Post-radiation reactive changes in a single vertebral body mimicking metastatic pineoblastoma

Case report

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This 18-year-old woman presented with headache and diplopia over several months and was found to have an enhancing pineal tumor with resultant obstructive hydrocephalus. Following standard preoperative diagnostic tests, including spinal axis imaging, the patient was taken to the operating room for an endoscopic third ventriculostomy to relieve hydrocephalus and then subsequently underwent a craniotomy for gross-total resection of the pineal mass. The patient was discharged after an uneventful hospital course and received standard adjuvant cranial-spinal radiation and chemotherapy as an outpatient. Follow-up imaging 1 year after surgery demonstrated a metabolically active, lytic lesion in the C-3 vertebral body and new lung lesions suggesting a metastatic pineoblastoma. The patient underwent a C-3 anterior corpectomy and reconstruction without complication as aggressive therapy for presumed metastatic disease. Final pathological results from the vertebral lesion were consistent with radiation-induced reactive changes, not metastatic pineoblastoma as originally suspected. The patient recovered well and remains symptom free. To the authors’ knowledge this is the first reported case of reactive changes mimicking metastasis in a single vertebral body following standard therapy for resected primary pineoblastoma. (DOI: 10.3171/2009.6.PEDS09266)

KEY WORDS • spine • radiation therapy • metastatic pineoblastoma

In addition to maximal resection, standard adjuvant treatment for intracranial pineoblastoma includes cranial-spinal axis irradiation and systemic chemotherapy.3,11 Although radiation-induced changes in vertebral bone marrow can be observed on MR imaging following treatment,17 we report a case of focal C-3 vertebral body radiation changes that mimicked the clinical and radiographic features of extraneurial metastatic pineoblastoma.

Case Report

History and Presentation. This 18-year-old woman presented to the University of California, San Francisco, hospital with a 6-month history of headache and 4-month history of diplopia, nausea, and urinary urgency. Her physical examination, including a detailed neurological assessment, was notable only for a right cranial nerve VI palsy. Magnetic resonance imaging demonstrated moderate obstructive hydrocephalus with a 2 × 2 × 2.4–cm enhancing mass in the posterior third ventricle, consistent with a pineal region tumor (Fig. 1A and B). Concurrent imaging of the spinal axis was normal (Fig. 2A).

Operation and Postoperative Course. Initial therapy included performing an endoscopic third ventriculostomy to treat the patient’s hydrocephalus, and her CSF was obtained at that time for standard analyses. Her cytological results of the mass were benign and markers of germ cell tumors, including α-fetoprotein, β-human chorionic gonadotropin, and carcinoembryonic antigen were all negative. Subsequently, a craniotomy was performed for resection of the pineal mass via an infratentorial supracerebellar approach with the patient in a sitting position. Gross-total resection was achieved (Fig. 1C and D), and the patient was discharged home on postoperative Day 3 following an uneventful hospital course.

This article contains some figures that are displayed in color online but in black and white in the print edition.
Permanent pathology specimens showed hypercellularity of small, undifferentiated cells with delicate, blunt cytoplasmic processes and with Homer-Wright rosettes (Fig. 3A and B). Immunohistological staining revealed strong MIB-1 and synaptophysin levels and low glial fibrillary acidic protein levels, a pattern consistent with pineoblastoma, which was in concordance with the final pathological diagnosis.

Following confirmation of pineoblastoma, the patient received standard adjuvant cranial-spinal radiation consisting of 3600 cGy with a 5400 cGy boost to the surgical field. In addition, 6 cycles of adjuvant chemotherapy using 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea (CCNU), cisplatin, and vincristine was also completed without significant complications.

Post-radiation Changes. Routine serial follow-up MR imaging of the cranial-spinal axis was unremarkable for recurrence or metastases until 12 months after the initial surgery. At 1 year after surgery, a follow-up MR image demonstrated a T1-dark, T2-bright, Gd-enhancing lesion within the C-3 vertebral body (Fig. 2B–D, G, and H) concordant with a lytic lesion on CT of the cervical spine (Fig. 2F). A staging workup showed multiple new abnormal foci of hyperdensity in the lungs on CT (Fig. 4A–C). A bone scan also demonstrated a focus of increased uptake of 20.5 mCi technetium-99 methylene diphosphonate in the C-3 vertebral body (Fig. 2E). Taken together, these series of imaging findings were most consistent with metastatic spread of the primary intracranial pineoblastoma.

Because the patient was asymptomatic from the C-3 lesion, it was believed that the metastasis was discovered at an early stage. Thus, aggressive treatment of this lesion was recommended, and a C-3 anterior corpectomy with partial en bloc resection of the lesion and reconstruction was performed without complications (Fig. 5). Final pathology from the vertebral lesion showed only reactive changes in the surrounding bone marrow with no evidence of malignant cells (Fig. 3C). In addition, lung nodules were
not observed on a repeat CT scan of the chest (Fig. 4D–F), suggesting that the C-3 lesion was, in fact, a result of posttreatment reactive changes and that the C-3 and lung lesions were not metastases. The patient has undergone biannual follow-up MR imaging of her brain and spine, most recently at 2 years following her spine surgery for the C-3 lesion. At that time, there was no evidence of brain or spinal recurrence, and her vertebral bodies were notable only for postoperative changes. Her hypothyroidism (likely related to radiation therapy), chronic foot pain (related to vincristine), neuropathy, and (preexisting) depression were well controlled as of her last clinic visit.

**Discussion**

Pineoblastoma is the highest grade malignancy among the pineal parenchymal tumors and is typically noted in younger patient populations.\(^1\)\(^,\)\(^2\)\(^,\)\(^3\)\(^,\)\(^4\)\(^,\)\(^8\)\(^,\)\(^9\)\(^,\)\(^11\) Although they comprise < 1% of brain tumors, pineoblastomas harbor a very poor prognosis.\(^10\) Considered a PNET of the pineal region, pineoblastoma is well recognized to recur and spread throughout the CNS, resulting in both cerebral and spinal “drop” metastases. The standard of care in the US for these tumors includes maximal resection with adjuvant cranial-spinal irradiation and systemic chemotherapy.\(^11\)

Among primary brain tumors, extraneural metastases occur in 0.5% of cases.\(^20\) Glioblastoma multiforme is the most common primary source in these rare cases, followed by PNET.\(^6\)\(^,\)\(^10\)\(^,\)\(^12\)\(^,\)\(^21\) Glioblastoma multiforme most commonly spreads to the lung, while PNETs have a predilection for the bone and bone marrow.\(^1\)\(^,\)\(^4\)\(^,\)\(^14\) Osseous spread of primary CNS tumors is believed to occur via CSF pathways. Alternatively, some have hypothesized that hematogenous spread of tumor cells during surgery may be a route of dissemination, although this mechanism likely accounts for a minority of cases.\(^12\)\(^,\)\(^15\)\(^,\)\(^18\)

First reported in 1974,\(^2\) extraneural metastasis of pineoblastoma has been reported in the literature in only 9
Fig. 5. Preoperative (A) and postoperative (B) lateral cervical radiographs demonstrating successful reconstruction following C-3 corpectomy with partial en bloc resection of the lesion and placement of an expandable cage with C2–4 anterior cervical plating.

cases, with 6 showing vertebral or osseous spreading.\textsuperscript{4,5,8–10} In most cases of bone metastasis, pain is a frequent symptom.\textsuperscript{4,5,20} Although extraneural metastasis is an extremely rare event for pineoblastoma, early and aggressive treatment has been reported to result in durable control.\textsuperscript{5}

A radiation dose to the spinal column is inevitable during spinal axis radiotherapy.\textsuperscript{19} Specific changes in vertebral bone marrow signal intensity on MR imaging occur at both early (< 1 month) and late (> 1 month) time periods following radiation treatment. Within hours to days, bone marrow may become hypocellular with vascular congestion and hemorrhage.\textsuperscript{17} Typically, early changes reflect bone marrow edema, indicated by a decreased marrow signal on T1-weighted MR sequences and increased marrow signal on T2-weighted and STIR imaging. Late changes reflect altered distribution of red and yellow marrow with decreased hematopoietic cellularity and increased fat content. By 3 months following therapeutic radiation, marrow is generally replaced by fibrosis and fat, with increased signal on T1-weighted MR imaging (T1 shortening) and mixed signals on T2-weighted imaging.\textsuperscript{17} These changes occur somewhat variably in time depending on the dose of radiation. Typically, several contiguous vertebral levels included in the radiation field will demonstrate late radiation changes, while bone outside the field usually is unaffected. Thus, the present case, which demonstrates significant radiation-induced changes at a single vertebral level, is rather atypical. Finally, the most dramatic effect observed after spinal radiation is osteonecrosis, which is an extremely rare sequela.\textsuperscript{7} Because the radiation dose to the vertebral column is usually less than that given to the spinal cord in spinal axis irradiation, vertebral osteoradionecrosis is often present in the context of radiation-induced myelopathy to the spinal cord. There was no evidence of vertebral osteonecrosis in the C-3 vertebral body specimens of the present case.

Conclusions

We report a rare case of radiation-induced vertebral body changes to a single cervical vertebral body following cranial-spinal irradiation as standard adjuvant therapy for pineoblastoma. Given the focality of this lesion in conjunction with new lung findings, increased metabolic activity on a bone scan, and lack of spinal cord changes, the patient was treated aggressively for presumed metastatic pineoblastoma. However, the lesion was ultimately determined to be reactive bone marrow secondary to treatment with radiation and chemotherapy. Even though the bone pathology was favorable in this case, lesions in the vertebral column in a patient with pineoblastoma should be considered metastases until proven otherwise.

Disclaimer

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

References

Radiation-induced vertebral body changes


