

Synovial Sarcoma of the Palatine Tonsil: Report of Two Cases and Review of the Literature

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Abstract

Here, we describe young men with synovial sarcoma in the palatine tonsil, who presented with a 3-4 month history of progressive sore throat, tonsillar ulcerative mass and bleeding. Clinical and radiological examinations revealed that the tumors arose from the palatine tonsil and extended to the parapharyngeal space. Both tumors were too advanced to remove completely; therefore, they underwent surgical debulking during tonsillectomy and partial pharyngectomy. Histopathological and immunohistochemical studies confirmed the diagnosis of synovial sarcoma of the palatine tonsil. Despite postoperative radiotherapy and systemic chemotherapy, they relapsed 18 and 22 months later. The first patient died from unresectable local recurrent disease three years after primary diagnosis, and the second patient is alive after 36 months, but suffers from unresectable locoregional recurrent disease and is receiving palliative chemotherapy and supportive care.

Keywords: Synovial sarcoma, Palatine tonsil, Tonsillectomy, Radiotherapy, Chemotherapy

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Introduction

Synovial sarcomas account for 6% to 9% of all adult soft tissue sarcomas. These malignant soft tissue neoplasms primarily arise from the extremities during young adulthood.¹ The extremities constitute the vast majority (80%) of the primary sites of the disease, followed by the trunk

(8%) and retroperitoneal/abdominal region (7%), which are the most frequent non-extremity primary sites of disease.¹ The head and neck region is a rare primary site for this neoplasm and only 3-5% of all synovial sarcomas arise in this location. In the head and neck, the parapharyngeal space is the most



Figure 1. A 23-year-old man (case 1) with a diagnosis of left tonsillar synovial sarcoma.

frequent location for synovial sarcoma.^{2,3} Primary synovial sarcoma of the palatine tonsil is extremely rare and, to date, only 4 cases have been reported.⁴⁻⁷ Herein, we describe the clinical, radiological and histopathological findings in two men with synovial sarcomas in the palatine tonsil.

Case 1

A 23-year-old man presented with a three-month history of progressive sore throat, ear pain, left temporal headache and tonsillar mass. At the time of referral, physical examination revealed a large ulcerative left tonsillar mass, which filled the oropharynx and compromised the upper airway (Figure 1). The mass was fragile and hemorrhagic. The right palatine tonsil was normal and there was no palpable cervical lymph node. A computed tomography (CT) scan showed a large infiltrating tonsillar mass which extended to the parapharyngeal space and hypopharynx, encasing

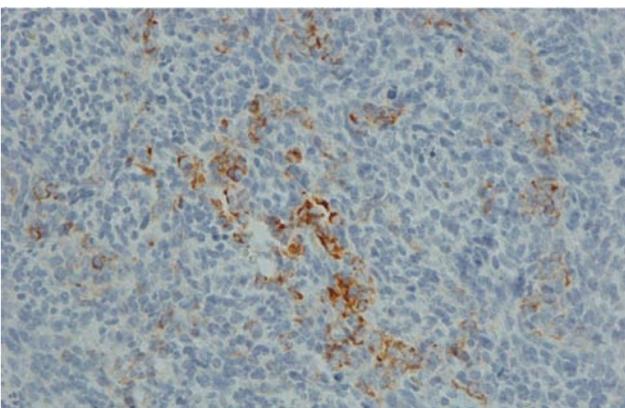


Figure 3. Positive cyokeratin immunostaining in scattered epithelial-like structures (250×) (case 1).

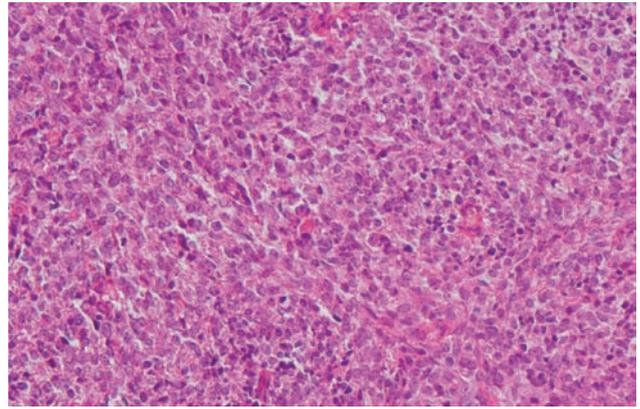


Figure 2. Spindle cell tumor with homogeneous appearance and plump nuclei (H & E stain, 250×) (case 1).

the carotid sheath and internal jugular vein. A preoperative incisional biopsy was performed prior to surgical planning. Surgical findings revealed complete encasement of the carotid sheath, internal jugular vein and accessory nerve. Therefore, only a debulking surgery (tonsillectomy and partial pharyngectomy) was performed.

Histopathologic examination showed monophasic synovial sarcoma (Figure 2). Immunohistochemical study with cyokeratin (Figure 3), vimentin (Figure 4), BCL-2 and MIC-2 (CD99) confirmed the diagnosis. Therefore, the patient received postoperative radiotherapy and a total dose of 60 Gy was delivered using megavoltage photons from a linear accelerator. He achieved a complete response and subsequently received systemic anthracycline-based chemotherapy which consisted of cyclophosphamide 600 mg/m², vincristine 1.4 mg/m², doxorubicin 50 mg/m² and dacarbazine 750 mg/m²

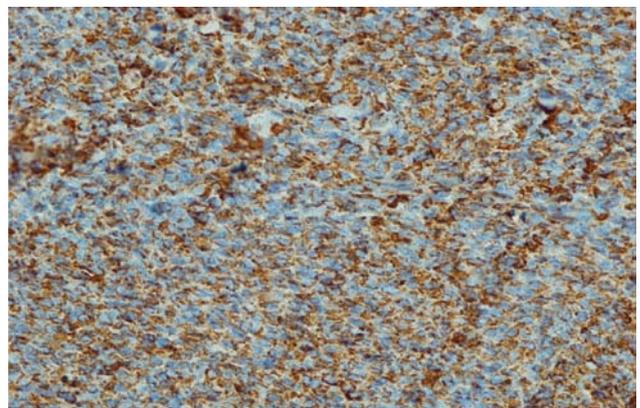


Figure 4. Diffuse vimentin immunostaining in sarcomatous areas of the tumor (250×) (case 1).

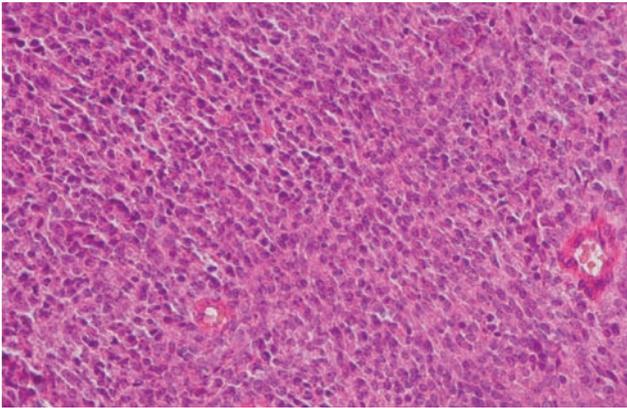


Figure 5. Occasional gland-like structures against a sarcomatous background (H&E stain, 250 \times) (case 2).

(CYVADIC regimen) for six cycles. Eighteen months later, the patient developed extensive local recurrent disease at the primary site. At that time, the recurrent tumor occupied the oropharynx, extended to the pterygoid space and skull base, and encased the carotid sheath. Debulking surgery followed by salvage ifosfamide-based chemotherapy which consisted of mesna 2500 mg/m²/d continuous infusion on days 1-4, doxorubicin 20 mg/m²/d continuous infusion on days 1-3, ifosfamide 2000 mg/m²/d continuous infusion on days 1-3 and dacarbazine 750 mg/m² via continuous infusion (MAID regimen), was considered for the patient. However, after four cycles of chemotherapy, he did not achieve a complete response. Three years after the initial diagnosis, he died due to progressive local recurrent disease.

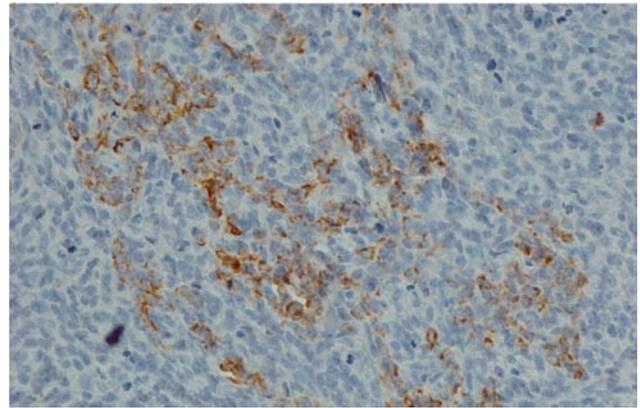


Figure 6. Positive cytokeratin immunostaining in scattered epithelial-like structures (250 \times) (case 2).

Case 2

The patient was a 26-year-old man who presented with a four-month history of throat discomfort, fullness and bleeding. On physical examination, there was a right hemorrhagic tonsillar mass, which caused remarkable airway narrowing with no cervical lymphadenopathy. A contrast-enhanced magnetic resonance image (MRI) showed a large infiltrating right tonsillar and parapharyngeal mass, which extended to the skull base. A preoperative incisional biopsy was performed before the surgical plan. The patient underwent surgery with curative intent. However, the disease was too extensive, and extended to the skull base and jugular foramen. Therefore, only a tonsillectomy and partial pharyngectomy was performed, leaving behind gross residual tumor, which could not be completely resected. Histopathological examination revealed occasional gland-like structures against a sarcomatous

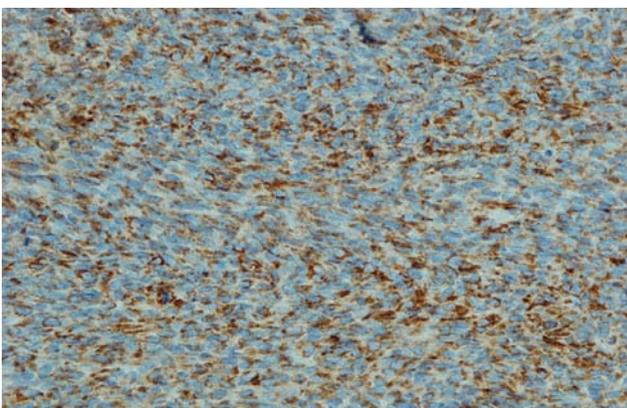


Figure 7. Diffuse vimentin immunostaining in sarcomatous areas of the tumor (250 \times) (case 2).

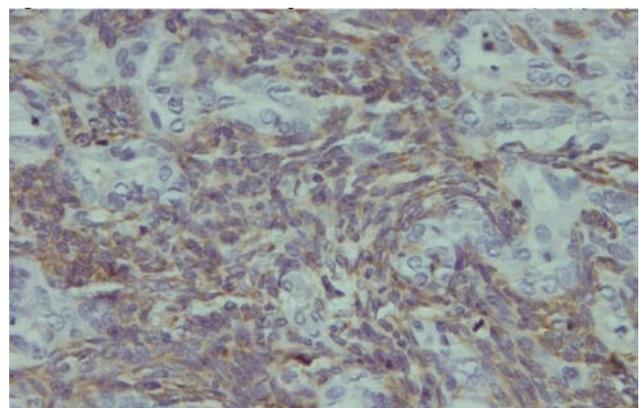


Figure 8. Positive BCL-2 immunostaining in sarcomatous areas of the tumor (400 \times) (case 2).

background (Figure 5). Immunohistochemical study for cytokeratin (Figure 6) revealed positive staining in the scattered epithelial component and that for vimentin (Figure 7) revealed positive staining in the sarcomatous cells of the tumor. Complementary immunohistochemical studies included BCL-2 (Figure 8) and MIC-2 (CD99) (Figure 9), which confirmed the diagnosis of biphasic synovial sarcoma. Therefore, the patient was treated with radiotherapy using megavoltage photons from a linear accelerator, and a dose of 60 Gy was delivered in 30 conventional fractions. Complete response was achieved by the end of radiation therapy. The patient subsequently received systemic anthracycline-based chemotherapy, which consisted of CYVADIC at the same doses as in the first patient for six months. Twenty-two months after the last cycle of chemotherapy, he developed extensive unresectable locoregional recurrent disease. Four cycles of salvage ifosfamide-based chemotherapy that consisted of mesna 2500 mg/m²/d continuous infusion on days 1-4, doxorubicin 20 mg/m²/d continuous infusion on days 1-3, and ifosfamide 2500 mg/m²/d continuous infusion on days 1-3 (AIM regimen) failed to achieve a significant response. At the time of this writing, three years after the initial diagnosis, he is alive and suffering from locoregional recurrent disease and lung metastases. The patient is receiving palliative chemotherapy and supportive care.

Discussion

Soft tissue sarcomas of the head and neck are a diverse group of rare and aggressive malignant neoplasms that constitute about 1% of all head and neck cancers, and 4-10% of all adulthood soft tissue sarcomas. The scalp, face and neck are the most frequent primary sites in the head and neck region.^{3, 8} Soft tissue sarcomas of the head and neck region tend to have a higher risk of local recurrence and a poorer outcome compared with other sites of the body.^{2, 9} Synovial sarcoma, a highly malignant soft tissue tumor, accounts for less than 1% of all head and neck malignant neoplasms.⁸ The parapharyngeal space and neck

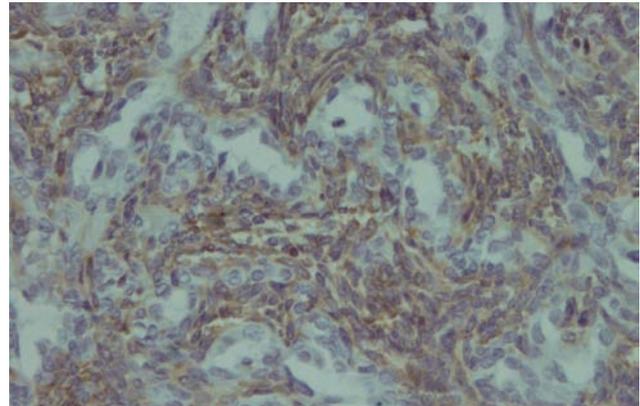


Figure 9. Positive MIC-2 (CD99) immunostaining of tumor cells (400×) (case 2).

are the most frequent sites affected by synovial sarcoma in the head and neck region. To date, about 100 cases of synovial sarcoma of the head and neck region have been reported in the literature.^{2,4,10} A literature review of PubMed using the search terms "synovial sarcoma" and "tonsil" yielded four previous reports.⁴⁻⁷ Therefore, our cases are the fifth and sixth cases, reported in this location.

Pretreatment clinical and imaging examinations should be considered for all patients with head and neck synovial sarcoma.^{11, 12} The clinical findings of these cases suggest that the extent of the resection should be determined through preoperative imaging studies, in particular CT and MRI, with the intent to select optimal surgical strategies and avoid suboptimal surgical resection. In addition, a preoperative incisional biopsy for future direct surgical planning is highly recommended.^{2, 11, 12}

Histologically, synovial sarcoma presents as monophasic, biphasic or uncommonly poorly differentiated subtypes. Synovial sarcoma may cause differential diagnostic challenges with other soft tissue sarcomas.¹ Special immunohistochemical stains are helpful for differentiating synovial sarcoma from other soft tissue sarcomas.¹ However, the precise diagnosis of synovial sarcoma can be difficult with histopathological and immunohistochemical studies alone.¹ In most cases of synovial sarcoma, there is a characteristic reciprocal translocation between chromosomes X and 18, which in about one-third of cases is the

only cytogenetic abnormality, i.e., translocation between chromosome X and 18, t(x; 18) (p11.2; q11.2).^{1,13} Detection of this specific chromosomal translocation is helpful in confirming the diagnosis of synovial sarcoma, particularly when histological studies are uncertain.^{1,13} Therefore, if the results of histopathological and immunohistochemical studies are inconclusive and there is a high clinical suspicion of synovial sarcoma, molecular genetic testing should be considered for diagnostic confirmation.^{1,13}

According to the general principles of high-grade soft tissue sarcoma, standard local therapy for synovial sarcoma consists of wide surgical resection and adjuvant radiotherapy when appropriate.^{1,7,11-13} Synovial sarcoma is one of the most chemosensitive soft tissue sarcomas, with about 50% response rates to ifosfamide- and doxorubicin-based regimens. In an effort to improve systemic disease control and survival, adjuvant chemotherapy is widely used.^{1,11,15} Currently, ifosfamide-based regimens with or without doxorubicin are considered the first choice of chemotherapy for patients with locally advanced and metastatic synovial sarcoma. CYVADIC (cyclophosphamide 500 mg/m², vincristine 1.4 mg/m², doxorubicin 50 mg/m² and dacarbazine 750 mg/m²), MAID (mesna 2500 mg/m²/d continuous infusion on days 1-4, doxorubicin 20 mg/m²/d continuous infusion on days 1-3, ifosfamide 2500 mg/m²/d continuous infusion on days 1-3 and dacarbazine 300 mg/m²/d continuous infusion on days 1-3), and AIM (doxorubicin 20 mg/m²/d continuous infusion on days 1-3, mesna 2500 mg/m²/d continuous infusion on days 1-4, and ifosfamide 2500 mg/m²/d continuous infusion on days 1-3) are the most common regimens used in soft tissue and synovial sarcomas.^{1,15}

Furthermore, synovial sarcoma is a unique soft tissue sarcoma with considerable promise for biologically targeted therapy. Recent studies have shown the interactions between fusion transcripts and cell cycle regulators or growth factors in synovial sarcoma. Potential novel drugs

that inhibit these fusion transcripts and epidermal growth factor receptor inhibitors are currently being investigated.^{1,16}

We described two extremely rare cases of locally advanced synovial sarcoma in the palatine tonsil with poor outcomes. The poor clinical course of these cases suggests that synovial sarcoma of the palatine tonsil is a highly aggressive tumor, and more effective adjuvant systemic treatment should be considered in high risk patients to control locoregional and distant failure.

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