monocentric study in the Department of Radiation Oncology at the National Institute of Oncology in Rabat, Morocco. The study included children treated for parameningeal rhabdomyosarcoma between January 2020 and December 2024.

Patient selection

All pediatric patients diagnosed with parameningeal rhabdomyosarcoma and referred for radiotherapy during the study period were eligible. Parameningeal sites included tumors arising from or extending to the nasopharynx, nasal cavity, paranasal sinuses, orbit, skull base, or adjacent head and neck regions at risk of meningeal proximity.

Patients were included if they had histologically confirmed rhabdomyosarcoma and available data regarding initial clinical presentation, tumor site, histological subtype, treatment modalities, radiotherapy dose, acute toxicity, response, and follow-up.

Data collection

Data were collected retrospectively from medical records. The following variables were analyzed: age at diagnosis, tumor site, histological subtype, risk group, chemotherapy protocol, radiotherapy technique, total dose, fractionation, acute toxicity, response to treatment, progression, death, duration of follow-up, overall survival, and progression-free survival.

Treatment strategy

All patients received systemic chemotherapy according to IVA +/- IVADO protocols. The IVA regimen, based on ifosfamide, vincristine, and actinomycin D, is widely used in European pediatric rhabdomyosarcoma protocols. The role of adding doxorubicin has been evaluated in high-risk non-metastatic disease, but dose intensification with doxorubicin did not show a significant improvement in outcome compared with standard IVA in the EpSSG RMS 2005 trial [8].

Radiotherapy was delivered using volumetric modulated arc therapy. The prescribed dose was 50.4 Gy in daily fractions of 1.8 Gy. This dose is consistent with commonly used definitive local treatment doses in pediatric rhabdomyosarcoma requiring radiotherapy, particularly for unresected or residual disease [6,7].

Radiotherapy planning was performed according to institutional practice. Target volumes were defined based on clinical examination, diagnostic imaging, initial tumor extension, response to chemotherapy, and anatomical risk structures. Particular attention was given to sparing organs at risk, including optic structures, brainstem, cochleae, pituitary region, oral cavity, salivary glands, and surrounding craniofacial structures.

Response and toxicity assessment

Treatment response was evaluated by imaging after completion of therapy and classified as complete remission, incomplete remission or partial response, tumor progression, or death during treatment.

Acute toxicity during radiotherapy was assessed clinically. The main toxicities recorded were radiomucositis and radiodermatitis. Other acute toxicities were recorded when available in the medical file.

Statistical analysis

Overall survival and progression-free survival were estimated using the Kaplan-Meier method. Because of the small sample size and retrospective nature of the study, results were reported mainly using descriptive statistics. Categorical variables were expressed as numbers and percentages. Continuous variables were expressed as medians and ranges.

Results

Patient characteristics

Nine children were treated for parameningeal rhabdomyosarcoma during the study period. The median age at diagnosis was 5 years, with a range from 4 to 9 years.

Tumor sites were predominantly located in the nasopharyngeal region, observed in four patients, corresponding to 44.4% of cases. Orbital localization was found in three patients, corresponding to 33.3% of cases. One patient had a sinus tumor and one patient had a nasal localization.

The predominant histological subtype was embryonal rhabdomyosarcoma, found in 88.9% of cases. According to the rhabdomyosarcoma risk group classification, most patients were classified as intermediate risk.

Treatment delivered

All patients received systemic chemotherapy according to IVA +/- IVADO protocols. Radiotherapy was delivered using volumetric modulated arc therapy in all cases. The total prescribed dose was 50.4 Gy, delivered in 1.8-Gy fractions.

The use of VMAT allowed conformal irradiation of complex parameningeal target volumes while attempting to reduce dose exposure to adjacent critical organs, particularly optic structures, brainstem, cochleae, oral cavity, and salivary glands.

Acute toxicity

The most frequently observed acute toxicities during treatment were radiomucositis and radiodermatitis. These toxicities were consistent with the expected profile of head and neck irradiation in children, particularly in patients receiving intensive chemotherapy.

Radiomucositis was clinically relevant because of its potential impact on oral intake, hydration, pain control, nutritional status, and treatment tolerance. Supportive care was therefore essential during treatment.

Tumor response and survival

Post-treatment evaluation showed complete remission in five patients. Two patients had incomplete remission or partial response. One patient experienced tumor progression, and one patient died during treatment.

The median follow-up was 12 months, with a range from 5 to 60 months. Among the eight patients with documented follow-up, the estimated 12-month overall survival was 87.5%.

Discussion

Parameningeal rhabdomyosarcoma remains one of the most difficult pediatric soft-tissue sarcomas to manage because of its deep anatomical location and proximity to critical structures. Tumors arising from the nasopharynx, nasal cavity, paranasal sinuses, orbit, and skull base are frequently unresectable or only partially resectable without unacceptable morbidity [3,4]. In our series, the majority of tumors were located in the nasopharyngeal region and orbit, confirming the complexity of local disease management in children.

The median age at diagnosis in our cohort was 5 years, which is consistent with the predominance of rhabdomyosarcoma in young children. Embryonal rhabdomyosarcoma was the predominant histological subtype, observed in 88.9% of cases. Embryonal histology is generally associated with a more favorable

prognosis than alveolar histology; however, parameningeal location is a recognized adverse prognostic factor because of the risk of skull-base involvement, intracranial extension, delayed diagnosis, and local failure [1,3,10].

The treatment delivered in our cohort was based on systemic chemotherapy combined with radiotherapy. This approach is consistent with international multimodal strategies for pediatric rhabdomyosarcoma, where chemotherapy is used to treat systemic microscopic disease and radiotherapy is used to achieve local control [1,6,7]. The use of IVA +/- IVADO protocols is in line with European treatment approaches. In the EpSSG RMS 2005 trial, the addition of dose-intensified doxorubicin to standard IVA chemotherapy did not significantly improve outcomes in patients with high-risk non-metastatic rhabdomyosarcoma, supporting IVA as a key backbone regimen [8].

Radiotherapy is particularly important in parameningeal rhabdomyosarcoma because surgical resection is often not feasible. Local failure remains a major pattern of relapse in rhabdomyosarcoma, especially in patients with gross residual disease or unfavorable local features [5,10]. In this context, adequate radiotherapy dose, precise target delineation, and avoidance of unnecessary treatment delays are essential components of local control.

All patients in our study received VMAT to a total dose of 50.4 Gy in 1.8-Gy fractions. Modern conformal radiotherapy techniques such as IMRT, VMAT, and proton therapy have become important tools in the management of pediatric head and neck rhabdomyosarcoma because they allow improved conformity around complex target volumes and better sparing of organs at risk compared with older conventional techniques [6,9]. Proton therapy has shown promising disease-control rates with favorable toxicity profiles in pediatric rhabdomyosarcoma, particularly for parameningeal tumors; however, access remains limited in many developing countries [9,11]. In such contexts, VMAT represents a realistic and valuable technique when proton therapy is unavailable.

The acute toxicity profile observed in our study was dominated by radiomucositis and radiodermatitis. These toxicities are expected in pediatric head and neck irradiation, especially when radiotherapy is delivered after or during intensive chemotherapy. Although generally manageable, mucositis can have major consequences in children, including pain, reduced oral intake, dehydration, weight loss, infection risk, treatment interruption, and psychological distress. Therefore, supportive care must be considered a central component of treatment rather than a secondary intervention.

The early tumor response in our cohort was encouraging, with five complete remissions and two incomplete responses. Nevertheless, one patient progressed and one death occurred during treatment, underlining the aggressive nature of parameningeal rhabdomyosarcoma and the vulnerability of this pediatric population. The estimated 12-month overall survival of 87.5% among patients with documented

follow-up is promising in a developing-country context. However, the short median follow-up of 12 months limits interpretation of long-term local control, progression-free survival, late relapse, and delayed radiation-related sequelae.

Several factors may influence outcomes in our setting. Delayed diagnosis remains a major concern. Early symptoms of parameningeal rhabdomyosarcoma may be nonspecific and may mimic benign ear, nose, throat, or orbital conditions. Nasal obstruction, epistaxis, otitis, orbital swelling, cranial nerve symptoms, headache, facial pain, or persistent sinusitis-like symptoms may not immediately lead to oncologic imaging. This delay can result in larger tumor volumes at diagnosis, more extensive local invasion, and higher risk of treatment complications [3,4].

Access to timely radiotherapy is another essential issue. In parameningeal rhabdomyosarcoma, delays in local treatment may compromise disease control, particularly in patients with high-risk features or incomplete response to chemotherapy. Therefore, reducing the interval between diagnosis, staging, chemotherapy initiation, radiotherapy simulation, planning, and treatment delivery should be a priority. For children, this also requires access to pediatric anesthesia, immobilization devices, nutritional support, and dedicated multidisciplinary coordination.

The management of pediatric parameningeal rhabdomyosarcoma in developing countries must also address social and logistical barriers. Families may face financial difficulties, long travel distances, limited accommodation near treatment centers, and emotional distress related to the child's diagnosis and prolonged treatment. These barriers may contribute to treatment interruption or delayed follow-up. For this reason, supportive care should include not only medical management, but also psychological, nutritional, and social assistance.

Long-term follow-up is essential in this population. Children treated with head and neck radiotherapy require surveillance for relapse, endocrine dysfunction, growth abnormalities, neurocognitive impairment, dental complications, visual and auditory toxicity, craniofacial development disturbances, and secondary malignancies [6,9,11]. Because several late effects may appear years after treatment, structured survivorship programs are necessary, particularly for children with expected long-term survival.

Our study has several limitations. Its retrospective and monocentric design limits the strength of conclusions. The sample size was small, reflecting the rarity of pediatric parameningeal rhabdomyosarcoma. The median follow-up was relatively short, preventing robust evaluation of long-term survival, progression-free survival, and late toxicity. In addition, molecular data such as FOXO1 fusion status were not available, although these markers are increasingly important for risk stratification and therapeutic decision-making [1,12]. Despite these limitations, this study provides real-life data from a

developing-country radiation oncology center and shows that modern multimodal treatment, including VMAT, can be delivered with encouraging early outcomes when protocols are respected.

In 2025, improvement in the management of pediatric parameningeal rhabdomyosarcoma in developing countries should focus on several priorities: earlier recognition of suggestive symptoms, faster access to diagnostic imaging and biopsy, systematic multidisciplinary tumor boards, availability of pediatric anesthesia for simulation and treatment, optimization of radiotherapy planning, integration of molecular risk stratification when possible, and reinforcement of nutritional, psychosocial, and family support. Establishing national or regional pediatric sarcoma networks could also help standardize treatment pathways, reduce delays, and improve outcomes.

Conclusion

Pediatric parameningeal rhabdomyosarcoma is a rare and aggressive disease requiring rapid, coordinated, and multidisciplinary management. In our experience, chemotherapy according to IVA +/- IVADO protocols combined with VMAT-based radiotherapy to 50.4 Gy provided encouraging early responses and acceptable acute toxicity despite the constraints of a developing-country setting.

The estimated 12-month overall survival of 87.5% among patients with documented follow-up is promising. However, longer follow-up and larger multicenter studies are needed to evaluate long-term disease control, late toxicity, functional outcomes, and quality of life.

Improving outcomes in pediatric parameningeal rhabdomyosarcoma requires earlier diagnosis, timely access to radiotherapy, optimized supportive care, and structured long-term surveillance. In developing countries, reinforcing pediatric oncology networks and multidisciplinary care pathways should be a major priority.

Declarations

Ethics approval

This retrospective study was conducted using anonymized patient data collected from medical records. Institutional approval should be obtained according to local requirements.

Consent for publication

Not applicable, as no directly identifying patient information is included.

Availability of data

The data supporting the findings of this study are available from the corresponding author upon reasonable request and according to institutional regulations.

Competing interests

The authors declare no competing interests.

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