Primary extraskeletal osteosarcoma in the pineal region

Case report

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Primary extraskeletal osteosarcoma occurring in the brain parenchyma is distinctly uncommon, with only five cases having been reported. The authors describe the case of a 45-year-old man who presented with progressive headache and diplopia. Computerized tomography scanning and magnetic resonance imaging results revealed a pineal region tumor with obstructive hydrocephalus. The patient underwent partial resection of the tumor. The histological examination showed large pleomorphic tumor cells embedded in osteoid matrix. Immunohistochemical analysis was negative for various antibodies and thus excluded a glial, germ cell, epithelial, and lymphoid tumor origin. Only vimentin showed strong positivity in most of the tumor cells. Ultrastructurally, the tumor cells were rich in dilated rough endoplasmic reticula. Clear zones between tumor cells and osteoid matrix were observed. The osteoid matrix was made up of small collagen fibrils and hydroxyapatite deposits. The tumor was not attached to the bone structure of the skull. These findings are consistent with the features of extraskeletal osteosarcoma. Data from complete medical and radiological studies excluded a metastatic origin for this tumor. Partial resection and postoperative radiotherapy had provided tumor control at 11 months after the onset of symptoms. This is the first reported case of a primary extraskeletal osteosarcoma occurring in the pineal region.

KEY WORDS • extraskeletal osteosarcoma • pineal gland • brain neoplasm

EXTRASKELETAL osteosarcoma is a rare tumor occurring most commonly in the soft tissue of the lower extremities.1,3,15,33 It tends to occur in older individuals in contrast to tumors of skeletal origin.3,7,15 Although extraskeletal osteosarcomas occasionally have been seen to occur as a group, their incidence as a primary intracerebral osteosarcoma is distinctly uncommon, with only five cases reported in the modern literature.5,6,14,21,25 Recently, we encountered a patient harboring an extraskeletal osteosarcoma occurring primarily in the pineal region together with obstructive hydrocephalus. To our knowledge, this is the first reported case of a primary extraskeletal osteosarcoma in the pineal region. We describe the clinical course, management, and pathological studies, including immunohistochemical and ultrastructural analyses.

Case Report

History. There was nothing remarkable in the medical and family histories of this 45-year-old left-handed man. He had never received cranial radiation. He was admitted because he had been suffering from headache and diplopia for a month. For a few days prior to admission, these symptoms had gradually worsened and he had experienced confusion with accompanying nausea and vomiting.

Examination. When the patient was examined at Siriraj Hospital, he was mildly drowsy and disoriented in all spheres. A positive Parinaud sign and bilateral papilledema were detected. Other examinations were unremarkable. Computerized tomography scans of his brain demonstrated obstructive hydrocephalus resulting from a partially bleeding mass located in the pineal region. On contrast-enhanced computerized tomography scans, the tumor was homogeneously enhanced. Admission T1- and T2-weighted MR images (Fig. 1) revealed a hypointense mass and a hemorrhagic portion at the pineal region. The tumor involved the midbrain tectum, splenium, and adjacent thalamus with compression of the aqueduct and displayed homogeneous enhancement on contrast study. Based on clinical presentation and imaging data, a differential diagnosis of germ cell tumor was made and serum tumor markers were studied, although all tumor marker levels were within normal limits.

Operation. On the day after admission, a right frontal ventriculostomy was performed to relieve the acute hydrocephalus. Tumor marker levels for germ cell tumors in the cerebrospinal fluid were within normal limits. On the 5th day of admission, a whitish-gray infiltrative tumor mass with firm consistency was confirmed at the pineal region via a right occipital transtentorial approach. Partial tumor removal was performed. The third ventricle was entered by removing the tumor portion involving the posterior end of the third ventricle. At the time of resection, no involvement of bone or dural structure was noted.

Histological Findings. Light microscopy examination disclosed hypercellular tissue composed of large pleomorphic tumor cells with vesicular nuclei, prominent nucleoli, and
some spindle cells embedded in eosinophilic trabeculated osteoid matrix (Fig. 2A–C). The tumor cells featured high mitotic activity.

**Immunohistochemical Findings.** Results of staining for CD3, CD20, CD30, CD43, CD68, kappa and lambda light chains, cytokeratin, epithelial membrane antigen, placental alkaline phosphatase, glial fibrillary acidic protein, and S100 protein were negative. Most tumor cells exhibited strong immunoreactivity for vimentin (Fig. 2D).

**Ultrastructural Findings.** The tumor cells contained numerous dilated rough endoplasmic reticula (Fig. 3). Clear zones between tumor cells and matrix were observed. The osteoid matrix was made up of small collagen fibrils of 35 to 45 nm and a small amount of hydroxyapatite deposit.

**Postoperative Course and Adjunctive Therapy.** The patient's postoperative course was good, and his symptoms were alleviated with only a positive Parinaud sign remaining. Complete medical and radiological evaluation, including a bone scan, revealed no primary skeletal or other extraskeletal osteosarcoma; therefore, a definitive diagnosis of primary pineal region osteosarcoma was made. Postoperative MR images obtained the 4th week after surgery demonstrated a decrease in tumor size. The patient received whole-brain fractionated radiotherapy at a total dosage of 41 Gy, and local boost radiotherapy was applied to the pineal region at a dosage of 20 Gy. He was discharged from the hospital and was observed on an outpatient basis. During the follow-up period, repeated medical and radiological evaluations, including a bone scan, confirmed the diagnosis.

Two months after surgery, the patient suffered headache and vomiting. Computerized tomography scans displayed a small amount of intraventricular hemorrhage, but the tumor had not grown. Hydrocephalus was demonstrated, indicating inefficiency in the opening of the third ventricle for the release of cerebrospinal fluid. After admission, a ventriculoperitoneal shunt was placed to improve the hydrocephalus. The patient's symptoms were immediately alleviated, and he was discharged from the hospital a few days after the operation. He remained in relatively good condition until the 10th month after the first admission; at that time he was readmitted following the gradual onset of drowsiness. Cerebral MR images revealed bilateral hemorrhagic tumors in the thalamus. The tumor had invaded the splenium of the corpus callosum and disseminated into the ventricles and basal cisterns. There was patchy enhancement of the tentorium and adjacent meninges (Fig. 4A–C). Soon thereafter, he became bedridden and died approximately 11 months after the onset of symptoms. An autopsy revealed generalized dissemination of the tumor into the subarachnoid space and extension of ill-defined grayish-white tumors in the thalamus, midbrain, and splenium (Fig. 5). There was no distant metastasis to other parts of the body.

**Discussion**

Extraskelatal osteosarcoma is a high-grade malignant
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sarcoma. It may be defined as a malignant mesenchymal neoplasm that produces osteoid, bone, or chondroid material and is located in the soft tissues without attachment to the skeleton, as determined on radiological examination or on inspection during the surgical procedure. Few data in the literature reveal the incidence of extraskeletal osteosarcoma, although it has been reported to constitute approximately 4% of all osteosarcomas and 1.2% or less of all soft tissue sarcomas. In contrast to osteosarcoma of the bone, extraskeletal osteosarcomas are rarely encountered in patients younger than 40 years. In two studies, in 26 and 40 patients with extraskeletal osteosarcoma, the mean patient ages were 53.5 and 50.7 years, respectively, and there was a male predominance (male/female ratio 1.9:1). Of the various anatomical sites, the thigh muscles were most commonly affected. There have also been reports of these lesions arising in unusual locations including the colon, tongue, mediastinum, penis, and scalp. Among these, only five cases with an intracerebral origin have been reported in the literature. Sarcomas of the central nervous system are uncommon and usually represent metastases, although several cases of primary sarcoma—including rhabdomyosarcoma, leiomyosarcoma, myeloblastoma, myxoid chondrosarcoma, and fibrosarcoma—have been reported to occur in the pineal region. To the best of our knowledge, the present case represents the first reported case of a primary extraskeletal osteosarcoma in the pineal region.

The absence of any skeletal lesion, which was determined by complete medical and radiological evaluations, including bone scan and postmortem examination, excluded a metastatic origin in this case. Based on preoperative imaging studies, the tumor was not attached to the bone structure of the calvaria and skull base and no lesion appeared in the dura mater. These results confirmed the extraskeletal origin of the tumor. Differentiating between primary extraskeletal osteosarcoma and gliosarcoma is mandatory. A biphasic tissue pattern with an area displaying gliomatous or mesenchymal differentiation is essential for the diagnosis of gliosarcoma. Histologically, the sarcoma in the featured case had large pleomorphic tumor cells embedded in osteoid matrix with no gliomatous component. The marked osteoid formation is characteristic of the diagnosis of osteosarcoma. Results of immunohistochemical studies excluded the lymphoid, epithelial, germ cell, and glial origins of this tumor given that only vimentin yielded a positive result. In addition, ultrastructural study results showed round tumor cells with numerous dilated rough endoplasmic reticula. The osteoid was composed of small collagen fibrils and hydroxyapatite crystal deposits. In addition, clear zones between tumor cells and the osteoid matrix were clearly observed. These findings are compatible with ultrastructural findings of osteosarcomas in other studies.

Data from one study demonstrated that the sarcomatous component in gliosarcoma is likely derived from undifferentiated cells with a broad differentiation into histiocytic, fibroblastic, chondroid, and osteoid metaplasia. It is less likely that endothelial cells and pericytes participate in sarcomatous development. The present case was studied using both immunohistochemical and ultrastructural methods whose results indicated a strong osteoblastic character of the tumor cells. In previous reports on primary intracerebral osteosarcoma, authors have speculated that primitive multipotential mesenchymal cells are the origin of such tumors. Nonetheless, an exclusively positive result for vimentin immunoreactivity in the present case did not provide enough information to presume an origin of multipotential mesenchymal cells.

In general, the prognosis of extraskeletal osteosarcoma occurring outside the central nervous system is poor, even in those patients who received what was considered adequate therapy. Many patients have developed a recurrent
growth or a metastasis within a few months after the initial diagnosis. The lungs, bone, lymph nodes, liver, and soft tissue represent common sites of metastases. Despite radical surgery and, in some cases, radiotherapy and chemotherapy, the outlook for those harboring extraskeletal osteosarcoma is grave, with approximately 50% of patients dying within 2 or 3 years after the first operation. Extra-skeletal osteosarcoma is grave, with approximately 50% of patients harboring extraskeletal osteosarcoma. The combination of resection, stereotactic radiosurgery, and chemotherapy yielded a good result in a case of primary extraskeletal osteosarcoma in the right temporal lobe; the patient survived without tumor recurrence after 18 months of follow up. Patel and Benjamin reported on the limited therapeutic benefit of cisplatin-based chemotherapy in the treatment of patients with extraskeletal osteosarcoma. The combination of resection, stereotactic radiosurgery, and chemotherapy yielded a good result in controlling primary extraskeletal osteosarcoma in the right temporal lobe: the patient survived without tumor recurrence after 18 months of follow up. The patient in the present case initially underwent tumor resection followed by whole-brain and local administration of radiation. The tumor’s infiltrative character and invasion into the midbrain and adjacent structures precluded radical resection. Metastasis to the ventricle and subarachnoid space indicated a limited role of radiotherapy in the local control of the tumor.

Conclusions
We assert that a multimodality treatment consisting of radical resection, high-dose radiation, and systemic chemotherapy should be considered and may provide a relatively good result in controlling primary extraskeletal osteosarcoma in the brain.

References

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