Sarcomas are malignant neoplasms that arise from mesenchymal tissues. Sarcomas of the meninges may originate primarily from mesenchymal cells or may be metastases of extracranial soft tissue sarcomas. Radiotherapy (RT)-related dural sarcomas are extremely rare, and the prognosis of RT-related sarcoma patients is worse than that of primary sarcoma. There is no consensus about the management of these very rare, malignant neoplasms. The authors herein report a patient with dural sarcoma and its management. Although the main treatment is surgery, re-irradiation, conventional chemotherapeutics, and targeted therapies are other options. Long term side effects of treatments should always be kept in mind and treatment decisions should be made accordingly.

Keywords: Sarcoma; dura mater; radiotherapy; antineoplastic protocols

Sarcomas are malignant neoplasms that arise from mesenchymal tissues. Sarcomas are a rare type of solid cancers, encompassing more than one hundred subtypes, and occur at any age.1 Sarcomas of the meninges may originate primarily from mesenchymal cells or may be metastases of extracranial soft tissue sarcomas.2 Symptoms such as nausea, vomiting, headache, seizure, and spinal cord compression may occur depending on the size and location of the tumor. Cranial magnetic resonance imaging (MRI) is often used for diagnosis. The primary treatment for sarcomas is surgery; other treatment options include radiotherapy (RT), chemotherapy (CT), targeted therapies, and immunotherapy.3 Though RT is one of the risk factors for sarcoma development, RT-related dural sarcomas are extremely rare.2 There is no consensus on the management of these extremely rare, malignant neoplasms. Here, the authors report a case of RT-related dural sarcoma and its management.

CASE REPORT

A 42-year-old woman presented with a headache and swelling on the scalp, growing gradually over the last three months. The physical examination did not reveal any abnormal finding except for the 4x2 cm swelling of the left parietal region. The patient presented a seven-year-old history of surgery for the left frontoparietal, intracranial mass originating from the calvarium. After the complete resection of the tumor, the pathological report was found to be consistent with atypical meningioma (WHO grade 2), and the patient received adjuvant RT with a total dose of 6000 centigray (cGy) external RT in 30 fractions.
Cranial MRI was performed, and the lesion appeared to be a lobulated, contoured mass adjacent to the bone graft, which measured 3.5x1.8 cm, in continuity with the bone in the subcutaneous fat tissue of the left parietal region (Figure 1 A, B, C). The patient underwent left frontoparietal dural mass excision. Pathological examination of the resected tumor demonstrated a highly cellular tumor characterized by spindle cells with pleomorphic fusiform nuclei (Figure 2 A). Numerous mitotic figures were observed, some of which were atypical. In histochemical reticulum stain, a well-defined, diffuse reticulum network was detected in the stroma (Figure 2 B). In immunohistochemical studies, most of the tumor cells showed nuclear p53 expression. GFAP (glial fibrillary acidic protein), S100, EMA (epithelial membrane antigen), PR (progesterone receptor), CD34, CD99, SMA (smooth muscle actin), desmin, H-caldesmon, HHV-8, myogenin were found to be negative in tumor cells. Ki-67 (MIB-1) proliferation index was detected as 60%. These findings were interpreted to be compatible with a malignant mesenchymal tumor, dural sarcoma (fibrosarcoma or undifferentiated pleomorphic sarcoma). In this case, the pathological images were obtained by the digital pathology systems supported by Ankara University (AU BAP A140230003). 18F-FDG positron emission computed tomography was performed to determine the staging; there was no pathological uptake except in the midline of the vertex (SUVmax: 11.4) and left parietal region (SUVmax: 25.2). The patient was evaluated in the multidisciplinary tumor council and treated with IMA (ifosfamide + mesna + adriamycin) chemotherapy (CT) every 21 days. After two cycles of IMA CT, clinical and radiological progression occurred, and second line docetaxel + gemcitabine CT was started. After three cycles of CT, partial radiological response was obtained, and treatment was continued. After the 5th cycle, the patient was hospitalized for meningitis and received intravenous antibiotics; complications in

![Fig 1](image1.png)

**FIGURE 1 A,B,C:** T1 axial, T1 coronal, and T2 fat axial MRI images of the lobular contoured lesion showing contrast enhancement with peripheral diffusion restriction in the continuation of bone in the left frontoparietal region of the bone graft.

![Fig 2A](image2a.png)

**FIGURE 2A:** A hypercellular tumor characterized by atypical cells with a pleomorphic large fusiform nucleus. Most tumor cells are spindle shaped, and uniformly arranged in short irregular bundles. Multiple mitotic figures can be noted (arrow); H&E, x37.2

![Fig 2B](image2b.png)

**FIGURE 2B:** Well defined, diffuse reticulum network (staining as black fibers) evident around tumor cells; modified Gomori’s reticulum stain x 24.5
wound healing persisted in the left frontoparietal region. Cranial MRI showed progression of the existing lesion and a newly developed lesion of 1 cm diameter in the left parietal region. After this, the patient was treated with pazopanib 800 mg/day, which was continued for 15 months; no progression of the lesion was reported after pazopanib therapy.

Informed consent of the patient was taken prior to the initiation of the treatment.

DISCUSSION

Sarcomas are heterogeneous, rare malignant tumors originating from mesenchymal tissues. Sarcomas account for less than 1% of all adult malignancies. Approximately 80% of all sarcomas originate from soft tissues, while the rest originate from bone.\(^1\)

Although advances in cancer treatment have prolonged survival, the frequency of long-term treatment-related complications has also increased. For many years, radiation has been known to be an inducing agent in the development of malignant neoplasms. RT may induce the development of secondary malignancies.\(^4\) According to recent data, RT-related sarcomas account for approximately 3–6% of all sarcomas, and the average age of diagnosis in RT-related sarcomas is between 50 and 67 years in adults.\(^5\) The most common subtype of RT-related soft tissue sarcomas are malignant fibrous histiocytomas. RT-related sarcomas can develop between several months to years after completion of RT.\(^4\) Factors such as age at the time of exposure to RT, a dose of RT, CT drugs used with RT, and genetic factors may contribute to the development of sarcomas. The prognosis for RT-related sarcoma patients is worse than that of primary sarcoma; the five-year survival rates are reported to lie between 10 and 50.\(^7\)

In the present case, the patient had adjuvant RT because of the WHO grade 2 atypical meningioma. However, there is no consensus for postoperative adjuvant RT in atypical meningioma. In a study on 99 patients diagnosed with atypical meningioma (WHO grade 2), RT was found to increase progression-free survival.\(^4\) Although the meningioma did not recur for seven years after surgery, in this case, adjuvant RT dural sarcoma related to RT was a late adverse effect.

Tumors originating from dura mater are morphologically, radiologically, and clinically diverse. The disease may originate primarily from the dura, or it may be metastatic, and survival results are poor in RT-related sarcomas. RT-related dural sarcomas are extremely rare and occur in 0.03–0.3% of patients treated with RT; different subtypes such as malignant fibrous histiocytoma, chondrosarcoma, leomyosarcoma, liposarcoma, fibrosarcoma have been observed.\(^2\) Meningeal sarcoma was detected after ten months in a patient with astrocytoma treated by RT.\(^9\) In the case of medulloblastoma treated by RT, malignant fibrous histiocytoma developed eight years later.\(^10\) In an ependymoma case postoperatively treated by RT, meningeal sarcoma developed seven and a half years later.\(^11\)

Surgery, re-radiation, CT, and targeted therapeutic agents may be considered as options for the treatment of RT-related sarcomas. Treatment decisions may vary depending on the morphological features, origin, and grade of the tumor. The main treatment modality is surgery. In this case, the patient was mainly treated surgically. It has been shown that adjuvant chemotherapy with doxorubicin and ifosfamide provides approximately 11% improvement in survival compared to the only resection.\(^12\) Treatment agents such as doxorubicin, ifosfamide, gemcitabine, docetaxel, trabectedin are used in the treatment of metastatic soft tissue sarcomas. There are also studies with pazopanib, sorafenib, regorafenib, sunitinib, which are targeted treatment agents.\(^3\) The patient was treated with doxorubicin and ifosfamide, and after progression, docetaxel and gemcitabine chemotherapy was given as the second line of treatment. In the third-line setting, the patient was treated with tyrosine kinase inhibitor pazopanib, and this treatment is still ongoing. Immunotherapy with pembrolizumab, nivolumab, and ipilimumab is also an option for patients with soft tissue sarcomas.\(^13\) If neurotrophic tyrosine receptor kinase fusion protein is positive, larotrectinib or entrectinib can be used.\(^14\)

In conclusion, the possible sarcoma development after RT to the central nervous system should be kept in mind by the clinicians. RT-related dural sarcomas are extremely rare, malignant neoplasms, and there is no consensus regarding the optimal choice of treatment.
The main treatment method is surgical, although RT and systemic treatment agents can also be used. Pazopanib may provide long term survival benefit in these patients. Further large-scale studies are required to determine survival benefit in these patients.

**Source of Finance**

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

**Conflict of Interest**

No conflicts of interest between the authors and/or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

**Authorship Contributions**


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