Case Report

rare tumors

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A rare case of extremely delayed osseous metastasis of pineoblastoma

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Abstract

Pineoblastoma is a rare, primitive, and malignant tumor arising from the parenchyma of the pineal gland. It typically metastasizes along the cerebral neural axis, with rare extraneural metastasis and even more rare intraosseous extraneural metastasis. A patient with pineoblastoma, initially treated with chemotherapy, presented 10 years after initial diagnosis with multiple osseous metastases including his pelvis, femur, and vertebrae, and is currently undergoing chemotherapy.

Keywords

Pineoblastoma, osseous metastasis, cancer, metastasis

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Introduction

Pineoblastoma is a rare, primitive, and malignant tumor arising from the parenchyma of the pineal gland. It comprises 0.4%–1% of all intracranial tumors and <25%–50% of pineal parenchymal tumors and typically occurs in the pediatric population.[1] Pineoblastoma is classified as a supratentorial primitive neuroectodermal tumor (PNET) and a Grade IV CNS tumor classified by the World Health Organization.[2] It is an aggressive tumor that commonly metastasizes along the craniospinal axes via the cerebrospinal fluid (CSF), manifesting as spinal drop and leptomeningeal metastases. Due to its high propensity of spreading into the subarachnoid space, initial evaluation with CSF analysis and magnetic resonance (MR) imaging are extremely important for detection as well as seeding.[3] Usual treatment includes maximal resection followed by adjuvant cranio-spinal irradiation and systemic chemotherapy. Neoadjuvant chemotherapy regimens with etoposide, cisplatin, and vincristine have been studied in small experimental cohorts and show potential benefit.[4] Survival rates vary widely depending on patient age, pathologic staging, and treatment but the overall median survival is 16–25 months.[1] Metastases in pineoblastoma typically presents along the cerebral neural axis, with rare extraneural metastasis, and even more rare intraosseous extraneural metastasis; only seven other cases of intraosseous metastasis of pineoblastoma have been described in literature.[5,6] In this report, we present a case of extraneural intraosseous metastasis of pineoblastoma to the pelvis and the spine 10 years after initial diagnosis and treatment.

Case presentation

In 2006, a 22-year-old man presented with worsening headache for 1-month duration with phonophobia, photophobia, and worsening lower extremity weakness. A computed

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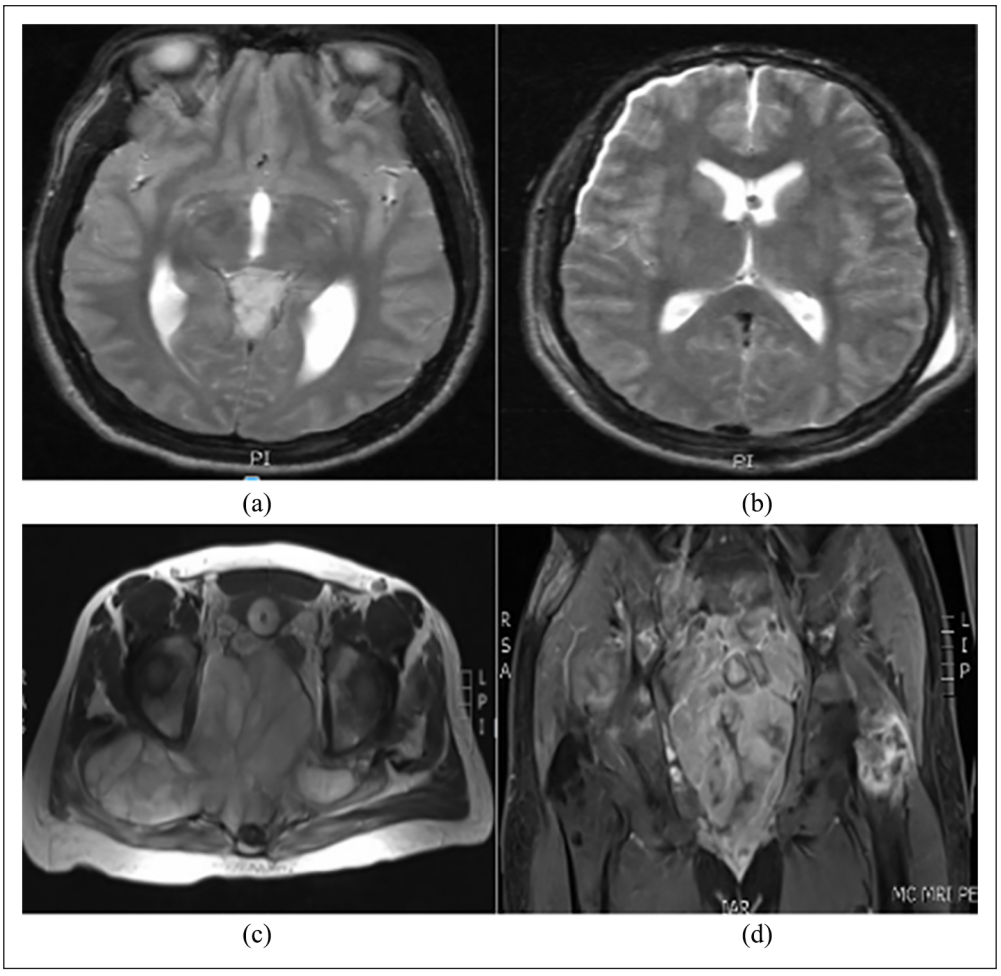

Figure 1. (a) large 3.5 × 2.5 × 2.6 cm mass arising from superior vermian region and effacing fourth ventricle, (b) right frontal VP shunt placement and pineoblastoma resection, (c) large multilobulated mass centered in sacrococcygeal spine with extension into pelvic bones, and (d) mass extends to the presacral space in the pelvis and superiorly extends to L5/21 spinal canal.

tomography (CT) and magnetic resonance imaging (MRI) of the head revealed a large supracerebellar, infratentorial large mass measuring 3.5 × 2.5 × 2.6 cm (Figure 1(a)). He underwent a suboccipital craniotomy with resection of the mass and a ventriculoperitoneal shunt (VP) was placed due to hydrocephalus (Figure 1(b)). Pathology from a biopsy taken from surgery confirmed a pineoblastoma.

The patient received concurrent chemotherapy and radiation with weekly vincristine and conventional proton radiation therapy for 5 weeks. Afterwards, he was referred for maintenance chemotherapy under pediatric protocol Children's Oncology Group 99701 regimen B but was ineligible due to his age and previous treatment with vincristine. After a prolonged hospital course which was complicated by pneumonia requiring a tracheostomy and dysphagia requiring a percutaneous endoscopic gastrostomy tube placement, he was discharged to an inpatient rehabilitation facility. He recovered well and his only residual effect from his treatment was a cerebellar gait.

He was admitted 9 years later in 2015 at the age of 31 after a seizure episode. He was found to have a left frontal mass measuring 7.2 × 5.2 × 3.4 cm with regional sulcal effacement, midline shift, effacement of the lateral ventricle, and rightward subfalcine herniation. The mass was resected and confirmed a grade 2 atypical meningioma. Post-operatively, he did not have major complications, but he developed intermittent seizures and traumatic brain injury symptoms and was treated with levetiracetam.

Ten years after the initial diagnosis of pineoblastoma and 1 year after the diagnosis of atypical meningioma in 2016, he was admitted for a 5-day history of severe hypogastric abdominal pain and worsening numbness and weakness of his lower extremities. CT and MRI imaging of his abdomen were obtained which showed a large pelvic mass with osteoblastic involvement of the bilateral proximal femurs, pelvis, and cervical, thoracic, and lumbar vertebral bodies (Figure 1(c) and (d)). Interventional radiology guided pelvic mass biopsies were consistent with his prior diagnosis of

pineoblastoma, and no surgical options were available due to the extent of disease. Genetic testing was not performed, as it was not indicated. To treat delayed intraosseous metastasis of pineoblastoma to the pelvis, he was started on the Pediatric Head Start II regimen with five cycles of induction chemotherapy with cisplatin, cyclophosphamide, etoposide, and vincristine with plans for an autologous stem cell transplant in the future. Immunotherapy was not considered, as patient had poor social support and would not have been able to adhere to close clinical monitoring. His chemotherapy course was complicated by pancytopenia, pneumonia, and deep venous thrombosis, and after his fifth cycle of induction chemotherapy, the patient was lost to follow-up.

Discussion

Pineoblastoma is an aggressive tumor that commonly presents with leptomeningeal metastases. Extraneural metastasis occurs in $<0.5\%$ of cases[7] and is associated with poor survival.[8] There are two mechanisms that primarily prevent extraneural invasion of neuroepithelial tumor cells: the immediate immune response and the inability of glial cell tumors to invade local lymphovascular structures.[9] When the malignancy is able to bypass these preventative measures, it is mainly due to surgical seeding of tumor cells beyond the dura and/or invasion of blood vessels, which can be done via hematogenous spread, VP shunt, or Batson's plexus.[5,6,10] Additionally, in patients who receive spinal arachnoid grafts, bone invasion may also occur through contiguous spread.[9]

This patient was at risk for recurrence likely related to two factors: incomplete maintenance chemotherapy treatment at initial diagnosis and through the VP shunt. However, his VP shunt was unlikely the route of metastasis since there was no evidence of peritoneal or abdominal metastasis, as most extraneural metastasis from the VP shunt is associated with peritoneal involvement.[10] Therefore, metastasis through Batson's plexus, which involves dissemination of malignant cells from the brain, through the spinal cerebrospinal fluid, then through the veins of Batson's plexus to the pelvis, likely accounts for our patient's pelvic and vertebral lesions.[3]

Batson's plexus was described in 1940 to explain tumor spread to osseous structures. It was described as a "third circulation" that bypassed the pulmonary, portal, and caval systems and instead used a valveless vertebral venous plexus to enter primary circulation.[11,12] It characterizes the veins surrounding the vertebral column draining to the pelvic bones and upper femora. It is hypothesized that due to the high pressure in the plexus around the spine and skeletal area, this can lead to metastatic tumor deposits.[13] Many malignancies, including prostate cancer and GI cancers, are thought use Batson's plexus for skeletal metastases.[14] In our case, the extensive pelvic and spinal metastases would correlate with the anatomy of Batson's plexus, and would most accurately reflect the mechanism of extraneural spread.

There have been seven other case reports of intraosseous metastasis, and only the case study by Constatine et al reported metastasis to the pelvis. The patient in their study showed complete regression of all lesions following conventional and consolidative chemotherapy and autologous hemopoietic stem cell rescue.[6] Two other case reports of intraosseous metastasis to acetabulum and the thoracic vertebral body also report disease free state being reached after standard chemotherapy and irradiation. Another case study showed disease progression with meningeal, spinal, and cranial invasion despite chemotherapy and death 2 years after recurrence.[7,9] The most recent case report by Golbin et al also reported multiple metastasis following surgery, chemotherapy, and craniospinal irradiation after initial diagnosis and tumor burden persistence after salvage chemoradiation and surgery.[5] Although difficult to predict the burden and the outcome of metastasis, Constatine et al suggests, isolated intraosseous metastasis, as seen in the patient in our case study, may potentially be curable.

This case demonstrates an extremely rare and delayed osseous metastasis of pineoblastoma. Usually, the time interval of osseous metastasis from initial diagnosis is 1 year, with one report documenting 4 years since diagnosis.[5,15,16] In our case, the patient did not present until 10 years after initial treatment of his pineoblastoma, making this case the longest time interval between initial treatment and recurrence. Given the favorable prognosis of isolated metastasis, the patient might have possibly reached complete remission following induction chemotherapy and hemopoietic stem cell rescue.

Conclusion

Osseous metastasis in patients with pineoblastoma is a rare presentation, and physicians caring for patients with pineoblastoma should be suspicious of this rare complication during the disease course. Case reports have pointed to a few risk factors of osseous spread, but more case studies of intraosseous metastasis will be needed to further elucidate various case presentations. Our case demonstrates a patient who presented with extensive osseous metastasis, with two risk factors: incomplete chemotherapy and VP Shunt, likely spread due to Batson's plexus. While our patient was lost to follow-up, studies suggest that osseous metastasis responds favorably to chemotherapy therapies. More studies regarding causal genetic mechanisms affecting the likelihood of metastasis is also an area of interest that may shed light onto the pathogenesis of osseous metastasis.

Author contributions

AN and SS performed clinical examination and designed the report. EC and JL designed the report and created drafts of the paper. HM designed the report. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

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Ethical approval

Ethical approval was not required, as this case report documents and studies patient's disease course and did not require the patient to be protected from any interventions by the authors

Informed consent

Written informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

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