Multifocal Eosinophilic Granuloma in an Adult With 20-Year Follow Up

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Introduction
Multifocal eosinophilic granuloma is a rare disease, usually found in young children or adolescents. It is most often a "self-limiting" condition, with spontaneous regression and healing of the lesions. Although usually occurring in children, this condition has been reported in adults. Adult cases may present a diagnostic challenge.

Case Report
A 50-year-old white male with multifocal eosinophilic granuloma has been followed at Wilford Hall USAF Medical Center for the past 20 years. When the patient developed right hip pain and a non-productive cough in 1965 he was on active duty and in good health as a 30-year-old flight engineer. He had no systemic symptoms such as fever, night sweats, chills, or weight loss, and no significant past medical history. Lab values, including a complete blood count and chemistries, were normal. Radiographs showed an oval radiolucent lesion in the right ischium, and a lesion in the left superior lung area. The patient smoked one to two packs of cigarettes per day. The initial diagnostic impression was lung carcinoma with metastatic disease to the bone. Biopsies of both areas were consistent with eosinophilic granuloma. He was treated with 500 rads to the lung and 500 rads to the ischium.

The patient did well until 1969, when he began to have left shoulder pain and was noted on radiographs to have an oval radiolucent lesion of the left clavicle. Biopsy material was consistent with eosinophilic granuloma, and the lesion was treated with curettement and bone grafting. Similar lesions were noted in the maxilla and mandible in 1971, and were treated with curettement and grafting. followed by 1000 rads irradiation. In the ensuing years, the patient developed the following areas of involvement and received the treatment shown in the Table: no chemotherapy was given.

Except for the lung, the patient's lesions have been skeletal. No liver, spleen, nor lymph system involvement has been noted. No significant systemic symptoms have been associated with the bone lesions. All biopsy material from the various sites have been consistent with eosinophilic granuloma, although with each new lesion, the diagnosis of metastatic carcinoma or lymphoma has been considered. All of the patient's metastatic evaluations have been negative.

Discussion
Eosinophilic granuloma is a benign, tumor-like disorder of histiocytes and eosinophils. The predominant cell is the histioocyte and the pathologic picture may be similar to an inflammatory reaction. Its etiology is unknown. Lichtenstein and Jaffe, in 1940, used the term eosinophilic granuloma of bone for what they considered a new entity. Green and Farber concluded that this was not a new entity, but was related to the previously described Hand-Schuller-Christian and Letterer-Siwe diseases. In 1953, Lichtenstein coined the term histiocytosis X for the three disorders of eosinophilic granuloma, Hand-Schuller-Christian and Letterer-Siwe diseases. Eosinophilic granuloma was initially defined as a localized benign histiocytic disorder with a lytic lesion, confined to the skeleton and not involving other systems. This definition has been expanded to include more than one lytic lesion of the skeleton as well as extraskeletal involvement by some authors.

Nomenclature and classification of these histiocytic disorders have been a problem. Other suggested terms have included the reticuloendothelioses and histiocytic granulomas. In 1969, Lieberman reviewed 113 cases diagnosed as having abnormal histiocytic disorders or reticuloendothelioises. He classified the cases of solitary bone lesions as unifocal eosinophilic granulomas, and those of multiple sites of bone involvement and various...
TABLE

<table>
<thead>
<tr>
<th>Date</th>
<th>Location</th>
<th>Irradiation</th>
<th>Surgery</th>
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<tbody>
<tr>
<td>1972</td>
<td>Left proximal femoral lesion</td>
<td>1000 rads</td>
<td></td>
</tr>
<tr>
<td>1973</td>
<td>Vertex of skull</td>
<td>450 rads</td>
<td></td>
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<tr>
<td>1974, April</td>
<td>Right anterior ribs</td>
<td>900 rads</td>
<td></td>
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<tr>
<td>1974, September</td>
<td>Occipital skull</td>
<td>900 rads</td>
<td></td>
</tr>
<tr>
<td>1981</td>
<td>Left proximal femur</td>
<td>IM not for impending fracture</td>
<td>1250 rads</td>
</tr>
<tr>
<td>1983</td>
<td>Right ilium</td>
<td>1250 rads</td>
<td></td>
</tr>
<tr>
<td>1985</td>
<td>Patient well at age 50</td>
<td>1250 rads</td>
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degrees of soft tissue abnormalities as multifocal eosinophilic granulomas, rather than Hand-Schuller-Christian disease. We have used Lieberman’s classification for our case. Other authors have adopted the term multifocal eosinophilic granuloma for cases of multiple bone involvement with varying degrees of soft tissue involvement including diabetes insipidus, lymphadenopathy, splenomegaly, hepatomegaly, dermatitis, and otitis media.

In 1973, Cline and Golde proposed a classification of histiocytic disorders based on the maturity or differentiation of the histiocytes themselves. They proposed that the histiocytic cell series is a continuum of progressive maturation from the monoblast to the monocyte of the peripheral blood, to the immature and mature tissue macrophages. Examples of diseases with minimal cellular differentiation were acute monocytic leukemia and undifferentiated reticulum cell sarcoma. Those with the mature histiocytes included Hand-Schuller-Christian disease and localized histiocytoma. Our patient had mature-apparing histiocytes of relatively homogeneous appearance with some eosinophils and giant cells present. Katz states that the histiocytoma of eosinophilic granuloma may be confused with large cell lymphoma. However, our patient had no apparent liver, spleen, nor lymph node involvement consistent with a lymphoma.

It is interesting to note that the patient had eosinophilia in his bone marrow in 1981, even though his peripheral blood smear was normal. The radiographs showed no apparent bone lesion in the iliac area at that time. Bone marrow eosinophilia, with eosinophilic granuloma of bone, but normal peripheral smear has been reported in the past in two cases reported by Marcove. The significance of this is not known.

As previously mentioned, most patients with multifocal eosinophilic granuloma are children (usually less than age 10) and few are as old as the patient presented here (30 years old). Enríquez found only 15, in a series of 73 patients greater than 15 years old, with multiple eosinophilic granuloma over a 55-year period at the Mayo Clinic. Lieberman et al. in a series of 24 patients, found that only one patient older than 19 years was included. In Schajowicz's series of 121 patients, over 70% were less than 20 years of age. The oldest was 34 years old. Baldacci reported a 51-year-old patient with multiple lesions over a 3-year period. He could find only three cases of older patients in the literature. No patient with a 20-year follow up was found in our review of the literature.

Our patient has demonstrated that the overall prognosis in this condition is a benign, but chronically progressive course. This is somewhat similar to the clinical course of the adult patient with progressive bone and soft tissue lesions reported by Kaufman. Baldacci reported a case with 6-year follow up with similar progression. West reported a case of a 17-year follow up with a similar course which was chronically progressive.

Lichtenstein stated that with time, Hand-Schuller-Christian disease could change to eosinophilic granuloma, and that eosinophilic granuloma could change to Hand-Schuller-Christian disease. Some authors have reported that if a bone lesion remains solitary for 12 months, no other bone lesions are expected to appear. However, with our patient, it was 3 to 4 years after appearance of the initial bone lesion before the second bone lesion was discovered. Schajowicz felt that some cases of multifocal eosinophilic granuloma might later manifest themselves as histiocytic lymphoma and Lieberman and Mirra agreed that the multifocal eosinophilic granuloma may progress to malignancy. However, the usual course of multifocal eosinophilic granuloma is chronic, with waxing and waning of intensity. In many patients, the disease often burns out and then slowly heals. Less than 15% of patients with Hand-Schuller-Christian disease or multifocal eosinophilic granuloma have a fatal outcome.

The treatment of multifocal eosinophilic granuloma is controversial. Our patient was treated primarily with radiation therapy in low to moderate doses, but some of his lesions were curedtted and bone grafted. His proximal femoral lesion had an intramedullary rod fixation because of an impending pathologic fracture. In addition to radiation and curettage with grafting, chemotherapy has been used in some patients with multifocal eosinophilic granuloma; this has included agents such as methotrexate and vinblastine. Katz states that eosinophilic granuloma and Hand-Schuller-Christian disease are benign lesions which remit spontaneously and do not require extensive therapy. McGavran and Spady reported that in their series of 28 patients with eosinophilic granuloma, all healed regardless of treatment. In children, many lesions consistent with eosinophilic granuloma have shown spontaneous healing. Similar lesions may heal in the adult, but treatment is done for other reasons. The diagnosis in our patient was made by biopsy. A review of the patient's chart indicates that a diagnosis of malignancy was considered on each admission and workup.
Summary

A 50-year-old male with a 20-year history of eosinophilic granuloma is presented. His progressive chronic course is compatible with other reported cases. This is the first case of an adult with 20-year follow up.

References


Editorial Discussion

Orthopedics: Why was this patient not offered chemotherapy?

Eady: Chemotherapy was considered in this patient but it was felt by our oncology service that since he responded so well to relatively low dose radiotherapy of each bony lesion since presentation of the initial lesions, chemotherapy should be reserved for any manifestation of systemic disease or major organ involvement. We agreed with that and have been following him now for 5 years with good response to radiation therapy and no evidence of any systemic involvement.

Orthopedics: What is the risk of radiating numerous sites over a prolonged period?

Eady: The risk of radiating numerous sites over a prolonged period of time is hard to predict. The Mayo Clinic published a very erudite paper showing that radiation therapy for myositis ossificans after total hip procedures, in low dosages, had very little risks. It is true that radiotherapy is cumulative, but we believe that the low dosage that he has been given minimally increases his risk for malignant transformation into sarcoma in the areas of radiation. We believe that irradiation under 3,000 rads will not have the effect of creating sarcomatous transformation in tissues not previously irradiated.