Sporadic unifocal infantile myofibromatosis involving the skull

Case report

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Infantile myofibromatosis involving the skull is a benign disease if there is a solitary lesion. However, the multifocal form with skull involvement may portend a lethal course in the 1st year of life if there is involvement of the heart, lungs, or gastrointestinal tract. The authors report the case of a 3-year-old boy with an enlarging left parietal skull lesion that had been present since infancy. Increasing pain and the need to obtain tissue for diagnosis led to resection of the lesion by means of a small craniectomy. Further evaluation revealed no other lesions. A distinctly rare disease is presented, and the need for staging in children younger than 2 years of age is suggested to rule out cardiac, pulmonary, or gastrointestinal involvement.

KEY WORDS • congenital generalized fibromatosis • eosinophilic granuloma • infantile myofibromatosis • skull • children

The management of osteolytic skull lesions in the pediatric population requires knowledge of various possible diagnoses because infectious, inflammatory, and neoplastic processes can manifest similar presentations. The patient’s age at presentation, physical findings, concurrent physical disease, family medical history, and radiographic appearance of the lesion are needed to generate a differential diagnosis and to formulate a treatment plan.

Case Report

History. This 3-year-old boy was referred to the neurosurgical service because he had a painful mass in the left parietal area. According to the patient’s medical history, the mass had been present since the child was an infant. It had slowly increased in size and had become progressively more painful.

Examination. Physical examination revealed a tender, nodular enlargement of the left parietal region. The patient had no family history of skull or soft-tissue lesions. Plain lateral skull radiography (Fig. 1) and computerized tomography (CT) scanning (Fig. 2) demonstrated a solitary lytic lesion in the left parietal bone that involved both the inner and outer tables. A radiographic skeletal survey and a chest radiograph revealed no other lesions. Systemic examination revealed no cutaneous lesions.

A literature search revealed no deaths related to multicentric disease in patients younger than 2 years of age; therefore, no further diagnostic imaging was performed.

Operation and Histological Findings. The lesion was completely resected by means of a small craniectomy. The underlying dura and brain were not involved. Histological evaluation revealed nodules of myofibroblasts with vascular spaces that were similar to those seen in hemangiopericytomas (Fig. 3). The tumor cells were not immunoreactive for S-100 protein, and they did not stain in response to testing for muscle-specific actin. Factor VIII stained the vascular channels but not the intervening tumor cells. Vimentin staining and electron microscopy were not performed. A diagnosis of myofibromatosis was made. The specimen was sent to another pathologist who had experience with this lesion type, and he confirmed the diagnosis.

Postoperative Course. The patient is now healthy at 5 years of age and has had no recurrence of pain or mass at the resection site. No skin lesions have developed.
Discussion

In 1954 Stout introduced the term “congenital generalized fibromatosis.” He described two fatal cases with multicentric lesions that involved soft tissue, viscera, and bone. Other names have also been applied to this entity: “multiple congenital mesenchymal hamartomas,” “congenital multiple fibromatosis,” and “multiple vascular leiomyomas of newborn.” In 1981 Chung and Enzinger renamed the entity “infantile myofibromatosis” after characterizing the tumor cells as being myofibromatous with hemangiopericytoma-like vessels.

The etiology of infantile myofibromatosis is unclear. In cases with a familial presentation, both autosomal-dominant and autosomal-recessive inheritance have been implicated. In most cases, however, there is no significant family history.

The natural history of multicentric infantile myofibromatosis is predicated on the location of the lesion(s). Cardiac, pulmonary, or visceral lesions can be lethal in the first year of life. In most reports, the exact cause of death has not been defined clearly. In a few cases, however, respiratory failure, cardiac failure, and bowel obstruction seemed to be the likely causes. The more common clinical course with multicentric infantile myofibromatosis, however, is spontaneous regression during the first few years of life, although lesions may persist throughout childhood. Proper diagnosis prevents the removal of other lesions, unless symptomatic, which can be mistakenly diagnosed as metastatic disease.

Need for Staging

When viewed on radiographic studies, infantile myofibromatosis can easily be confused with eosinophilic granuloma. It is important that a tissue diagnosis be made to define the appropriate treatment protocol. Whereas resection of a single lesion is curative in both diseases, in cases in which there are multiple lesions, the treatment and prognosis are distinctly different. At present, multicentric infantile myofibromatosis is followed without treatment because its natural history is usually spontaneous regression. Histopathological examination does not distinguish between the solitary and multicentric form and does not help predict the time course of regression or which patients will have a fatal course. Consequently, when cranial infantile myofibromatosis is diagnosed, patients should undergo a rigorous physical examination and skeletal survey or bone scan to search for other lesions. Given the risk of a fatal cardiac, pulmonary, or gastrointestinal event in children younger than 2 years of age, imaging of these organ systems should be strongly considered.

Radiation therapy, which has been used for the treatment of systemic histiocytosis X, is not beneficial in the treatment of infantile myofibromatosis. In fact, irradiation has been shown to induce myofibroblast formation. Similarly, chemotherapy has no role in the treatment of this disease.

Histopathological Findings

Solitary and multicentric variants of infantile myofibromatosis have the same histological characteristics and affect the same tissues. Two characteristic histological patterns are used to diagnose infantile myofibromatosis. First, the spindletype cells are arranged in whorls and their appearance is intermediate between muscle cells and fibroblasts. Second, the vascular spaces exhibit a hemangiopericytoma-like appearance. No histopathological finding predicts a fatal course.

In our case, the specimen was not stained for vimentin. Vimentin positivity is seen in all mesenchymal cells and would be present in many of the neoplasms included in the differential diagnosis. Consequently, vimentin staining is unnecessary in the evaluation of this tumor. The diagnosis of infantile myofibromatosis is based on the growth pattern and cytological features of the tumor demonstrated in hematoxylin and eosin–stained specimens. The immunohistochemical staining pattern of these tumors varies significantly. From an academic perspective, electron microscopy would have been interesting, but both electron microscopy and immunohistochemical analysis are supplemental rather than necessary to the diagnosis.
Infantile myofibromatosis

Most tumors have features that permit them to be distinguished from infantile myofibromatosis. Eosinophilic granuloma is excluded by the absence of a significant component of eosinophils and the fact that the nuclei do not demonstrate the typical grooves. In addition, the tumor cells in infantile myofibromatosis are S-100 protein negative, whereas cells in eosinophilic granuloma are S-100 positive.\(^1\)\(^,\)\(^2\) Epidermoid and dermoid cysts are excluded by the absence of a squamous epithelium and, in the case of dermoid cysts, dermal appendages. Hemangioma is excluded by the absence of dilated mature capillaries as a component of the neoplasm. Furthermore, an infantile myofibromatosis tumor is a solid mesenchymal process rather than a vascular lesion. Osteoblastomas and fibrous dysplasia are excluded from the diagnosis by the absence of the characteristic bony features of each tumor and the absence of multinucleated osteoclastic giant cells. Lipomas are excluded by the absence of fat. Neurofibromas do not demonstrate typical wavy spindle-cell nuclei and wavy fibrous stroma. The vasculature of infantile myofibromatosis is also more prominent than is typical for neurofibromas. Finally, neurofibromas are S-100 protein positive. Although leiomyoma is a serious consideration in the differential diagnosis, the absence of muscle-specific actin staining of tumor cells is inconsistent with leiomyoma, and the overall architecture is more consistent with myofibromatosis.

The possibility of hemangiopericytoma is always the greatest concern in the differential diagnosis. Both tumors can have a similar microvasculature. However, the pattern in hemangiopericytomas is typically diffuse. In myofibromatosis and in our tumor, areas of more solidly “fibromesenchymal proliferation” did not show a hemangiopericytoma pattern. Ultimately, it is this growth pattern that distinguishes these tumors.\(^3\)

Skull Involvement

With the multicentric form, the skull is often involved, but reports of solitary lesions of the cranium are rare.\(^4\)\(^,\)\(^5\)\(^,\)\(^6\)\(^,\)\(^7\) The clinical differential diagnoses based on skull radiography and CT scanning include eosinophilic granuloma (histiocytosis X), osteomyelitis, metastasis, epidermoid cyst, hemangioma, and fibrous dysplasia. Incompletely resected lesions recur, whereas those that are completely resected have a low recurrence rate (approximately 10%).\(^4\)\(^,\)\(^5\)\(^,\)\(^6\)\(^,\)\(^7\)

Chung and Enzinger\(^8\) reviewed data obtained in 61 patients with either unifocal or multicentric infantile myofibromatosis, which were obtained from the Armed Forces Institute of Pathology. Their study covered 24 years and included seven patients with lesions involving the skull. Five of the patients had solitary lesions and two had multifocal lesions. A solitary lesion of the head or neck was present in 16, the trunk in 15, the upper extremities in six, and the lower extremities in eight patients.

Inwards and colleagues\(^1\)\(^,\)\(^8\) reviewed the Mayo Clinic experience with infantile myofibromatosis involving bone treated over four decades. Approximately 70% of the patients presented before the age of 2 years. There were nine boys and five girls. There were eight cases of unifocal involvement of the skull; three of the lesions were grossly excised with no recurrence over a 2- to 5-year follow-up period.

Conclusions

Infantile myofibromatosis is an extremely rare cause of skull lesions in the newborn and pediatric population. Their radiographic appearance is not pathognomonic and can mimic infectious, inflammatory, and neoplastic processes, necessitating the need for biopsy and possible resection of the lesion. Total resection is usually diagnostic and curative. Tissue diagnosis is important to prevent inappropriate therapy such as radiation therapy or chemotherapy. The diagnosis of cardiopulmonary or gastrointestinal involvement can yield important prognostic information that could prove life saving in patients with the multicentric form of the disease. We suggest that imaging studies be performed on these organ systems in all patients with the multicentric form of this disease who are younger than 2 years old. Imaging of the neuraxis should be performed if a patient with infantile myofibromatosis develops any neurological deficits.

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