



Rare Adult-Onset Nasopharyngeal Botryoid Embryonal Rhabdomyosarcoma: A Case Report and Review of Literature

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ABSTRACT

Botryoid embryonal rhabdomyosarcoma (RMSs) is a rare malignant tumor typically seen in children, with common sites including the vagina, bladder, and nasopharynx. Its occurrence in adults, is extremely rare, with a very limited number of cases in the nasopharynx. This case report highlights the unusual presentation of the disease and its treatment follow-up. A 46-year-old male presented with a painless neck mass and weight loss. Imaging revealed a parapharyngeal mass with cervical lymphadenopathy, and biopsy confirmed nasopharyngeal botryoid embryonal RMS. Due to the tumor's proximity to critical structures, surgical resection was not feasible. The patient received vincristine, actinomycin-D, and cyclophosphamide, chemotherapy followed by radiotherapy, achieving complete radiological remission. However, regional recurrence was detected three months post-treatment, necessitating a switch to ifosfamide and etoposide chemotherapy. This case highlights the challenges of diagnosing and treating adult-onset nasopharyngeal botryoid embryonal RMS, emphasizing the importance of vigilant follow-up and tailored treatment strategies. Given its rarity, this report provides valuable insights into the management of adult RMS.

Keywords: Botryoid embryonal rhabdomyosarcoma; adult rhabdomyosarcoma; nasopharyngeal tumor; VAC chemotherapy; radiotherapy

INTRODUCTION

Rhabdomyosarcomas (RMSs) are malignant neoplasms arising from immature myogenic stem cells, comprising less than 5% of all soft tissue tumors. While RMS is predominantly diagnosed in children and adolescents, approximately 40% of cases occur in adults.¹ In children, RMS most commonly occurs in the head and neck region, with an incidence rate of approximately 40%.²⁻⁴ However, in adults, RMS is more frequently observed in the extremities, showing a distinct distribution pattern compared to pediatric cases.

Head and neck RMSs (HNRMS) primarily arise from orbital, parameningeal, or non-orbital non-parameningeal regions. These tumors spread via direct invasion, hematogenous routes, or lymphatic metastasis. At diagnosis, metastases are

present in fewer than 25% of cases, most involving a single site.⁵

RMSs are classified into four histologic subtypes: embryonal, alveolar, pleomorphic, and spindle cell/sclerosing. The embryonal subtype, accounting for 50-60% of cases, includes the rare botryoid variant, typically seen in the vaginal and bladder walls of infants and, less commonly, in the nasopharynx of children. To date, nasopharyngeal botryoid RMS has not been reported in adults.

Nasopharyngeal RMS poses significant mortality risks due to its potential for intracranial invasion and distant metastasis.⁵ Advances in systemic therapies have improved 5-year survival rates for parameningeal tumors from 20% in the 1970s to 50-75%. However, surgical options remain limited by proximity

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to critical structures, making radiotherapy essential for local control.^{6,7}

In this report, we present a case of nasopharyngeal botryoid embryonal RMS in an adult who achieved complete radiologic response following curative chemotherapy and radiotherapy.

CASE REPORT

A 46-year-old male presented with a neck mass. He had no significant medical history, and his family history was unremarkable. A review of systems indicated a 10% weight loss over the past three months, but no other symptoms, such as shortness of breath, epistaxis, headache, or dizziness, were reported. On physical examination, fixed and painful lymphadenopathy was noted in levels I, II, and III according to Robbins' classification.⁸ The largest node, measuring approximately 3 cm, was located posterior to the left sternocleidomastoid muscle. The otolaryngologic evaluation revealed a mass in the nasopharynx, prompting a tru-cut biopsy of both the nasopharyngeal mass and the cervical lymph node. In this case, the tumor invades adjacent structures and involves regional lymph nodes without distant metastasis, classifying it as T3N1M0 according to the tumor, lymph node, metastasis (TNM) staging system. Percutaneous core needle biopsy (CNB) is a minimally invasive, highly accurate diagnostic tool, achieving 87-92% accuracy for malignancy and 80-83% for histological subtypes, comparable to incisional biopsy but with fewer complications.⁹ CNB provides sufficient tissue for diagnosing head and neck sarcomas while minimizing morbidity, particularly when guided by imaging modalities. Its cost-effectiveness, reduced recovery time, and safety make it ideal for deep-seated tumors like parapharyngeal masses, as in this case, where a precise, low-risk approach was essential.

Pathology

Pathological examination revealed neoplastic cells that were consistent with a diagnosis of botryoid embryonal RMS, as shown in Figure 1. Given the rarity of this condition in adults, particularly in the nasopharyngeal region, a second opinion was sought from a specialized center, which confirmed the initial diagnosis.

Imaging

Neck MRI revealed a 48x30 mm parapharyngeal mass occupying the left Rosenmüller fossa of the nasopharynx. The mass exhibited indistinct borders with the soft palate and extended distally into the inframaxillary fossa. Additionally, a 25x20 mm soft tissue lesion, shown in Figure 2, was identified at the level of the left lacrimal sac, extending into the nasolacrimal duct. Systemic imaging with thoracic and abdomen computed tomography (CT) revealed no evidence of distant metastasis.

Treatment

The patient was started on a chemotherapy regimen consisting of: vincristine, actinomycin-d, and cyclophosphamide (VAC), with doses of Vincristine 1.4 mg/m², Actinomycin-D 1.5 mg/m², and Cyclophosphamide 1,500 mg/m², administered every 3 weeks. After three cycles, clinical regression of the cervical lymph nodes and the nasopharyngeal mass was observed. Follow-up neck CT demonstrated near-complete regression of both the nasopharyngeal mass and the cervical lymphadenopathy shown in Figure 3.

Following this, the patient received an additional course of VAC chemotherapy and proceeded to radiotherapy. A total of 50.4 Gy of radiotherapy was delivered to the primary tumor and the involved lymphatic regions over 28 fractions. The treatment resulted in grade 1 and grade 2 acute radiodermatitis in the neck region and grade 1 esophagitis. These adverse effects were resolved with symptomatic management, and the patient continued with follow-up care without further medication.

Follow-up

A CT of the nasopharynx, performed three months after the completion of radiotherapy, revealed a soft tissue lesion measuring approximately 13-14 mm in diameter. This mass extended from the medial canthus plane into the deep subcutaneous tissue of the dorsum of the nose within the medial aspect of the left orbit. The lateral pharyngeal recess appeared narrower on the left side compared to the right, and the soft tissue density in the left parapharyngeal-retropharyngeal region showed mild heterogeneity in comparison to the right side. The piriform sinus was also narrowed on the left, though no significant pathological density was noted on the mucosal surfaces.

A soft tissue biopsy confirmed a diagnosis of embryonal RMS. Immunohistochemical analysis showed diffuse positive staining for MYO-D1, desmin, and CD56, while negative staining was observed for CD20, CD3, TTF1, chromogranin, and synaptophysin. Myogenin staining did not contribute to the diagnosis. The Ki-67 proliferation index was approximately 50%, indicating a high rate of cellular proliferation.

The treatment plan included three additional cycles of VAC chemotherapy, ensuring that the cumulative dose of Adriamycin would not exceed 550 mg/m². Following the completion of VAC, the patient was scheduled for ifosfamide 1,800 mg/m²/day, etoposide 100 mg/m²/day, and mesna 1,080 mg/m²/day (IE) administered over five days, with cycles planned every three weeks.

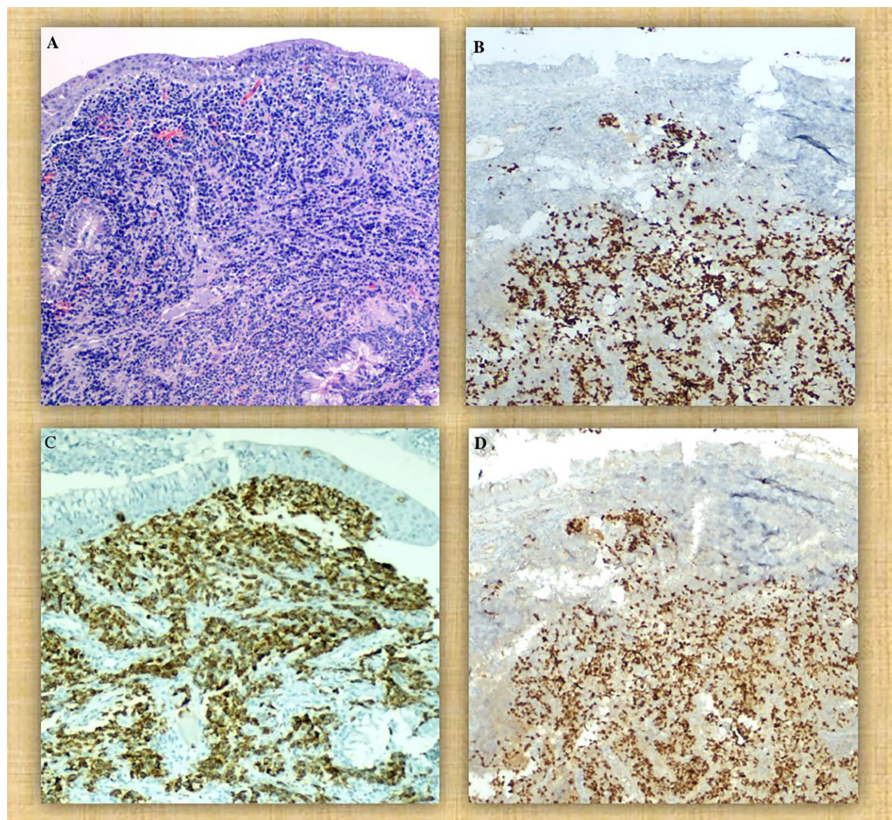


FIGURE 1: Histopathological features of nasopharyngeal botryoid embryonal rhabdomyosarcoma.

Representative histopathological images of the tumor at diagnosis.

(A) Hematoxylin and eosin staining demonstrates the characteristic morphology of tumor cells, including round to spindle-shaped nuclei and hypercellularity (400×).

(B) Immunohistochemical staining for MyoD1 shows diffuse positivity (400×).

(C) Positive desmin staining highlights the skeletal muscle differentiation of the tumor cells (400×).

(D) Myogenin staining further confirms the myogenic origin of the tumor (400×).



FIGURE 2a: Magnetic resonance imaging (MRI) of the parapharyngeal mass at diagnosis. Axial T1-weighted MRI shows a 48×30 mm irregular parapharyngeal mass (white arrow) originating in the left Rosenmüller fossa. The lesion demonstrates cystic and necrotic components, with poorly defined borders extending into the infratemporal fossa and soft palate. Infiltration of adjacent structures, including the medial pterygoid muscle, is evident, suggesting advanced local invasion.

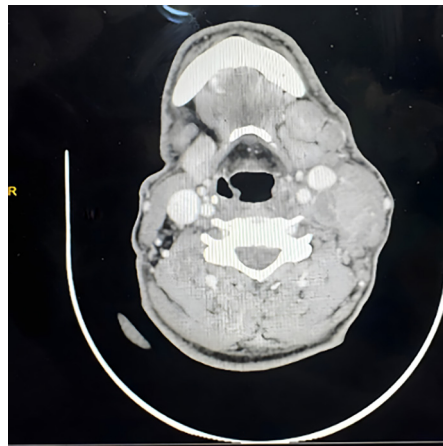


FIGURE 2b: Computed tomography (CT) Imaging of cervical lymphadenopathy at presentation. CT imaging reveals multiple enlarged cervical lymph nodes in levels I, II, and III. The largest node measures approximately 25 mm in diameter, located posterior to the left sternocleidomastoid muscle. The nodes exhibit heterogeneous signal intensity, indicative of metastatic involvement.

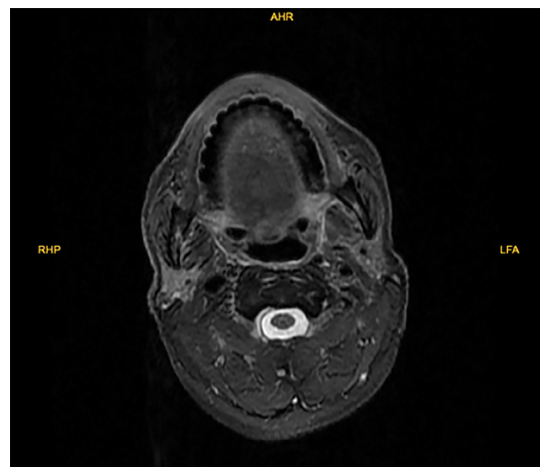


FIGURE 3a: Post-treatment magnetic resonance imaging (MRI) indicating radiological resolution of the nasopharyngeal tumor. MRI imaging after three cycles of vincristine, actinomycin-d, and cyclophosphamide chemotherapy demonstrates near-complete regression of the nasopharyngeal tumor. The Rosenmüller fossa and adjacent structures, including the soft palate and infratemporal fossa, show normal anatomical contours with no evidence of residual tumor or abnormal signal.

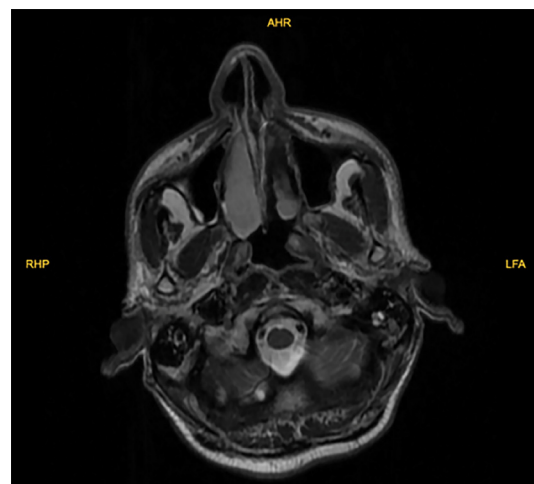


FIGURE 3b: Follow-up magnetic resonance imaging (MRI) showing complete resolution of cervical lymphadenopathy. MRI imaging obtained after combined chemotherapy and radiotherapy depicts complete regression of cervical lymphadenopathy. Levels I, II, and III show no residual nodal enlargement or abnormal signal, confirming effective treatment of regional metastases.

DISCUSSION

RMS is a malignant tumor originating from myogenic stem cells and represents a small fraction of all soft tissue tumors. Immunohistochemical evaluation typically reveals positive staining for desmin, actin, and myosin. This tumor is most commonly observed in children, particularly between the ages of 0 and 4, with an incidence of approximately 4 cases per million. Around 20% of cases occur in adults.¹⁰ The majority of RMS cases are sporadic, although mutations in the RAS and Hedgehog signaling pathways have been identified as predisposing factors.¹¹

RMSs commonly occur in the head and neck region in children and adolescents, whereas in adults, they are more frequently found in the extremities. These tumors originate from undifferentiated mesodermal cells and exhibit phenotypic and biological characteristics of primitive skeletal muscle. There are four recognized histologic subtypes: embryonal, alveolar, pleomorphic, and spindle cell/sclerosing, with the alveolar type being the most common. Within the embryonal subtype, a rare variant known as botryoid RMS exists. This distinct subtype is typically localized in the vaginal and bladder walls of infants and the nasopharynx of older children.¹² Fewer than 10 cases of childhood nasopharyngeal botryoid embryonal RMS have been documented in the literature. This case represents the first reported instance of botryoid embryonal RMS occurring in an adult. Reported

adult-onset embryonal RMS cases are listed in Table 1 and Table 2.

Microscopically, botryoid embryonal RMS is characterized by spindle to round cells with hypercellularity, significant mitotic activity, and areas of necrosis. Immunohistochemically, the tumor typically stains positive for desmin, myogenin, and MyoD1. The absence of *FOXO1* gene fusion is a key feature that helps differentiate it from the alveolar subtype of RMS. In alveolar RMS, small, circular rhabdomyoblasts are typically arranged in nests or cords, separated by connective tissue trabeculae, with focal areas displaying alveolar architecture.⁵ In our study, the tumor's morphology was consistent with RMS, and immunohistochemical analysis revealed diffuse staining for desmin, myogenin, and MyoD1. The diagnosis was independently confirmed by two pathologists, further supporting the findings.

HNRMS presents significant prognostic challenges, primarily influenced by the metastatic potential of the primary tumor site. Orbital RMS, the least aggressive subtype, is associated with a favorable 5-year survival rate of 84% and minimal incidence of distant metastasis. In contrast, parameningeal RMS, involving regions such as the paranasal sinuses and nasopharynx, demonstrates regional lymph node involvement in 45.2% of cases and distant metastasis in 11.9%, leading to a 5-year survival rate of 49.1%. Non-orbital, non-parameningeal RMS shows an intermediate prognosis, with a 5-year survival

TABLE 1: Adult-onset nasopharyngeal embryonal rhabdomyosarcoma cases.

Age/sex	Head and neck location	Presentation	Treatment	Outcome	Reference
58/male	Maxillary sinus	Numbness/swelling of the left cheek	Surgery	No recurrence	Liu et al. ²³ 2023
51/male	Right nasal cavity, nasopharynx, cervical	Unilateral painless neck mass and nasal obstruction	Chemoradiotherapy	Spinal metastasis after 6 months and death	Alaraifi et al. ²⁴ , 2022
18/female	Right nasal cavity	Right side nasal obstruction for 5 months	Surgery	No recurrence after 4 months	Fatah et al. ²⁵ , 2022
34/male	Left nasal cavity extending to sphenoid sinus	Left nasal cavity mass, nasal obstruction	Chemotherapy	Death after 2 weeks	Kwatra et al. ²⁶ , 2020
25/male	Sinonasal area extending to right frontal lobe	Headache, nasal congestion, right sided vision impairment	Chemoradiotherapy+surgery	No recurrence after 2 years	Palacios et al. ²⁷ , 2013
58/female	Between rosenmüller fossa and base of the tongue	Sore throat, dysphagia and temporary hoarseness	Chemoradiotherapy+surgery	No recurrence after 4 years	Osuch-Wójcikiewicz et al. ²⁸ , 2004
28/male	Paranasal sinus invading the left cavernous sinus	Headache, abducent nerve palsy	Chemoradiotherapy	No recurrence	Arita et al. ²⁹ , 2001
78/female	Left nasal cavity and nasopharynx	Nasal congestion	Chemotherapy+surgery	No recurrence after 1 year follow-up	Jund et al. ³⁰ , 1998

Number of cases	Age range	Subtypes	Outcome	Reference
27	18-65	14 embryonal, 7 alveolar, 6 mixed	No outcome data	Liu et al. ³¹ , 2023
35	No age data	22 embryonal, 13 alveolar	The 5-year overall survival rate of adult nasal sinus rhabdomyosarcoma was 2.9% after 9-62 months of follow-up.	Li et al. ³² , 2020
13	19-86	3 embryonal, 9 alveolar, 1 unknown	33% mortality rate with approximately 2 years follow up	Montone et al. ³³ , 2009

rate of 70.3%. Survival outcomes are closely tied to disease extent. Localized RMS achieves a 5-year survival rate of 92.4%, which decreases to 60.1% with regional spread and further to 36.6% in cases of distant metastasis.^{13,14} Distant metastasis is a primary cause of treatment failure in HNRMS, with common metastatic sites including the lungs (25%) and bones (50%). Larger tumor sizes (greater than 5 cm) and lymph node involvement significantly reduce locoregional recurrence-free survival (LRFS), with rates decreasing from 85% in node-negative patients to 50% in those with node-positive disease. The alveolar subtype, more likely to metastasize than the embryonal subtype, is associated with poorer outcomes. Although systemic chemotherapy is a cornerstone of treatment, its ability to prevent metastasis remains limited, with an overall response rate of 51.8%. A combination of surgery and radiotherapy improves local control, achieving a 5-year LRFS of 73.6% compared to 64.2% for radiotherapy alone. These findings highlight the importance of early diagnosis, comprehensive multimodal management, and exploration of novel systemic therapies, including targeted agents and immunotherapy, to better address the metastatic spread and improve survival outcomes in HNRMS.^{13,14} The rates of lymph node metastasis (LNM) in RMS vary significantly based on histological subtype and primary tumor location, highlighting the biological and anatomical factors influencing lymphatic spread. Among histological subtypes, alveolar RMS (ARMS) demonstrates the highest rate of LNM at 60 percent, followed by other subtypes, including spindle cell, sclerosing, and pleomorphic variants, at 48.2 percent, and embryonal RMS (ERMS) at 32.6 percent. These variations reflect the more aggressive nature of ARMS compared to ERMS. Regarding tumor location, parameningeal tumors exhibit a significantly higher rate of LNM with 47.7 percent compared to 11.1 percent in non-parameningeal tumors. The rich lymphatic network in parameningeal regions, such as the nasopharynx and Waldeyer's ring, facilitates regional nodal involvement, while proximity to the midline promotes contralateral and bilateral spread.¹⁵

The symptoms of RMS vary based on its anatomical location. Parameningeal RMSs, such as those in the nasopharynx, often present with epistaxis, nasal obstruction, rhinorrhea,

or recurrent otitis media. Superficially located RMSs typically appear as either painless or painful masses. Tumors arising from the paranasal sinuses may present with local pain, epistaxis, nasal obstruction, hearing loss, or sinusitis. The interval from symptom onset to diagnosis is generally under 9 months. In our case, the patient presented with a painless, palpable neck mass, and a subsequent evaluation revealed a history of weight loss.

Prognosis for RMSs is influenced by several factors, including histologic subtype, age at diagnosis, surgical resection status, tumor stage, and location. Positive prognostic indicators include the botryoid subtype, complete (R0) resection, diagnosis between the ages of 1 and 9, and early-stage disease. Conversely, tumors located in the extremities are associated with a less favorable prognosis.¹⁶

In this case, the tumor was classified as T3N1M0 under the TNM staging system, indicating a locally advanced tumor with regional lymph node involvement but no distant metastasis. Surgical resection was a cornerstone in managing RMS but was not pursued due to several factors. The tumor's location in the nasopharynx and invasion into adjacent critical structures, such as the infratemporal fossa and surrounding soft tissues, posed significant challenges for achieving a complete (R0) resection. Additionally, the involvement of level II and III lymph nodes further complicated surgical feasibility, highlighting the necessity of addressing regional disease through systemic and local therapies. Given the functional and cosmetic implications of head and neck surgeries, particularly in sensitive areas like the nasopharynx, a multimodal approach combining systemic chemotherapy and radiotherapy was deemed optimal. For radiotherapy planning, especially when lymphatic regions are included, a dose of 50.4 Gy over 28 fractions is recommended.⁵ Systemic therapy is another strategy of RMS management, though optimal chemotherapy regimen has not been universally established. In the present case, the patient was classified as stage 3 at diagnosis and initially assessed for local intervention. However, surgical resection was not feasible due to tumor involvement with vital structures. After three cycles of VAC chemotherapy, the patient demonstrated a

complete radiological response. Following a fourth cycle of VAC, definitive radiotherapy was administered to consolidate treatment. Despite initial success, regional recurrence was detected shortly after completing therapy, showing the challenges of local disease control in advanced-stage RMS.

Due to the poor prognosis of RMS, novel strategies being developed to improve outcomes for patients. These treatment strategies include immunotherapies and novel targets for nanomedicine.^{17,18} Because of the non-immunogenic nature of RMS, immunotherapy must be carefully selected for each case. Bertolini et al.¹⁹ and Gabrych et al.²⁰ investigated programmed cell death protein 1 and programmed death-ligand 1 (PD-L1) expression in RMS cases by immunohistochemistry and tumor microarray. In both cases, PD-L1 expression was detected in the tumor microenvironment but not in neoplastic cells. enhanced PD-L1 expression was observed in some post-chemotherapy samples, suggesting a different role for chemotherapy.

Ongoing clinical trials with nivolumab or ipilimumab have not shown any objective tumor response in phase 1 results.^{21,22} At this point, there hasn't been any clinical trial containing immune checkpoint inhibitors, cancer vaccines, or nanomedicine that has shown better results than standard chemoradiotherapy regimens. New surgery and radiotherapy techniques are also being developed to treat this disease.¹⁷

In this article, we present a case of botryoid embryonal RMS arising in the nasopharynx of an adult patient who presented with a neck mass, along with a concise review of the relevant literature. Botryoid embryonal RMS, which is exceedingly rare and typically found in the vagina, bladder wall, and nasopharynx during infancy and childhood, very rarely seen in the nasopharynx of an adult patient, as in this case.

CONCLUSION

We have reported a very rare nasopharyngeal botryoid embryonal RMS in an adult patient. This case highlights the significant diagnostic and therapeutic challenges posed by such a rare entity. Although the patient demonstrated an excellent initial response to a standard pediatric-based protocol of VAC chemotherapy followed by radiotherapy and achieved complete radiological remission, the disease recurred regionally within three months. This outcome underscores the aggressive nature of RMS in adults and emphasizes the critical need for active surveillance following initial treatment. The management of this rare tumor in adults remains complex, and this report contributes valuable data to the limited literature, importance of the multidisciplinary approach and the ongoing search for more effective, tailored therapeutic strategies to improve patient outcomes.

Ethics

Informed Consent: Informed consent was obtained.

Footnotes

Authorship Contributions

Surgical and Medical Practices: F.C., E.K., Y.A., B.Y., Concept: F.C., A.K.T., Design: F.C., A.K.T., Data Collection or Processing: F.C., B.Y., Analysis or Interpretation: Y.A., B.Y., Literature Search: F.C., A.A.Ü., Y.A., B.Y., Writing: F.C., A.K.T.

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