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(CASE REPORT)

Ethmoidal–nasal alveolar rhabdomyosarcoma in an adolescent: The contribution of radiotherapy in a high-risk case

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Abstract

Alveolar rhabdomyosarcoma (ARMS), a histological subtype associated with a poorer prognosis, represents an aggressive form of the disease. In the ethmoidal–nasal region, the proximity of critical structures such as the orbit and the skull base presents significant diagnostic and therapeutic challenges.

We report the case of a 15-year-old adolescent presenting with sudden-onset right exophthalmos secondary to an alveolar RMS with orbital, sinus, and basifrontal extension. A multimodal treatment approach was initiated, including ifosfamide–vincristine–actinomycin (IVA) chemotherapy followed by intensity-modulated radiation therapy (IMRT) delivered concomitantly with chemotherapy. The treatment was overall well tolerated. Immediate post-treatment imaging showed slight tumor regression, and at 18 months a marked regression of both the tumor and cervical lymphadenopathies was observed after maintenance therapy combining actinomycin, cyclophosphamide, and vinorelbine.

This case highlights the importance of a multimodal therapeutic strategy and multidisciplinary management in high-risk ethmoidal–nasal RMS. Long-term surveillance remains essential to optimize prognosis and allow early detection of recurrence.

Keywords: Alveolar Rhabdomyosarcoma; Ethmoidal Tumor; Orbital Extension; IMRT Radiotherapy; Multidisciplinary Approach

1. Introduction

Rhabdomyosarcoma (RMS) is the most common soft-tissue sarcoma in children and adolescents, accounting for approximately 5% of all pediatric cancers [1]. It arises from primitive mesenchymal cells with myogenic differentiation and includes several histological subtypes. Among these, the alveolar form is distinguished by greater biological aggressiveness and a less favorable prognosis compared with the embryonal subtype [2]. Head and neck tumors represent nearly one-third of all cases, but sinonasal involvement particularly ethmoidal is rare, accounting for only a small proportion of pediatric RMS [3].

Due to the rarity of sinonasal RMS, the literature relies mainly on small case series and isolated clinical reports. Optimal management requires a multidisciplinary approach involving pediatric oncologists, surgeons, radiologists, and radiation oncologists, in order to best tailor therapeutic sequences and optimize tumor control.

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We report here the case of a locally advanced ethmoidal–nasal alveolar rhabdomyosarcoma in a 15-year-old adolescent, revealed by right-sided exophthalmos and characterized by orbital and intracranial extension. The patient was treated with a combined chemotherapy (CT) and radiotherapy strategy, achieving good local control during follow-up.

2. Case report

We report the case of a 15-year-old child with no significant medical history who had presented for one month with sudden and progressive right-sided exophthalmos (Figure 1) along with transient spontaneous redness of the eye, the rest of the physical examination being unremarkable, a cervicofacial magnetic resonance imaging (MRI) scan revealed a lesion centered on the right ethmoidal cells measuring 55 × 35 × 50 mm (AP × T × H) with the following extensions and anatomical relationships: laterally it breached the orbital floor and ipsilateral lamina papyracea extending into the orbit and causing grade I ipsilateral exophthalmos and it came into contact with the medial and inferior rectus muscles with loss of the intervening fat plane, medially it eroded the nasal septum and extended into the left posterior ethmoidal cells, superiorly it eroded the right cribriform plate and the posterior wall of the ethmoid with intracranial basifrontal extension, inferiorly it widened the right maxillary sinus meatus with intrasinus extension resulting in fluid retention and eroded the ipsilateral superior and middle nasal turbinates, posteriorly it eroded the anterior wall of the sphenoid sinus with intrasinus extension and associated fluid retention (Figure 2)

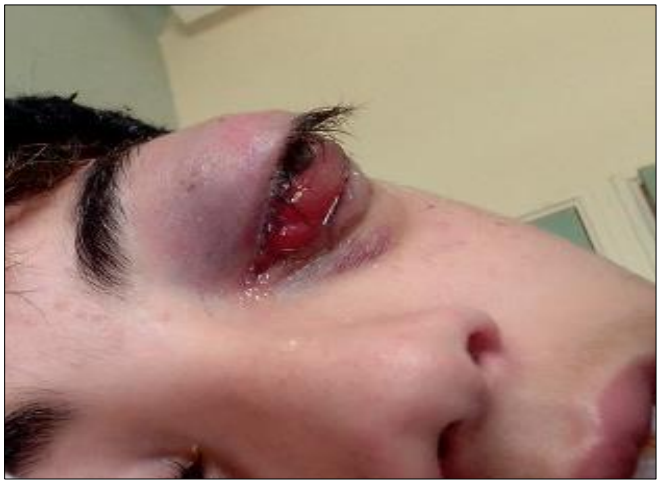

Figure 1 Clinical image showing right-sided exophthalmos

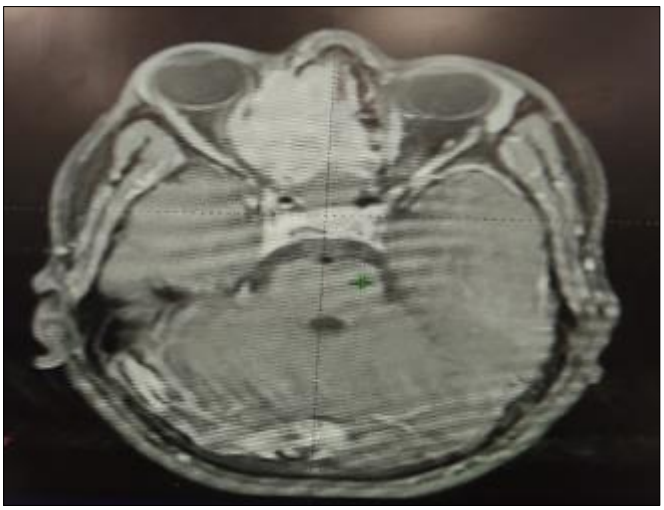

Figure 2 Initial T1 GADO sequence showing the T1 isointense tumor exerting a mass effect on the right orbit

A nasosinusal biopsy performed under general anesthesia (GA) showed, on pathological examination, bone infiltration by an undifferentiated malignant small round cell tumor. Immunohistochemical analysis supported a diagnosis of alveolar RMS, with diffuse and strong nuclear expression of myogenin; the cytoplasm showed strong positivity for desmin; CD99 expression was moderate and likely nonspecific; there was no expression of the lymphoid markers CD20 and CD30, no expression of HMB45, and no expression of synaptophysin or chromogranin.

A staging workup consisting of cervico-thoraco-abdomino-pelvic computed tomography (CTAP) revealed right lateral cervical lymphadenopathies (levels 3, 2A, and 2B). Given that the patient was classified as very high risk (N+), the workup was completed with a bone marrow biopsy (BMB), scintigraphy, and lumbar puncture (LP), all of which returned negative results.

Due to the tumor size and the risk of local functional damage, surgery was not indicated, and chemotherapy was initiated, consisting of six cycles combining ifosfamide, vincristine, and actinomycin (IVA). A treatment response assessment was performed after four cycles: the orbital CT scan showed clear regression in the size of the tumor centered on the right nasal cavity, now limited to the ipsilateral ethmoidal cells. However, there was an increase in the size of the right spinal cervical lymph nodes (25 mm versus 14 mm). Two additional cycles of IVA were added, and no follow-up imaging was performed at that stage

Radiotherapy was delivered using an IMRT technique following a strategy of hierarchical sequential volumes. The first dose level consisted of 41.4 Gy administered to the initial tumor volume (gross tumor volume (GTV), pre-chemotherapy) as well as to the cervical lymph node regions at risk. A first boost (total dose 50.4 Gy) was delivered to the residual tumor visible after induction CT and to the right spinal lymph node. Finally, a second boost focused on the tumor residue brought the total dose to 55.8 Gy (figure 3-4), concomitant with three cycles of CT combining ifosfamide and vincristine, without actinomycin given the risk of pulmonary toxicity. During treatment, the patient developed bacterial conjunctivitis of the right eye and febrile neutropenia requiring hospitalization.

A cranio-cervical CT scan performed immediately after concomitant radiochemotherapy (CRT) showed a slight decrease in the size of the tumor centered on the right ethmoidal cells, as well as complete regression of the right cervical lymphadenopathies. The patient then received maintenance CT consisting of three cycles of actinomycin followed by six cycles of cyclophosphamide plus vinorelbine, with an evaluation CT scan showing disease stability (DDC on 09/08/23). Eighteen months after completion of radiotherapy, a follow-up MRI showed no evidence of recurrence (Figure 5). A long-term radiation-induced adverse effect was right-eye cataract, which was managed surgically.

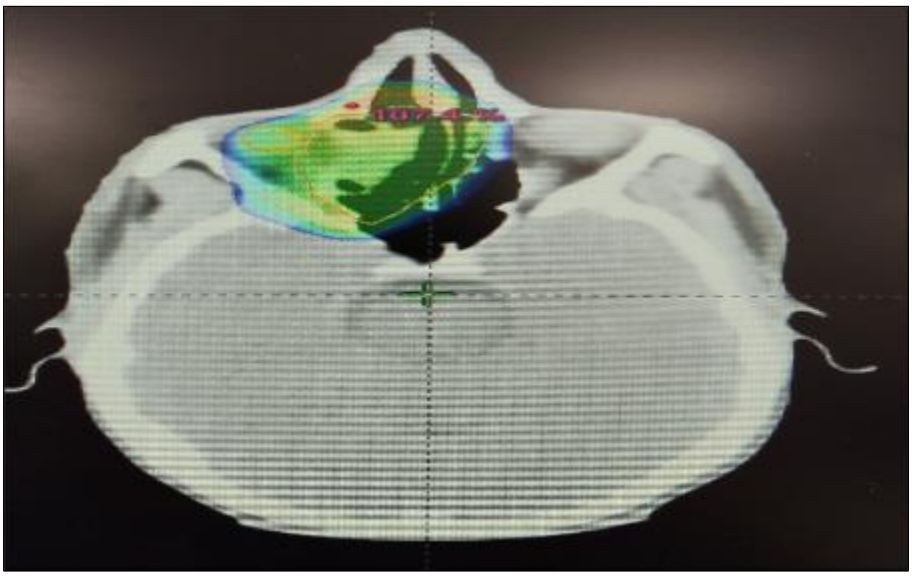

Figure 3 Dose distribution on the residual ethmoidal–nasal tumor volume

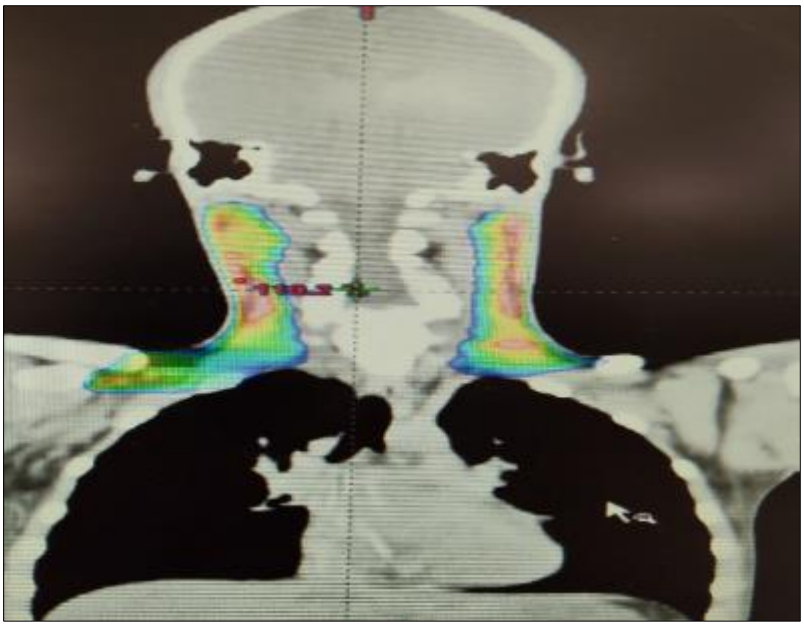

Figure 4 Dose distribution on the cervical target volumes

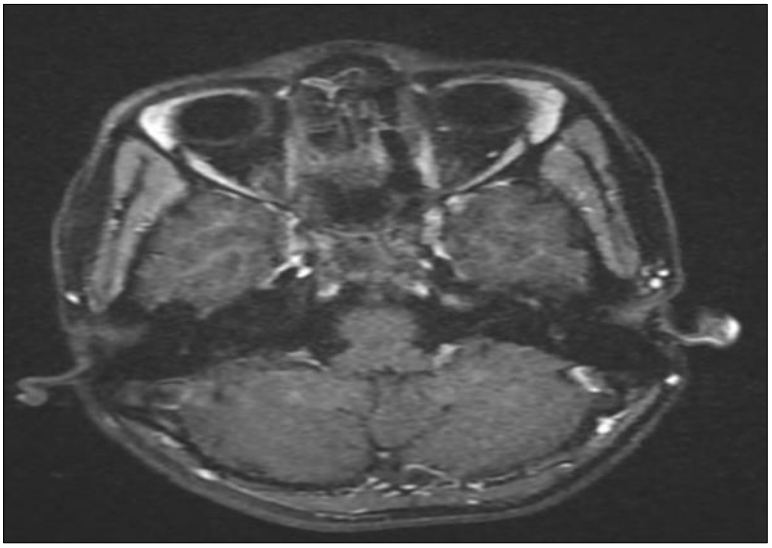

Figure 5 T1 GADO MRI sequence showing complete tumor regression two years after treatment

3. Discussion

ARMS is an aggressive form of pediatric RMS, accounting for approximately 20% of cases. It is characterized by increased aggressiveness and a high propensity for lymph node involvement, particularly in cervicofacial forms, which often leads to an advanced presentation at diagnosis [4].

Head and neck locations are common, but ethmoidal–nasal involvement remains rare and presents diagnostic challenges due to the anatomical complexity of the region and the proximity of critical structures, notably the orbit and skull base [5]. In this confined anatomical context, the clinical presentation may become rapidly suggestive because of the absence of a large expansile space: the exophthalmos observed in our patient thus reflects early orbital invasion, which is frequently associated with ethmoidal tumors. Several series have reported similar rapidly progressive presentations, including nasal obstruction, epistaxis, or ocular protrusion [6].

Our case fits fully within this pattern, with rapidly progressive symptoms and significant locoregional extension at the time of diagnosis. Parameningeal extension, widely described in pediatric ethmoidal and paranasal tumors, represents a well-documented unfavorable prognostic factor: studies have shown that skull base erosion, intracranial extension, and age >10 years are associated with a significant decrease in survival rates [7].

From a histopathological standpoint, ARMS is characterized by strong and diffuse expression of muscle differentiation markers, particularly myogenin and MyoD1, which is a key element for diagnosis and helps distinguish it from other small round-cell tumors of the ENT region [8]. Moreover, the identification of PAX3-FOXO1 or PAX7-FOXO1 fusions further supports the diagnosis of the alveolar subtype and carries important prognostic significance, as these alterations are strongly associated with a more aggressive tumor biology [8,9]. In our case, although molecular analysis was not performed, the immunoprofile (diffuse myogenin and desmin expression, absence of lymphoid and neuroendocrine markers) was typical of an alveolar RM. This subtype, combined with the presence of cervical lymph node involvement, places the patient in the high-risk group according to the European recommendations of the European Paediatric Soft Tissue Sarcoma Study Group (EpSSG), thereby guiding the choice toward a more intensive multimodal therapeutic strategy [10].

In our observation, surgical excision was not considered because of the major functional risk associated with orbital and intracranial extension. This approach is consistent with data from the literature on RMSs arising from parameningeal sites, particularly the paranasal sinuses, where surgery plays a limited role due to the proximity of critical structures and the difficulty in achieving complete resection without significant morbidity. Merks et al. [7] indeed report that, in these locations, the impact of surgery on tumor control is limited, thus justifying the preferential use of chemotherapy and radiotherapy to ensure local control.

The patient was therefore treated according to the European EpSSG/Frontline and Relapsed RhabdoMyoSarcoma (FaR-RMS) recommendations, which advocate an induction regimen of the IVA type, currently considered the standard protocol for high-risk pediatric or adolescent forms [11].

Guidelines from the European Society for Paediatric Oncology (SIOPE) confirm that vincristine–actinomycin–cyclophosphamide (VAC) and IVA protocols constitute the cornerstone of initial systemic therapy in locally advanced rhabdomyosarcoma [12].

Similarly, recent reviews emphasize that vincristine–actinomycin cyclophosphamide/ifosfamide-based combinations represent the conventional reference chemotherapy in RMS, including the alveolar subtype [13].

Local control therefore relied on radiotherapy, in accordance with EpSSG and FaR-RMS recommendations, which advocate its early integration for all high-risk tumors, regardless of the feasibility of a surgical procedure [11,12]. In line with these standards, our patient received irradiation of the initial tumor volume using a hierarchical sequential strategy, a commonly favored approach for paranasal locations to optimize target-volume coverage while respecting dose-constraint thresholds for organs at risk. The delivered doses fully adhered to SIOPE and FaR-RMS recommendations for high-risk forms: an initial level of 41.4 Gy to the pre-chemotherapy GTV and involved lymph node regions, followed by a first boost bringing the dose to 50.4 Gy, and then a second boost targeted at the residual tumor reaching 55.8 Gy. This regimen is consistent with contemporary approaches recommending doses between 50.4 Gy and 59.4 Gy for unresected or incompletely resected tumors [11,12]. The technique used—IMRT/VMAT (Volumetric Modulated Arc Therapy)—is currently the preferred modality for tumors of the skull base and paranasal sinuses. Guidelines emphasize the use of highly conformal techniques to ensure an optimal dose gradient around sensitive structures such as the optic nerve, orbital contents, and frontal lobes [11,12]. In this type of location, proton therapy represents a potentially advantageous alternative thanks to its substantial reduction in dose to healthy tissues. However, its indication depends on availability and on individual dosimetric evaluation [14,15]. In our case, IMRT enabled treatment planning that met ophthalmic and neurological dose constraints while maintaining satisfactory tumor control. Irradiation of the regional lymph node areas is also consistent with current recommendations, as any documented N+ involvement must be treated with radiotherapy, with radical lymph node dissection now discouraged in most pediatric cases [11,12].

The concomitant integration of chemotherapy—here vincristine and ifosfamide—is likewise in accordance with FaR-RMS protocols and contributes to potentiating the locoregional effect of radiotherapy. As part of the continued management and in order to reinforce systemic control, maintenance chemotherapy was initiated in accordance with recent recommendations. Maintenance therapy has indeed emerged as an essential component in the treatment of high-risk RMS, supported by the results of the RMS2005 trial, which demonstrated the efficacy of a 6-month regimen combining vinorelbine and oral cyclophosphamide in reducing the risk of relapse [16]. In our case, the patient was

treated following this therapeutic principle, receiving first actinomycin D and then a vinorelbine–cyclophosphamide sequence in accordance with FaR-RMS protocols.

At the end of treatment, radiological assessment showed a marked regression of the ethmoidal lesion and complete disappearance of lymphadenopathy an encouraging outcome in a location known to be particularly difficult to control. Finally, prolonged surveillance remains indispensable, especially for alveolar RMS, which carries a risk of late relapse. The absence of recurrence at one and a half years in our case is an indicator of good locoregional control, although long-term follow-up remains an essential requirement according to international FaR-RMS recommendations.

Abbreviations

- **ARMS**: alveolar rhabdomyosarcoma;
- **IVA**: ifosfamide–vincristine–actinomycin regimen;
- **IMRT**: intensity-modulated radiation therapy;
- **CT**: chemotherapy;
- **MRI**: magnetic resonance imaging;
- **GA**: general anesthesia;
- **CT CAP**: cervico-thoraco-abdomino-pelvic computed tomography;
- **BMB**: bone marrow biopsy;
- **LP**: lumbar puncture;
- **CCRT**: concurrent chemoradiotherapy;
- **EpSSG**: European Paediatric Soft Tissue Sarcoma Study Group;
- **FaR-RMS**: Frontline and Relapsed RhabdoMyoSarcoma;
- **SIOPE**: European Society for Paediatric Oncology;
- **VAC**: vincristine–actinomycin–cyclophosphamide;
- **VMAT**: Volumetric Modulated Arc Therapy

4. Conclusion

Ethmoid–nasal ARMS represents a rare entity with an unfavorable prognosis, particularly when associated with lymph node involvement and complex locoregional extensions. This case highlights the importance of an integrated therapeutic strategy based on effective induction chemotherapy, rigorous conformal radiotherapy, and maintenance chemotherapy consistent with recent protocols. The complete response obtained underscores the impact of modern therapeutic approaches, although prolonged surveillance remains essential given the risk of late relapse characteristic of this aggressive subtype.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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