

Neuroblastoma with mandibular metastasis: a case report

Douglas R. Reich, DMD
Theodore P. Croll, DDS
Frederic T. Serota, MD
John Powers, BS

Abstract

Neuroblastomas with mandibular metastases have been reported in the literature. A case is reported in which a patient with neuroblastoma displayed unusual symptomatology and radiographic changes, and underwent bone marrow transplantation therapy.

Introduction

Neuroblastoma is a malignant neoplasm of infancy and childhood. The tumor is of undifferentiated embryonic neural tissue usually derived from the adrenal gland, but may originate anywhere along the sympathetic chain.^{1,6} Some neuroblastomas are functional and laboratory testing may reveal elevated urinary or serum catecholamines. Neuroblastoma accounts for 10 percent to 50 percent of all neonatal malignancies, ranking fourth in frequency after leukemia, lymphoma, and central nervous system tumors.^{4,7,8}

The etiology of neuroblastoma is unknown. Epidemiologic research in Great Britain revealed a seasonal increase in mortality rates, and the investigators theorized a viral etiology.⁹ Such findings have not been corroborated in the United States.¹⁰ A genetic pattern for neuroblastoma has not been shown, but males are reportedly affected slightly more than females.⁴

Neuroblastoma usually occurs in the first decade of life. Snyder and Cawson reported that 80 percent of affected children develop the disease before the age of five, and rarely after 15 years of age.⁵ Angelopoulos et al. noted that 50 percent of neuroblastomas occur in the first three years of life,³ and Chakrabarty and Dash reported a case of neuroblastoma with mandibular metastasis in a 23-year-old male.¹¹ Stern et al. reviewed 83 cases of neuroblastoma and found a

median age of three years at time of initial diagnosis.¹²

Neuroblastoma spreads by local extension and invasion. Metastasis of neuroblastoma occurs by circulatory or lymphatic routes, with blood-borne metastases diagnosed by bone marrow aspiration. The tumor may be characterized by its metastatic pattern. The "Pepper" type results from metastases throughout the soft tissues, while the "Hutchinson" type results from spread to cranial bones and skeletal structures.^{13,14}

Signs and symptoms of neuroblastoma include palpable abdominal masses, weight loss and elevated temperature. Anemia is a common laboratory finding. Oral involvement may include facial and/or intraoral swelling, mobile or displaced teeth, and dysfunction of affected cranial nerves.¹²

Radiographically, the lesion may show ill-defined borders and expansion of dental follicles.¹² De Leon et al. observed that the lesion appears "moth-eaten,"¹⁵ while Worth noted that radiographic appearance varies and is not pathognomonic for the disease.¹⁶ From the time of radiographic diagnosis of neuroblastoma in the maxilla or mandible, patient survival rarely exceeds a year.¹⁷

To date, the results of treatment for neuroblastoma have been disappointing. The current 32 percent overall survival rate is the same as it was prior to the use of chemotherapy, though the median survival time appears to have been prolonged by a few months.¹⁸ For this reason, supralethal doses of chemotherapy and radiotherapy, followed by bone marrow rescue are being investigated in patients demonstrated to be refractory to conventional therapy.^{19,21}

In 1933, Colville and Willis first reported neuroblastoma with mandibular metastasis. Their patient was an eight-year-old female who died six weeks after surgery and radiotherapy, and was found to have suf-

ferred extensive metastatic involvement of the cranial osseous structures, including the mandible.²² Nine years later Rosendal reported two other cases of very young children with "sympathicoblastoma" with cranial and mandibular lesions.²³

Since the early reports of neuroblastoma with confirmed mandibular metastasis, there have been numerous others.^{1,3,5,11,15,24-29} A variety of unusual oral findings are recorded including metastatic pulpal involvement,⁵ gingival alterations,^{24,25} osseous expansion,^{1,7} tooth mobility,¹⁵ and in one unique case, a 23-year-old male had a radical hemimandibulectomy due to extensive mandibular involvement.¹¹ In all the cases reviewed the usual treatment was a combination of surgery and radiotherapy, and in recent years, adjunctive chemotherapy. All reported cases of neuroblastoma with mandibular metastasis have in common early demise of the patient after detection of the jaw lesion, despite subsequent therapy.

Case Report

S.K. was a 13-year-old Caucasian female who was well known to the Division of Dentistry at Children's Hospital of Philadelphia. She had a history of stage IV neuroblastoma and had undergone autogenous bone marrow transplantation in 1978.

Chief Complaint — In June, 1979, the patient complained of intermittent "tingling" of the gingiva and teeth, on the right side of the mandible in the region of the permanent first molar and premolars.

History of Present Illness — S.K. had been examined by dental staff in September, 1978, and again four months later. She complained only of dryness of the mouth at both visits. The patient was again examined in May, 1979, when she first complained of intensifying paresthesia in the tissues of the right mandible anterior to the second molar region.

Past Medical History — In April of 1973 S.K. was diagnosed at eight years of age with left suprarenal neuroblastoma. A urinary test for catecholamines was strongly positive and lytic lesions were evident in thoracic and lumbar vertebrae, and in the left femur. A bone marrow aspirate from the posterior iliac crest revealed neuroblastoma cells. Chemotherapy was initiated including dimethyl trazene imidazole carboximide (DTIC), vincristine, and cyclophosphamide. One thousand, four hundred rads of radiotherapy were administered to the lower thoracic and lumbar spine and left femur. In April, 1975, two years after primary diagnosis, the patient was thought to be free of active disease, and the chemotherapeutic regimen was withdrawn. She remained in remission for one year when a vanilmandelic acid spot test (VMA) was again found to be positive, and a bone scan revealed lytic lesions of the cervical and thoracic spine, the skull, and the left ileum. Radiotherapy was again administered, this

time to the skull and cervical spine, and chemotherapy was reinstated. In April, 1978, a new lesion was discovered in the right femur and it was irradiated with 1,500 rads.

In August, 1977, and January, 1978, when S.K. was in remission and the bone marrow was determined by histologic technique and gradient analysis to be free of tumor, bone marrow was harvested and cryopreserved. In September 1978, the patient was conditioned with vincristine, cis-platinum, nitrogen mustard, and total body radiation. Rescue (infusion) with autogenous bone marrow followed. Her hospital course was complicated by renal failure, presumed sepsis, and hemorrhagic cystitis. Bone marrow engraftment was slow and incomplete. In December 1978, the patient was discharged, 61 days after the transplantation procedure. She was then followed in the oncology out-patient clinic, receiving blood and platelet transfusion support as required.

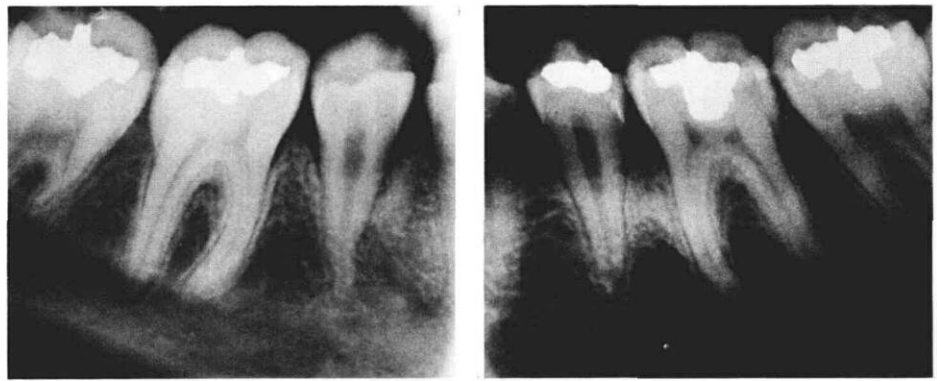
Oral Findings — S.K. demonstrated a complete permanent dentition with unerupted third molars. There were no remarkable oral soft tissue findings in May or June of 1979 with the exception of generalized chronic marginal gingivitis, and the patient's reports of paresthesia in certain regions. Saliva was seen to flow freely from the major glands.

There existed multiple Class I carious lesions and several silver amalgam restorations which had been placed three to four years previously. The second premolar and first molar in the mandibular right quadrant were loosened in their sockets, with no periodontal pathosis or traumatic occlusal forces apparent to explain the abnormal mobility.

The patient reported discomfort and paresthesia extending from the mandibular right first molar to the canine, along with "tingling" in the mandibular lip from the midline to the area of the right commissure. The patient did not claim profound numbness, but had difficulty discerning pin prick testing in the soft tissues of the region. The tongue and other orofacial soft tissues displayed no motor or sensory abnormalities.

Radiographic Findings — Radiographs from May, 1979, showed a diffuse thickening of the periodontal ligament space at the apex of the distal root of the right mandibular first molar (Figure 1a), while the left molar appeared normal (Figure 1b). The panoramic radiograph revealed no abnormal radiolucencies but demonstrated alterations in premolar root formation consistent with changes caused by chemotherapy and radiotherapy.³⁰ In June, 1979, new radiographs revealed a large irregular radiolucency surrounding the roots of the mandibular right first molar (Figure 2a). That finding coincided with the patient's complaint of increased discomfort and paresthesia. The distal root of the contralateral first molar and surrounding tissues again appeared radiographically normal (Figure 2b).

Figure 1. Periapical radiographs from May, 1979, reveal no obvious osseous changes (left, patient's right; right, patient's left).



Dental Treatment — The patient was scheduled for restorative dental care and consideration for biopsy of the osseous mandibular lesion, however she expired in July, 1979, before dental services could be performed.

Autopsy Findings — Postmortem examination was performed 2½ hours after death. The autopsy confirmed the diagnosis of neuroblastoma, stage IV. Metastases were found in the liver, spleen, visceral pleura, lungs, pancreas, lymph nodes, calvarium, dura, meninges, and ribs. Microscopic examination of the skull, mandible, and vertebrae revealed "... dense infiltration by tumor, with no normal marrow elements seen," and the examiner noted, "... considering the extent of disease at diagnosis (autopsy), her long survival was remarkable." Photomicrographic documentation of the mandibular lesion was not available for this report.

Discussion

This case of mandibular metastasis of neuroblastoma is interesting in several respects. At initial diagnosis, S.K. was considerably older than the median age of three years as reported by Stern.¹² Although S.K. was first diagnosed with neuroblastoma at eight years of age, evidence of mandibular metastasis did not appear until much later. Since the patient was closely followed clinically and radiographically, the authors were able to observe no diagnostic evidence of

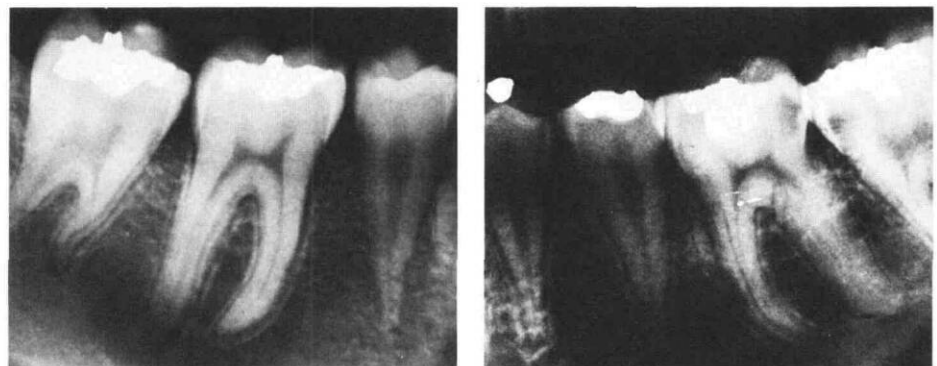
jaw metastasis until six years later. At that stage, the mandibular lesion was aggressive and the patient was near death.

In other reported cases of neuroblastoma with jaw metastasis, swelling of the cortical plate or dental follicle was often observed. The authors of this report were able to find only one other case where sensory nerve dysfunction is reported,¹² and that patient had confirmed tumor involvement of the inferior alveolar nerve. In considering S.K.'s anatomical and symptomatological findings, it is likely that she suffered from tumor extension into the neurovascular tissues of the mandibular canal.

Radiographically, the lesion appears to surround the roots of the mandibular right first molar. There are various patterns of radiographic changes around teeth with neuroblastoma, including small rarefactions,²³ dental follicular expansion and osteolytic lesions,¹² multiple radiolucencies,³¹ and a "moth-eaten" osseous appearance.¹⁵ It is doubtful that the lesion appearing in Figure 2a could have had odontogenic etiology. Even though Kotzet et al. noted that methotrexate, among other chemotherapeutic agents, prevents localization of inflammation,³² there existed no apparent reason for pulp inflammation in the right first molar. There were no dental caries and the restoration was of long duration.

An experimental means of treating neuroblastoma was used for S.K. Bone marrow was harvested from

Figure 2. Periapical radiographs from June, 1979. Left, reveals osteolytic changes around the roots of the mandibular right first molar; right, reveals no abnormal findings of the left molar region.



the patient's own marrow during episodes of remission. Later, after total body irradiation, the marrow was reinfused. To date, the outcome of bone marrow transplantation procedures are promising for treatment of some disorders. Patients with aplastic anemia and leukemia are improving and much research is underway in this novel treatment mode. Since such therapy for neuroblastoma patients is in its nascent stages, no information on its efficacy is currently available, and the effect of bone marrow transplantation on mandibular metastasis of neuroblastoma is not known.

Dr. Reich is lecturer and Dr. Croll is clinical associate, department of orthodontics/pedodontics, University of Pennsylvania School of Dental Medicine, 4001 Spruce Street A1, Philadelphia, PA 19104, and both are staff pedodontists, Children's Hospital of Philadelphia. Dr. Serota is assistant clinical professor, division of oncology, Children's Hospital of Philadelphia. Mr. Powers is a senior student of dentistry, University of Pennsylvania School of Dental Medicine. Requests for reprints should be sent to Dr. Reich.

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