Primary Ewing's Sarcoma of the Skull

Kafatasında Birincil Ewing Sarkomu

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Abstract: A six year-old girl with primary Ewing's sarcoma in the right temporal fossa is reported. Computerized tomography disclosed a non-homogeneous contrast enhancing mass with necrosis. At operation, the tumour was situated in the epidural space, and has penetrated into the brain parenchyma through an opening of dura caused by tumour invasion. Both the tumour and invaded dura were removed, and the patient received radiotherapy postoperatively. After 27 months, a recurrence developed in the original tumour bed. Although the initial tumour had originated from temporal bone, recurrence arose from a focus of the frontal region. Differential diagnosis and reccurrence of this rare tumour of skull are discussed with a review of the literature.

Key Words: Ewing's sarcoma, radiotherapy, skull

Özet: Sağ temporal çukur yerleşimli birincil Ewing sarkomu olan 6 yaşında bir kız çocuğu sunuldu. Bilgisayarlı beyin tomografisinde nekroz içeren ve kontrast maddeyi non-homojen tutan lezyon görüntülendi. Ameliyatta, tümörün epidural yerleşimli olduğu ve dura materde oluşan bir açıklıktan beyin parankimine yayıldığı görüldü. Tümör ve tümörlü dura çıkarıldı ve hasta ameliyat sonrası dönemde radyoterapi aldı. Yirmi yedi ay sonra özgün tümör yatağında nüks gelişti. Tümör başlangıçta temporal kemikten köken almasına rağmen, nüks frontal bölgedeki bir odaktan gelişti. Kafa içinde nadir görülen bu tümörün ayırıcı tanısı ve nüksü, ilgili yayımlar gözden geçirilerek tartışıldı.

Anahtar Sözcükler: Ewing sarkomu, kafatası, radyoterapi

INTRODUCTION

Ewing's sarcoma is a potentially fatal bone sarcoma and constitutes about 5 % of biopsy-proven bone tumours with a predilection for long bones or the pelvis, the skull as primary site is rare and seen in only about 1 % of cases (17, 20, 25). The majority of patients are under the age of 30, with the highest frequency between 10-15 years of age (17, 20). Total excision of the lesions plus radiotherapy and chemotherapy may be effective in the treatment of these tumours (16, 17, 25, 28). The aim of this report is to draw attention to regrowth of Ewing's sarcoma of the skull together with a review of the literature.

CASE REPORT

A six-year old girl with a two week history of headache, nausea and vomiting was admitted in October 1993. No abnormality was found on physical examination. Fundoscopic examination showed bilateral papilloedema. A palsy of the seventh cranial nerve on the left was observed.

The skull radiogram did not show any abnormality. Computerized tomography (CT) scans revealed a patchy, enhancing mass in the right temporal fossa with scattered hypodense areas. The lesion was well circumscribed with a hyperdense rim

of contrast material enhancement, which was connected with the nidus (Figure 1).

She underwent a right temporoparietal craniotomy. On removing the bone flap, we encountered a soft, reddish- grey mass situated in the epidural space. The inner tabula of temporal bone had been softened by the lesion, and its colour had changed. The dura was intact except for one opening, through which the nidus of tumour in reddish colour penetrated into the cerebrum. The tumour and invaded dura were removed and the defect was repaired with a dural graft.

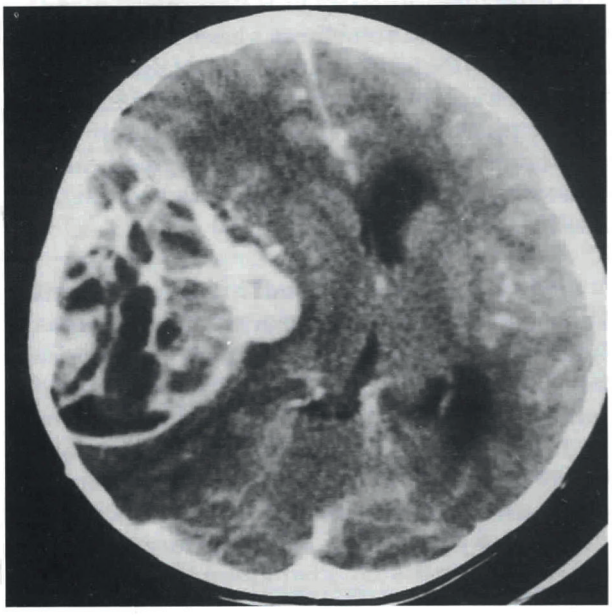

Figure 1: Axial CT scan showing a well circumscribed, irregular contrast enhancing mass with nidus.

Histological examination showed a tumour of high cellularity composed of monotonous sheets of small cells; the cells had little discernible cytoplasm, some had vesicular angulated nuclei, and occasionally ill-defined rosette like structures, formed by the tumour cells. There was PAS positive material in some sheets of tumour cells (Figure 2). Occasional clusters of lymphocytes were present, and large clusters of tumour cells infiltrated the bone and dura. Preliminarily the tumour was recognized to be a round cell sarcoma.

Immunocytochemistry studies showed positive labelling for MIC-2 (a marker for Ewing's sarcoma and primitive neuroectodermal tumours)

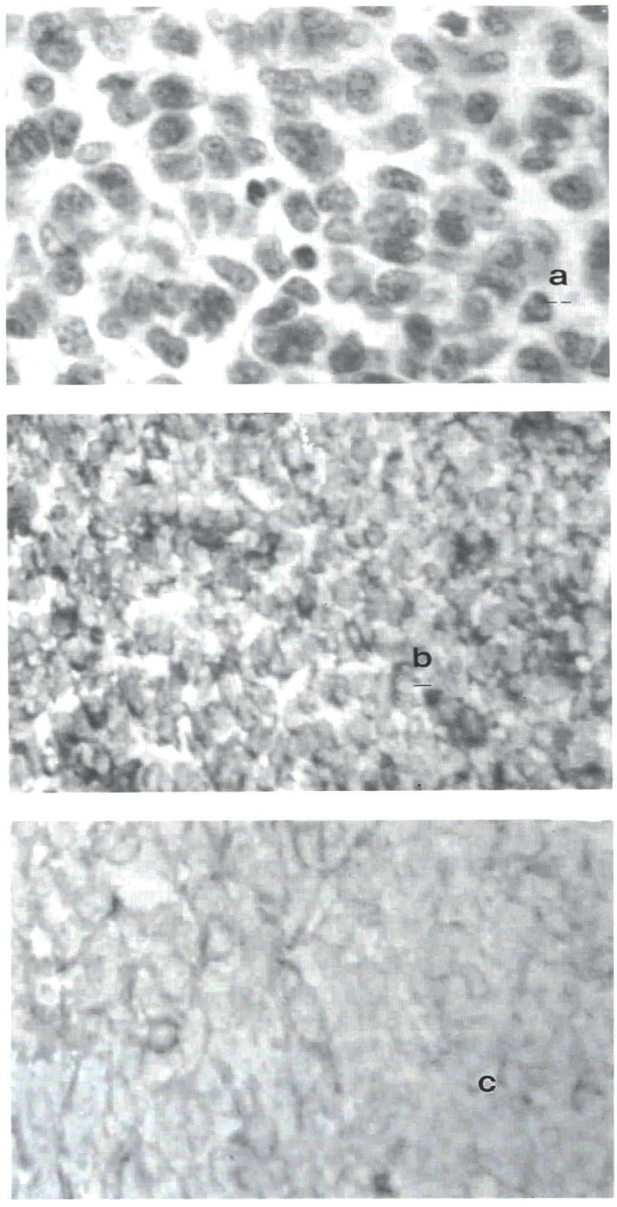

Figure 2, a)Photomicrograph showing uniform sheets of small cells with round, ovoid or vesicular angulated nuclei and indistinct, pale staining cytoplasm (H+E, X40), b) tumor cells stained for glycogen, showing abundant deposits within the cytoplasm (PAS, X25), c) tumor cells stained for MIC-2 (Immunoperoxidase, X25).

(Figure 2), neuron specific enolase (NSE), vimentin and weak positivity with synaptophysin. Glial fibrillary acidic protein (GFAP), epithelial membrane antigen (EMA), leukocyte common antigen (LCA) and desmin were negative.

The total dose of 3600 cGy was given locally over a period of six weeks. She received no

chemotherapy. As a follow up, computed tomography of the head was taken once every 6 months. A whole bone scintigraphy which was not performed initially was also made to identify any metastases of tumour after the definite immunohistochemical diagnosis of Ewing's sarcoma during the follow up. She was in a good health up to March 1996. Then, she begun to suffer from headache, and her CT scans showed a huge recurrent mass in the original tumour bed, originating from orbital roof of frontal bone (Figure 3). Bone scintigraphy revealed uptake of radionuclide on the supra orbital rim of the right eye, but no metastases in others parts of the skeleton. The right carotid arteriogram displayed that, the recurrent tumour's nodule was being fed by ophthalmic artery and the intracerebral part of tumour was mainly by middle cerebral artery and also anterior cerebral artery (Figure 4). The tumour received no supply from the external carotid artery. Direct radiograms and CT scans of the chest were normal.

At the second operation, the tumour appeared to be red coloured, fragile and soft, except for a hard nidus at the junction of the right orbital roof and the zygomatic arch of the frontal bone. The tumour was removed totally and histopathologic examination of specimens was the same as the initial diagnosis. The patient received radiotherapy and chemotherapy including vincristine (1.5 mg/m^2), cyclophosphamide (1200 mg/m^2) and adriamycin (30 mg/m^2) in a month postoperatively. This chemotherapy regimen was completed over a period of two months. The patient was in good health 9 months after the reoperation.

DISCUSSION

Primary Ewing's sarcoma of calvarial bone is extremely rare. To our knowledge only 24 individual cases were reported in the literature (1,3,6,8-12,14,18,19,21-23,26,29,30,33-37). Since Ewing's sarcomas have a capacity for rapid growth , those arising from the skull frequently produce the signs and symptoms of intracranial hypertension, with a short history and sometimes a need to be removed urgently (14,29,30). Local swelling of the head may be the first sign of Ewing's sarcoma (3,14,26,29,33,36). Our patient had a short history of 15 days, no local swelling was palpated on the head and there was no abnormality on plain radiogram of the skull.

A CT scan showed an epidural mass surrounded by the regular margin of the dura on the inner side. Contrast enhancement of the lesion may be homogeneous (21,30,33,34) or irregular as seen in our case (1,19,37). In addition, an invading tumour nodule to the brain parenchyma was seen at the border of lesion, which has not been reported previously. This is of interest, as Ewing's sarcoma originates from bone, the nodule generally is

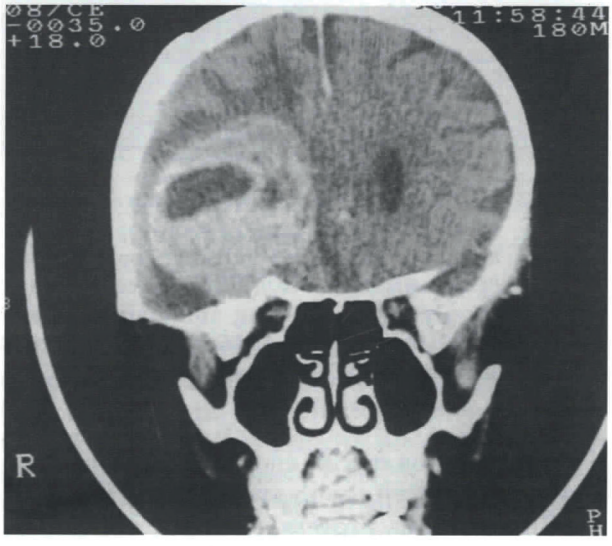

Figure 3: A huge recurrent mass which developed 27 months after first operation.

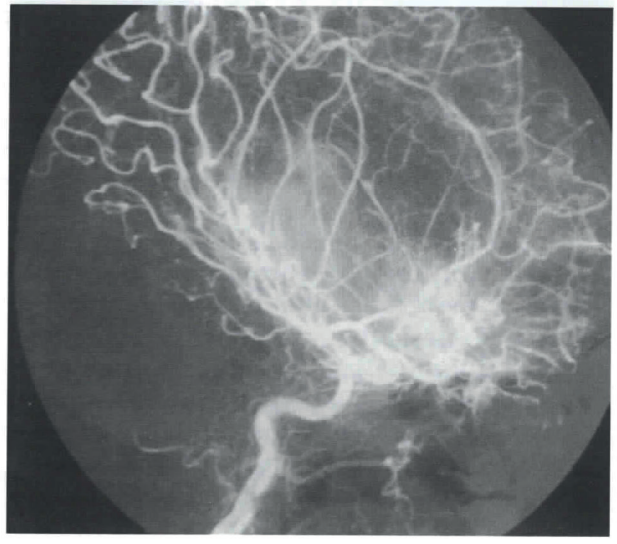

Figure 4: Right carotid arteriogram shows that the nodule of recurrent tumor is being supplied mainly by the ophthalmic artery and the intracerebral part of tumour by the middle and anterior cerebral arteries.

expected on or at the border of bone, like the recurrent tumour in our case.

Since the tumour was preliminarily reported as round cell sarcoma on the basis of light microscopy, Ewing's sarcoma, peripheral neuroepithelioma, neuroblastoma and non-Hodgkin's lymphoma were included in the differential diagnosis (20). The histogenesis of Ewing's sarcoma is still controversial, however there is convincing evidence for the potential of Ewing's sarcoma cells to undergo neural differentiation in vitro (4). Ewing's sarcoma and peripheral neuroepithelioma which are classified as poorly differentiated round cell, primitive neuroectodermal neoplasms have similar morphological, immunohistochemical features and identical cytogenetic anomalies (2,7,13,27,32). In the cases where tumour shows well defined rosettes of Homer-Wright or Flexner-Wintersteiner type and has two or more neural marker expression such as NSE, Leu-7, synaptophysin, S-100 protein, chromogranin and neurofilament protein, the diagnosis is more favoured as neuroepithelioma rather than Ewing's sarcoma (5,15). Whereas the presence of intracellular glycogen by PAS stain with diastase control and vimentin expression renders the diagnosis as Ewing's sarcoma (7).

Neuroepithelioma must be distinguished from the metastases of neuroblastoma. The localization of these tumours shows also some differences: Peripheral neuroepithelioma arises usually from peripheral nerves in extremities, on the other hand, neuroblastoma originates in the neural crest cells of the sympathetic nervous system and typically appears as an abdominal mass with frequent bone metastases (7). Mic-2 gene product expression is seen in neuroepithelioma and Ewing's sarcoma rather than neuroblastoma (24). The presence of intracellular glycogen in neuroblastoma cells is very rare and may be possible to discern only with the electron microscope (31).

In our case, there was no primary tumour focus as to be diagnosed neuroblastoma, which is excluded for diagnosis. The location of tumour, vimentin and Mic-2 expressions and PAS positivity for glycogen have strongly favoured Ewing's sarcoma with neural differentiation. Since LCA was negative, non-Hodgkin's lymphoma was excluded.

The patients with Ewing's sarcoma without metastases have a 5 year survival of 22 % and the most important factors associated with survival are the surgical resection and localization of tumour (25). The co-operative Ewing's sarcoma study (CESS 81) group defined a four-drug combination of chemotherapy, prior to local control of lesion by surgery or radiation with the disease-free interval rate 60 % at 36 months. They also observed that local failure has been occurred mostly in patients treated with radiotherapy only (16). The intergroup Ewing's Sarcoma Study (IESS) reported that Ewing's sarcoma of head and neck have a better prognosis than those of other parts of the skeleton, with a mean 3 years of follow-up (28). The majority of the cases with Ewing's sarcoma of the skull, without metastases and recurrences, had a follow up duration of less than two years (1,9,12,19,21,26,33,34,37). But, the follow up duration was longer than two years we encountered two recurrences (6,36). One of these patients was treated with radiotherapy and chemotherapy after radical excision of tumour (36), and the other patient treated with radiotherapy and chemotherapy without surgical excision of the lesion, died from intracranial extension 46 months later (6). Since there is no report of case with distant metastases, local control of intracranial tumour seems to be essential for longer survival.

Jayaram et al. reported that radiotherapy can reduce about 30 % of tumour size (14). However with radiotherapy and chemotherapy, the tumour can regress to 5 % of the initial size (1). Local recurrences were seen in 33 % of patients who had received radiotherapy alone, but only in 5 % of those who had received radiotherapy and chemotherapy (25). Therefore, the fact that our patient (who was transferred to a department of oncology for radiotherapy and chemotherapy treatment in another hospital) did not receive chemotherapy, may have played a role in tumour recurrence. Ewing's sarcoma may be multilocal, including shoulder, knee and skull vault (30). In our patient, although involved bone was removed in the first operation, regrowth of the lesion was observed at the junction of the orbital roof and zygoma. This suggested that the tumour has spread along the flat bone.

Ewing's sarcoma arising from the skull is mainly fed by external carotid artery (9). In some cases, it can be supplied by the branches of internal carotid, like the callosomarginal artery (26). In our case, tumor nodule was mainly be supplied by the ophthalmic artery and the intracerebral part of tumour was by both the middle and anterior cerebral arteries.

In conclusion, the patients with Ewing's sarcoma of skull carry a high risk of local failure and the invasion of the brain may occur. We recommend that these patients follow by CT or magnetic resonance imaging every 6 months.

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