Solitary Eosinophilic Granuloma of Mandibular Condyle: Literature Review and Report of a Rare Case

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Abstract Solitary eosinophilic granuloma (EG) is traditionally included as 1 of the 3 clinical manifestations of the histiocytosis-X group of diseases, which also encompasses Hand–Schuller–Christian disease and Letterer–Siwe disease. EG is the most common lesion in the spectrum of disorders under the classification of Langerhans cell histiocytosis. EG represents the monostotic form of the disease with the head and neck region representing the most common site of initial presentation. We report a rare case of solitary EG involving mandibular condyle in a 49-year-old male patient, which is the first reported case in Indian literature.

Keywords Eosinophilic granuloma · Mandible · Condyle · Histiocytosis-X

Introduction

Histiocytosis-X, recently termed Langerhans cell histiocytosis, is histologically characterized by an abnormal proliferation of histiocytes and usually a massive aggregation of eosinophilic leukocytes [1, 2]. Eosinophilic granuloma (EG) of bone has traditionally been included as one of three clinical manifestations of the histiocytosis-X group of diseases, which also encompasses Hand–Schuller–Christian disease and Letterer–Siwe disease [3]. This grouping has been based on the similarities of the histopathologic appearance of the histiocytic and eosinophilic

proliferations. EG is the most common benign lesion of the triad commonly known as histiocytosis-X and accounts for 50–60 % of all cases of this disease [4, 5]. Histiocytosis-X is also called “Langerhans cell disease” because it has recently been shown to involve Langerhans cell precursors. The cause and pathogenesis of histiocytosis-X remains unclear. Possible etiologic factors include infection, inflammation, or immunologic response [6]. Skeletal lesions of histiocytosis-X can occur in any bone. However, they are most common in the pelvis, ribs, skull, long bones, vertebrae, and facial bones [7]. It has been reported that the incidence in the jaws is 7.9 %. In the mandible, the body and angle are the most commonly affected sites [8]. Only 12 cases of EG of the mandibular condyle have been reported in the literature till now. Ultrastructural and immunohistochemical studies have implicated the dendritic antigen-presenting Langerhans cell of the skin, mucosa, and other organs as the proliferative cell of this disorder. Electron microscopic studies have shown the presence of similar cytoplasmic structures that occur in the Langerhans cells; specifically Langerhans cell (Birbeck) granules. The function of the Langerhans cells in the immune response is to present antigen to T lymphocytes. Because these diseases are now known to involve Langerhans cell precursors, a change of terminology to Langerhans cell histiocytosis (LCH) has been proposed [9]. The cause and pathogenesis of LCH remains unclear. Both macrophage and dendritic Langerhans cells have a common lineage, arising from the bone marrow stem cell containing CD34 surface antigen. Using ultra structural and phenotypic cell markers, and molecular or chromosomal markers of malignancy, Cline has developed a classification for histiocytic diseases [4]. The four major groupings include reactive and malignant macrophage histiocytosis and reactive and malignant LCH. EG is classified as a reactive

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LCH. Recent evidence that all lesions of LCH are clonal however, suggests that this disorder should be classified under the malignant disorders of histiocytes. The clinical expression of this disease is diverse. EG, or the chronic localized form of LCH, is the most common and least severe form; solitary or multiple bone lesions are evident [10]. Hand–Schuller–Christian disease, or the chronic disseminated form of LCH, may present as a complete triad of calvarial bone defects, exophthalmus, and diabetes insipidus in only a few patients, and is usually the result of granulomatous infiltration of the skull and pituitary gland. Patients also may show lymph node, visceral, and skin involvement. Letterer–Siwe disease, or the acute disseminated form of LCH, is most likely an aggressive malignancy. It is characterized by a rapidly progressive course with widespread multiple organ system involvement and a usually fatal clinical course in infants. Skeletal lesions of LCH have been well documented, especially in the skull, facial bones, long bones, pelvis, vertebrae, and ribs [11, 12]. In the mandible, lesions occur more commonly in the body, followed by the ramus. It can affect almost any bone and commonly involves the mandible when the jaws are affected. It is usually managed empirically with surgery, radiotherapy, chemotherapy, and intralesional steroid injection, because its etiology remains mainly unknown [12]. We report a rare case of solitary EG involving mandibular condyle in a 49-year-old male patient which is the first of its kind in Indian literature.

Case Report

A 49-year-old male patient was referred to the Department of Oral and Maxillofacial Surgery for evaluation of a left preauricular swelling (Fig. 1). The lesion had been slowly increasing in size since it was first noticed. There was no history of trauma, pain, paresthesia or lymphadenopathy. There was no significant facial asymmetry caused by an approximately 2×1.5 cm mass involving the preauricular region. The mass was firm and nontender to palpation and not adherent to the overlying skin. On further examination, the patient showed no limited mouth opening and no temporomandibular joint (TMJ) noise. A panoramic radiograph showed a well-defined unilocular radiolucent lesion measuring approximately 1 cm in diameter involving the left condyle (Fig. 2). Computed tomography (CT) scan showed central lytic unilocular radiolucent lesion surrounded with sclerotic border and small discontinuities in the peripheral cortex (Figs. 3, 4). A radiologic diagnosis of EG was made based on the central lytic lesion and periosteal new bone reaction. Under general anesthesia, a standard preauricular approach to the TMJ was used to expose the left condyle (Fig. 5). The outer cortex was

Fig. 1 Frontal view photograph showing slight obvious swelling in the left preauricular region

Fig. 2 Orthopantomograph (OPG) showing unilocular radiolucent lytic lesion involving the left condyle

found to be missing, and the condyle was largely replaced with a soft tissue mass. Aggressive curettage along with condylectomy was performed and the excised tissue was subjected to histopathological examination (Fig. 6). Histopathological examination confirmed the diagnosis of solitary EG of mandibular condyle revealing fibrous connective tissue with plasma cells, lymphocytes, eosinophils, histiocytes, and focal accumulation of multinucleated giant

Fig. 3 Axial CT scan view showing unilocular radiolucent lytic lesion in the left condyle causing thinning and perforation of the cortex

Fig. 4 3D CT scan view showing unilocular radiolucent lytic lesion in the left condyle

cells (Fig. 7). The patient was discharged from the hospital on second post-operative day and sutures were removed after 1 week. Patient was followed-up for 1 year during which no recurrence was observed.

Discussion

Histiocytosis-X, recently termed Langerhans cell histiocytosis, is histologically characterized by an abnormal

Fig. 5 Intraoperative photograph showing the lesion, which is exposed using preauricular approach

Fig. 6 Photograph showing the excised specimen along with the condylar neck

proliferation of histiocytes and usually a massive aggregation of eosinophilic leukocytes [12]. EG of bone has traditionally been included as one of the three clinical manifestations of the histiocytosis-X group of diseases, which also encompasses Hand–Schüller–Christian disease and Letterer–Siwe disease [13]. We report a rare case of solitary EG of mandibular condyle possibly the first reported case in Indian literature. Previously there are only 11 reported cases in the literature (Table 1).

Eosinophilic granuloma of bone, or chronic localized LCH, occurs primarily in children and young adults, with the highest incidence in the first decade of life [12, 13]. Men are affected twice as much as women. Monostotic EG occurs more frequently than polyostotic EG in most studies, and any bone of the skeleton may be affected except the hands and feet [14]. The sites most commonly involved by the bony lesions of EG are the skull, ribs, vertebrae,

Fig. 7 Photomicrograph showing histopathological findings revealing fibrous connective tissue with plasma cells, lymphocytes, eosinophils, histiocytes and focal accumulation of multinucleated giant cells (hemotoxylin and eosin stain, $\times 200$)

pelvis, long bones and mandible. In adults, there may be a higher frequency of involvement of the ribs and the mandible [14, 15].

Hartman [16] reviewed 114 cases of histiocytosis-X with lesions in the jaws and noted that 76 % occurred in the mandible, with two-thirds located in the posterior region. Dagenais et al. [10] reviewed 29 cases of LCH of the jaws and reported that 28 cases (96.6 %) occurred in the mandibular body and ramus. Of 14 solitary intraosseous lesions (48.3 %), excluding lesions of the alveolar process, 13 cases involved the lower jaw and were evenly distributed

between the body and ramus. The mandibular body lesions were situated below the inferior alveolar nerve. The ramus lesions were mostly located on the lateral aspect of the jaw. The most frequent complaints in patients were pain and swelling. Intraoral symptoms include gingival inflammation, hyperplasia, oral ulceration and leukoplakia [17]. Mobile teeth in the affected alveolar area were a common occurrence, mimicking a dental infection or periodontal disease [18]. Occasionally, lesions can result in pathologic fractures [6, 11].

In the jaws, solitary lesions of EG appear as radiolucencies. Dagenais et al. [10] documented several common radiographic characteristics. Solitary intraosseous lesions unrelated to the alveolar process were circular or elliptical and usually located on the lateral aspect of the jaw when occurring in the ramus. They were always solitary, unlike the alveolar lesions. The periphery of these lesions was usually well defined but uncorticated, with the term “punched-out” referring to other bony lesions. Whereas bone sclerosis commonly occurred in alveolar bone lesions, this was not considered a feature in other bones. Because sclerosis is a frequent response to inflammatory lesions of the jaws, oral contamination of alveolar lesions is a likely explanation. Intraosseous lesions without oral communication did not show evidence of cortication or sclerosis. Periosteal new bone formation was seen in a significant number of intraosseous lesions, indicating a good characteristic for use in identification of LCH. Because EG can be a multifocal bone disease, it is reasonable to proceed with technetium bone scan, which is a sensitive method for detecting polyostotic lesions. Although radionuclide

Table 1 Reported cases of EG of the mandibular condyle

Author	Age/sex	Radiological presentation	Treatment
Makek and Sailer [6]	38 F	Poorly demarcated osteolysis of entire condyle; periosteal new bone formation; pathologic fracture	Aggressive surgical curettage; low condylectomy
Donazzan et al. [13]	17 F	Radiolucent lytic lesion involving condyle.	Aggressive surgical curettage
Tant et al. [7]	33 F	Complete lysis of condyle	Aggressive surgical curettage
Zachariades et al. [8]	8 F	Small radiolucency with ill-defined borders	Surgical exploration
Peckitt and Wood [9]	32 M	Radiolucency with central opacity in condyle	Aggressive surgical curettage; low condylectomy and costochondral graft
Bhaskar et al. [11]	44 M	Radiolucency with pathologic fracture	Aggressive surgical curettage; condylectomy
Wong et al. [12]	36 M, 27 M, 20 M	Radiolucent lytic lesion with periosteal reaction.	Aggressive surgical curettage; condylectomy
Miyamoto et al. [27]	34 M	Well defined radiolucent lytic lesion	Aggressive surgical curettage; condylectomy
Kazunari et al. [30]	53 F	Radiolucent lytic lesion involving the condyle	Aggressive surgical curettage
David et al. [28]	11 M	Radiolucent mass causing local destruction of the condyle	Aggressive surgical curettage; condylectomy

scanning is the most sensitive method, complementary studies using radiographic skeletal surveys may be indicated for complete evaluation [16]. Differential diagnosis include giant cell tumour, aneurysmal bone cyst, ameloblastoma, osteomyelitis and benign and malignant cartilaginous tumours, also may show similar signs.

Extra skeletal involvement is more likely in patients with multiple bony lesions. Patients with EG may require further evaluation for other affected sites, including skin, liver, spleen, lung, bone marrow and pituitary gland. Microscopic examination shows sheets of histiocytes together with focal collections of eosinophils and other chronic inflammatory cells, including lymphocytes and plasma cells. Another group of mononuclear phagocytes exhibiting foamy, vacuolated cytoplasm is frequently present. Multinucleated giant cells and foci of necrosis also may be evident. Electron microscopic examination of the proliferative cell has identified Birbeck granules, which are normally present in Langerhans cells. Further immunohistochemical studies support the origin from Langerhans cells [1]. Positive immunostaining for S-100 protein and CD1a antigen can help distinguish LCH from other histiocytic lesions [12, 17]. As the lesion matures, fibrosis occurs, with a reduction of the histiocytic and eosinophilic component and with gradual replacement by nests of granular to foamy macrophages. Several currently accepted treatment modalities for EG of bone include vigorous surgical curettage, low dose radiation, and chemotherapy. These methods have been used either alone or in combination with good results. Surgical curettage has been recommended for those lesions in accessible areas. Although aggressive surgical curettage should be performed, total removal of the lesion has not always been necessary for a favorable response [19]. The use of an ultrasonic surgical aspirator in the extirpation of an EG of the mandible can be useful in avoiding major nerves and vessels [20]. In some situations, immediate bone grafting can be performed after surgical curettage of large lesions in which a pathologic fracture may be imminent [14]. A response to surgical biopsy alone has also been reported [21, 22].

Conservative treatment for solitary EG of bone by intralesional injection of steroids has been reported with good results [23–26]. The mechanism of action is unknown, but the rapid relief of pain and rapid resolution of lesions radiographically have supported this as a possible treatment alternative. Low-dose radiation therapy also has been used as an adjunct to initial surgical curettage [21, 27] in the management of recurrent lesions [28] or in the primary management of localized lesions [29]. The potential risks of low-dose radiation therapy include secondary malignant transformation and the disruption to growth centers, the lens, and dental follicles, especially in children. These risks must be carefully weighed against the complications of the

disease. Intralesional injections of triamcinolone acetonide (Tricort 40 mg/ml, 6 injections at weekly intervals over 6 weeks), leading to complete resolution of the lesion have been reported in the literature.

Chemotherapy has been used as an adjunct to initial surgical curettage or low-dose radiation therapy [28, 29]. Because surgical curettage and low-dose radiation usually provide a good response in EG of bone, chemotherapy is generally used only in treatment failures, or for widespread disease including visceral involvement [30]. Surgical management also was the preferred treatment in earlier reports.

Conflict of interest None declared.

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