

Case Report

Neo-Adjuvant Chemotherapy Followed by Surgery for Extensive Calvarial Metastases of a Neuroblastoma

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Neuroblastoma is a common tumor of children. We report a patient with extensive calvarial metastases of a neuroblastoma as an initial presentation. A 2-year-old girl presented with a history of gradually increasing head size and fever. A brain CT showed a multilobulated, large, extra-axial tumor involving both frontotemporoparietal areas with a sunray-spiculated hyperostosis of the skull and marked contrast enhancement. A brain MRI demonstrated extensive calvarial lesions with simultaneous involvement of the orbits. A biopsy was performed and a ganglioneuroblastoma was diagnosed. On systemic evaluation, an enlarged abdominal mass was detected. After neo-adjuvant chemotherapy, most of the tumors disappeared except for a tumor in the left parietal area; there was a corresponding decrease in the circumference of the head. We performed surgery for the remnant mass. Intensive chemotherapy was administered and a bone marrow transplantation was performed. Adequate neo-adjuvant chemotherapy followed by surgery to the neuroblastoma with extensive metastases to the skull and orbit may be helpful.

Key Words : Calvarium · Chemotherapy · Neuroblastoma · Metastasis.

INTRODUCTION

Neuroblastomas constitute 10% of all pediatric malignancies and 75% present in children under 2 years of age.⁵⁾ This tumor accounts for approximately 10% of all pediatric neoplasms and 15% of cancer deaths in children. Seventy-five percent of neuroblastomas arise in the abdomen and pelvis, 20% originate in the thorax, and 5% are derived from the neck.¹⁾ Metastases from neuroblastomas characteristically occur in a disseminated fashion, with the common sites being liver, lymph nodes, bones, and bone marrow.⁵⁾ Skull vault metastases are generally more common in adults and infrequent in children. Calvarial metastases are characteristically occurred on multiple lesions with simultaneous involvement of the orbits and isolated metastasis rarely occur.¹¹⁾ As described above, skull vault metastasis is very rare in children. We report a 2-year-old girl who initially presented with extensive calvarial and orbit masses, which were successfully controlled by neo-adjuvant chemotherapy followed by surgery for the residual mass.

CASE REPORT

The patient was a 2-year-old girl who presented with a history of gradually increasing head size, proptosis, and fever. The head circumference was in the 97th percentile. On examination, the child had an average build and there was no lymphadenopathy or organomegaly. There was no history of trauma, convulsions, vomiting, limb weakness, abnormal bleeding, or bladder/bowel disturbances. There was no tenderness or signs of inflammation over the swelling of the scalp. A brain CT showed a multilobulated, large, extraaxial tumor involving both frontotemporoparietal areas with a sunray-spiculated hyperostosis of the skull, which presented as a hyperdensity on the pre-enhanced film and markedly homogenous contrast-enhanced on the post-enhanced film (Fig. 1A, B). A brain Magnetic resonance imaging demonstrated extensive calvarial lesions with simultaneous involvement of the orbits (Fig. 1C, D). On T1-weighted images the tumor showed iso-signal intensity, and on T2-weighted image, the tumor had a hyper-signal intensity with irregular margins. On the contrast image, the tumor was shown to be a large, heterogeneous, enhancing mass-like lesion. A biopsy was performed. The histologic features showed sheets of small, round cells divided by a delicate fibrovascular stroma. The tumor was also positive for neuronal markers, such as CD56, chromogranin, and synaptophysin (Fig. 2). A ganglioneuroblastoma was diagnosed. On systemic evaluation, an International Neuroblastoma Stag-

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ing System stage IV neuroblastoma with an adrenal mass and involvement of the bone marrow and skull was confirmed. Cisplatin, etoposide, CPM, and adriamycin (CCG) 3,891 induction chemotherapy was initiated. Five months later, the head circumference was in the 75th percentile and the proptosis had resolved. On the brain MRI, most of the tumors had disappeared except for the left parietal area, and T2WI showed a low-signal intensity (Fig. 3). The consistency of the tumor had changed after chemotherapy. Surgery was performed for the remnant mass. Intra-operatively, the tumor was very hard, and it presented in the epidural space, which was firmly attached to the dura mater. The inner table of the skull showed severe osteolytic changes, spiculated bone formation, and extuberant new bone formation causing bony spiculation was noted arising from the inner table of the parietal bone (Fig. 4). Post-operative follow-up imaging showed no recurrent or remnant metastatic lesions in the calvarium. Intensive chemotherapy was administered and a bone marrow transplantation was performed.

DISCUSSION

A neuroblastoma is a type of cancer that begins in the embryonic cells which normally develop into parts of the nervous system. These cells are referred to as neuroblasts. The tumor arising from these cells is a neuroblastoma. The cause of neuroblastomas is unknown. We do know that neuroblastomas are not hereditary, do not result from injury, and are not infectious. The most common clinical presentation of a neuroblastoma is an abdominal mass. Metastases may also be the primary presentation of neuroblastomas and the common sites of such manifestations are the liver, lymph nodes, bone, and bone marrow.⁵⁾ The skeletal sites of predilection for metastases are skull, facial bones, pelvis, and proximal long bones.^{1,7)} Two hypotheses have been advanced regarding the metastatic behavior of neuroblastomas (the “soilseeded” hypothesis of Paget and the mechanical theory of Ewing). According to Paget’s hypothesis, tumor cells circulate in the vascular tree, but only seed areas which have a favorable microenvironment or growth advantage (i.e., the “proper soil”). Ewing proposed that the pattern of metastases is related to blood flow to tissues; thus, tissues with more flow have a higher incidence of metastases. In 1907, Hutchinson reported the tendency of neuroblastomas to metastasize to the calvarium and orbit (Hutchinson’s form of neuroblastoma).^{3,10)} This case initially presented with extensive calvarial and orbit masses. The characteristic radiographic pattern of sk-

elethal metastases in neuroblastomas is of permeative destruction.^{7,9)} Calvarial involvement in neuroblastomas has a classic multiple lucency appearance; other patterns include diastasis of cranial sutures and “sunray spiculation” or a “hair brush appearance.”^{9,9)} The latter is a rare presentation, known to have poor prognosis with early death.⁵⁾ The differential diagnosis in a child with a solitary calvarial mass and underlying osteolysis includes

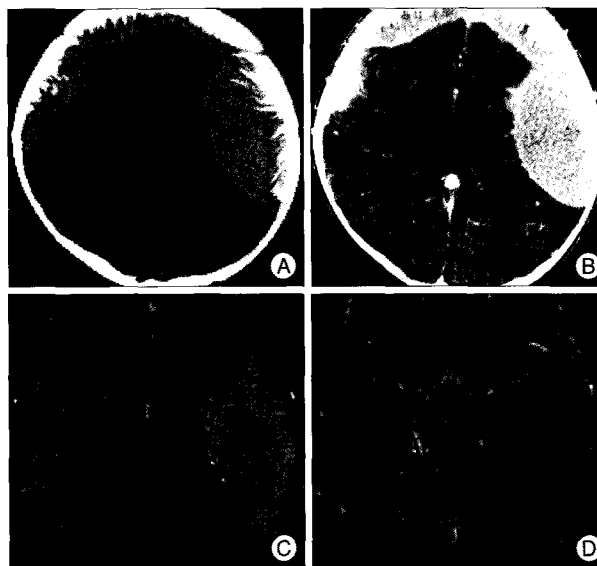


Fig. 1. Pretreatment CT and MRI showing extensive calvarial involvement. CT scans showed multilobulated, large, extraaxial tumor involving both frontotemporoparietal areas with spiculated hyperostosis of the skull (A) and markedly homogenous contrast-enhanced tumor on the post-enhanced film (B). Magnetic resonance imaging (MRI) shows high signal intensity on T2WI and heterogeneous enhancement after gadolinium enhancement (C). The mass into both orbits is shown (D).

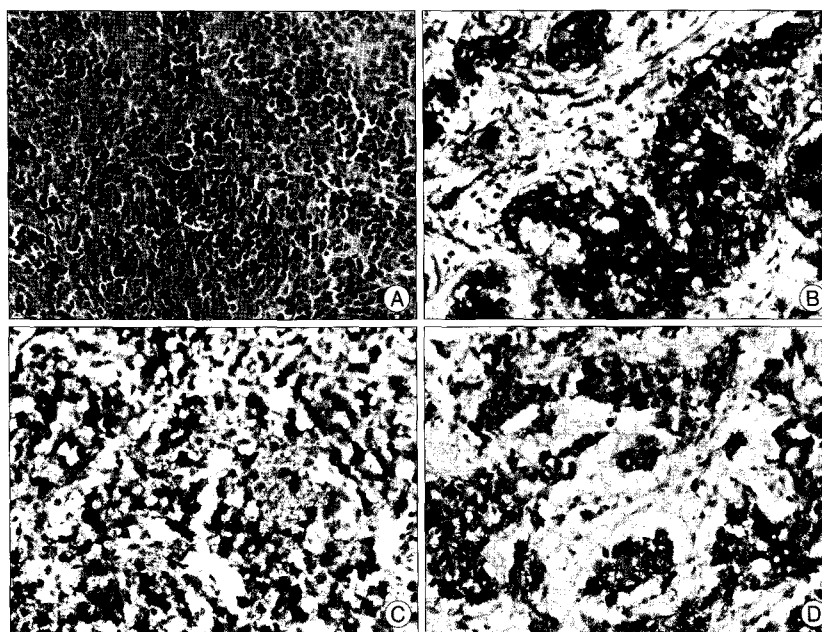


Fig. 2. Pathologic findings. The histologic features show sheets of small, round, cells divided by delicate fibrovascular stroma (A). It is also positive for neuronal markers, such as CD56 (B), chromogranin (C), and synaptophysin (D) (Original magnification $\times 400$).

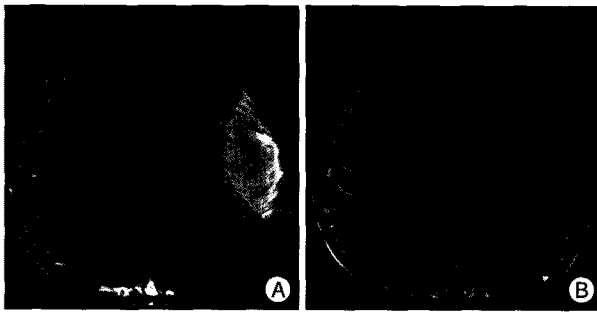


Fig. 3. Postchemotherapy MRI showing partial remission with residual mass. On brain MRI, most of the tumors had regressed, except the left parietal area (A) and T2WI showed low-signal intensity (B).

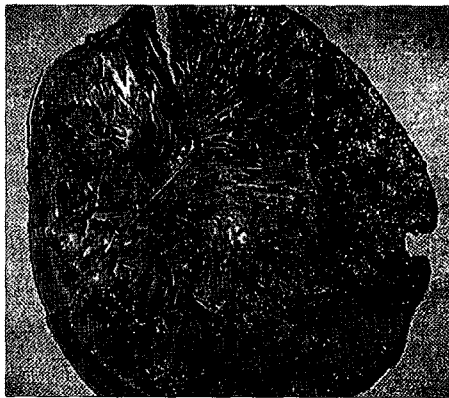


Fig. 4. Operative findings. The inner table of the skull shows severe osteolytic changes and speculated bone formation (A). The tumor is very hard, and it occupies in the epidural space, which was firmly attached to the dura mater (B).

osteomyelitis, eosinophilic granuloma, and malignant deposits from leukemia or lymphoma. Spiculated new bone formation is usually a feature characteristic of metastases from leukemia, lymphomas, melanotic prognomas, osteosarcomad, or Ewing's sarcomas, rather than neuroblastomas.⁵⁾ Since calvarial metastases are uncommon in children compared to adults, a primary pathology and surgical resection may usually be considered clinically for a child with an isolated calvarial mass. An isolated calvarial deposit with a large soft tissue component and sunray spiculation as a leading presentation of neuroblastoma has been described only once in a report by Egelhoff and Zalles. Spiculated new bone formation has also been reported in mandibular metastases of a neuroblastoma by Haddad et al.⁷⁾ Our patient presented with extensive calvarial metastases which had a spiculated bone reaction.

In 2005, Gaetani et al.⁸⁾ reported calvarian metastases of renal cell carcinoma. They reported two cases. Both patients underwent open surgery without chemotherapy or radiotherapy. In both cases, a wide craniectomy based on neuronavigation was performed, allowing detection of the margins of bone involvement using CT scanning for bone. The limits of the craniectomy were larger than the extension of the tumor in order to create an island of non-pathologic bone and dura around the lesion, carefully avoiding entry into the mass during surgery, and removing the mass "en bloc" together with bone and dural components. They

recommended the use of bone wax and the removal of a wide dural flap to minimize blood loss and the risk of local recurrences.

In our case, neo-adjuvant CCG chemotherapy was used for the calvarian lesion for 5 months and was effective. The tumors that had extended to both frontotemporoparietal areas had regressed, except the left parietal area, which showed a well-circumscribed feature. After following the surgery for the remnant mass and continuing systemic chemotherapy, there were no recurrences. Neo-adjuvant CCG chemotherapy to the calvarian metastases of the neuroblastoma was successful and the localized calvarial mass through chemotherapy was treated by surgery.

CONCLUSION

We experienced an extensive calvarial metastasis of neuroblastoma which was successfully controlled by neo-adjuvant chemotherapy followed by surgery for the residual mass.

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