CELL WITH A GIANT NAME:-GIANT CELL LESION OF THE ORAL CAVITY-AN UPDATE

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ABSTRACT
Diagnosis of many lesions of the oral cavity is challenging to most clinicians because of their uncommon prevalence. A number of cystic, metabolic, osteodystrophic, microbial, tumour and tumour like lesions of the oral cavity present with characteristic giant cell lesions; which makes their diagnosis and study simpler. We have attempted to classify the common giant cell lesions of the oral cavity, giving a brief account of their clinical, histological and diagnostic features, along with their recent treatment modalities.

KEYWORDS: Giant cell, tumors, diagnosis.

INTRODUCTION
Cell is defined as the fundamental, structural & functional unit of all known living organisms. The term “cell” was coined by Robert Hooke[¹] It is derived from the Latin word “cellula” which means ‘small compartment.’[²]
Cells usually contain a single nucleus. But certain tissues contain cells in which several nuclei are present within the same cytoplasm. These are termed as multinucleated giant cells. These cells were first reported in tuberculous granulomas by Rokitansky and Langhans over a century ago.

Giant cells are large multinucleated cells of different lineage and the lesions containing giant cells fascinate clinicians, radiologists and pathologists. Multinucleated giant cells are broadly classified into physiologic & pathologic giant cells.

**Classification**

1. Microbial lesions: Tuberculosis, Leprosy, Actinomycosis, Sarcoidosis
2. Tumour and tumour like lesions: Central giant cell granuloma, Peripheral giant cell granuloma, Giant cell fibroma, Giant cell tumour, Osteosarcoma, Rhabdomyosarcoma, Hodgkin’s lymphoma
5. Osteodystrophic lesions: Noonan-like multiple giant cell lesion syndrome.

1. **MICROBIAL LESIONS**

**TUBERCULOSIS**

Tuberculosis is a communicable chronic granulomatous disease which is caused by Mycobacterium tuberculosis. Tuberculosis of the oral cavity is an uncommon occurrence.

**Clinical features**

In a review of 20 cases of tuberculosis of the head and neck, oral TB was found in 13 patients (11 males and 2 females, male to female ratio of 5.5:1.0). The patients ranged in age from 7 to 78 years, with an average of 53.4 - 20.1 years.

**Histopathological features**

Histopathological examination showed stratified squamous epithelium with presence of multiple necrotizing epithelioid cell granuloma and Langhans’ type of giant cells containing nuclei arranged in a horseshoe shaped pattern at cell periphery.
**Treatment**

First-line drugs likely to be used for treatment of TB include isoniazid, rifampin, pyrazinamide and ethambutol. Oral lesions would be expected to resolve with treatment of the patient’s systemic disease. Bacille Calmette Guerin (BCG) is effective in controlling childhood TB but loses efficacy in adulthood.\[10\]

**LEPROSY**

Leprosy, eponymously known as Hansen’s disease is a chronic infectious disease caused by Mycobacterium leprae, an acid-fast bacillus that presents a peculiar tropism for the skin. The oral lesions are generally asymptomatic and secondary to nasal changes.\[11\]

**Clinical features**

Patient age ranged from 39 to 55. All were male patients. They presented skin and mucosal lesions. Mucosal disease was found in the palate and nasal mucosa. The soft palate, hard palate and tongue are also affected.\[12\]

**Histopathological features**

Histological examination of the oral lesions showed epithelial hyperplasia with areas of ulceration and a dense lymphohistiocytic inflammatory infiltrate with the presence of histiocytes showing foamy cytoplasm vacuoles with large amounts of acid-fast bacilli.\[12\]

**Treatment**

Patients were treated with multidrug therapy for multibacillary leprosy consisting of rifampicin, clofazimine once a month/50 mg daily, and 100 mg dapsone daily, for a total of 24 doses.\[12\]

**ACTINOMYCOSIS**

Actinomycosis is a chronic infectious disease caused by the organisms of the order Actinomycetaceae. Actinomyces The most common clinical forms of actinomycosis are cervicofacial and abdominal.\[13\]

**Clinical features**

Actinomycosis is commonly said to be found in young adults with 80% of the cases reported in patients above 20 years, with low incidence in children. Most authors report a mean age of 40 years. A predilection for male subjects is observed with a male: female ratio of 4:15.\[14\]
Histopathological features
Histological examination reveals acute or chronic inflammation and granulation. Neutrophils, foamy macrophages, plasma cells and lymphocytes surrounding dense fibrotic tissue are usually found. A hallmark of actinomycosis is the presence of sulphur granules.[13]

SARCOIDOSIS
Sarcoidosis is a chronic, multiorgan inflammatory disorder of unknown etiology, characterized by non-caseating granulomas, that primarily affects the lungs and the lymphatics. The term sarcoidosis in Greek means, ’flesh-like condition’ (Chesnutt, 1995).[15]

Clinical features
Oral involvement in sarcoidosis is uncommon. Schroff (1942) reported the first suspected case of sarcoid granulomas in the oral mucosa. The common clinical presentations were as localized swelling or nodules, ulcers, swelling with multiple ulcers, gingivitis, gingival hyperplasia and gingival recession.[15]

Treatment
Multiple methods were employed in the treatment of oral sarcoidosis ranging from no treatment (Cohen et al, 1981; Hayter and Robertson, 1988) to radiation therapy (Hoggins and Allan, 1969).[15]

2. TUMOR AND TUMOR LIKE LESIONS
CENTRAL GIANT CELL GRANULOMA
The WHO has defined central giant cell granuloma as an intraosseous lesion consisting of cellular fibrous tissue that contains multiple foci of hemorrhage, aggregations of multinucleated giant cells and occasionally trabeculae of woven bone.[6]

Clinical features
Central giant cell lesion is described as usually a painless, slow growing swelling of the jaw. Displacement of teeth occurs frequently and can lead to malocclusion.[16]

Histopathological features
Central giant cell granuloma is made up of a loose fibrillar connective tissue stroma with many interspersed proliferating fibroblasts and small capillaries. The collagen fibers are not usually collected into bundles; however, groups of fibers will often present a whorled
appearance. Multinucleated giant cells are prominent throughout the connective tissue, but not necessarily abundant.  

Treatment
surgical, by means of excision and curettage. Recent approaches for the treatment of large or multiple lesions have included weekly intralesional corticosteroid injection, daily subcutaneous or intranasal administration of calcitonin, and the use of interferon alpha-2a.

PERIPHERAL GIANT CELL GRANULOMA
The PGCG, also known as osteoclastoma, giant cell reparative granuloma, or giant cell hyperplasia, are reactive exophytic lesions found in the oral cavity.

Clinical features
PGCG’s may present itself as polypoid or nodular lesions, predominantly bluish red with a smooth shiny or lamillated surface. They are variable in size, though reportedly rarely exceed 2 cm in diameter and are generally soft or rubbery to touch.

Histopathological features
It was reported that large number of multinucleated giant cells were seen in vascularized fibrocellular stroma. In some cases the giant cells were said to be present in lumen of capillaries. Hemorrhage, hemosiderin pigment, inflammatory cells & newly formed bone or mature calcified material throughout the cellular stroma may be seen.

Treatment
The treatment advocated has been surgical excision and elimination of possible irritant factors, with recurrence being infrequent (approximately 10%).

GIANT CELL FIBROMA
Giant cell fibroma or fibroblastoma is a benign fibrous neoplasm characterized by the presence of mono-, bi- or multinucleate spindle-shaped or stellate giant cells that are mainly found in subepithelial connective tissue. It was described for the first time by Weathers and Callihan.

Clinical features
It appears as an asymptomatic sessile or pedunculated nodule that is less than 1 cm in diameter. Often, it has a bosselated or somewhat papillary surface. Most cases are diagnosed
in persons aged 10-30 years. There is no gender predilection. The most common site is the mandibular gingiva, followed by the maxillary gingival, the tongue and the palate.\(^{[17]}\)

**Histopathological features**

Histopathological features of Giant cell fibroma showed large, stellate shaped, mononuclear and multinucleated giant cells.\(^{[6]}\) Microscopically, GCFs consisted of fibrous, usually loose connective tissue and mono-, bi- or multinucleated spindleshaped or stellate giant cells that are mainly located in the papillary lamina propria.\(^{[21]}\)

**Treatment**

In a study, the treatment recommended is conservative surgical excision.\(^{[6]}\)

**GIANT CELL TUMOR**

It is a primary locally aggressive bone neoplasm characterized by stromal mononucleated cells associated with uniformly distributed osteoclast-like giant multinucleated cells.\(^{[22]}\)

**Clinical features**

The tumor is said to account for 4-5% of all primary bone tumors and 20% of benign bone tumors. Skeletally mature patients ranging from 20 to 45 years of age, especially women are affected.\(^{[22]}\)

**Histopathological features**

Histopathological the growth is found to be composed of large multinucleated giant cells loosely embedded in a stroma of smaller rounded, spindle and polygonal cells with large vesicular nuclei. In addition to the above components of the giant cell tumor, aggregates of endothelial leukocytes are present, filled with lipoid inclusions-the so called "foam cells".\(^{[23]}\)

**Treatment**

In a study it has been reported that the treatment includes scooping out the tumor (curettage).\(^{[6]}\)

**OSTEOSARCOMA**

Osteosarcoma or osteogenic sarcoma is defined as a primary intramedullary high grade malignant tumour in which the neoplastic cells produce osteoid.\(^{[24]}\)
Clinical features
In the mandible, the molar region, premolar region, and retromolar region are affected.\cite{25}

Histopathological features
Histopathological examination showed presence of malignant osteoid although the matrix formation varied from osteoblastic to fibroblastic. The majority of the cases were osteoblastic in type (n=30), followed by chondroblastic (n=19), fibroblastic (n=6) and telangiectatic (n=4).\cite{24}

Treatment
Osteosarcomas of the jaw are reported to be treated by surgery, chemotherapy or a combination of both.\cite{24}

RHABDOMYSARCOMA
Rhabdomyosarcoma is a mesenchymal malignant neoplasm that exhibits skeletal muscle cells with varying differentiation degrees. It occurs most often in the head and neck region.\cite{6}

It accounts for 5-10% of childhood cancers and for more than 50% of pediatric soft tissue sarcomas. About 35% of rhabdomyosarcomas are localized in the head and neck region.\cite{26}

Clinical features
The most frequently affected sites are orbit, paranasal sinuses, soft tissues of the cheek and the neck. In the oral cavity the most common sites are tongue, palate and buccal mucosa.\cite{6}

Histopathological features
Embryonal rhabdomyosarcoma was the most. The embryonal rhabdomyosarcoma is composed of several cell types and the mesenchymal cells tend to differentiate into cross-striated muscle cells. It is generally a moderately cellular tumor with loose myxoid stroma. The cell nuclei of embryonal rhabdomyosarcomas are smaller than those of an alveolar rhabdomyosarcomas and the nucleoli are difficult to visualize.\cite{26}

Treatment
Chemotherapy and radiotherapy was the treatment of choice.\cite{26}
HODGKIN’S LYMPHOMA

Lymphomas are malignant neoplasm of the lymphocyte cell lines. They mainly involve lymph nodes, spleen and other non-haemopoietic tissues. They are mainly classified as either Hodgkin's or Non-Hodgkin's lymphoma (NHL) and of either B-lymphocyte or T-lymphocyte origin.\textsuperscript{[27]}

Clinical features

It is stated that Hodgkin’s lymphoma is distributed in a bimodal pattern with a first peak in the third decade and a second peak after the age of 50; systemic signs and symptoms such as weight loss, fever, night sweats and generalized pruritis may be present.\textsuperscript{[28]}

Histopathological features

A study conducted in Los Angeles on 292 twin pairs with cancer, histology data was available only for 160 pairs out of which 54% had nodular sclerosis, 17% had mixed cellularity and 4% had predominance of lymphocyte.\textsuperscript{[28]}

Treatment

In most cases, extended field radiotherapy was curative in patients with localized disease at presentation. The development of combination chemotherapy with MOPP (nitrogen mustard, vincristine, procarbazine, and prednisone) was a milestone.\textsuperscript{[28]}

3. CYSTIC LESIONS

TRAUMATIC BONE CYST

In 1929, Lucas and Blum for the first time described traumatic bone cyst as a separate disease entity. It was later defined by Rushton as a single cyst that has no epithelial lining, has an intact bony wall, is fluid filled, and has no evidence of acute or chronic inflammation.\textsuperscript{[29]}

Clinical features

Traumatic bone cysts have an equal prevalence in both genders, present at a mean age of 18 years, are most prevalent among white persons, and most often affect the posterior mandible. The typical location for traumatic bone cysts is the mandibular body, whereas maxillary lesions tend to be uncommon, although the reasons for this are unclear.\textsuperscript{[29]}

Histopathological feature

Histologically, the lesion appears as a cancellous bone cavity that may be vacant and without a lining, or presents as a thin connective tissue layer with a scant liquid content.\textsuperscript{[6]}
Treatment
Simple curettage of the bone walls is performed, with healing after 6-12 months, exploration and excisional biopsy of the left mandibular body lesion with apicoectomy and retrograde filling of the tooth.

ANEURYSMAL BONE CYST
The WHO defines ABC as a benign intra-osseous lesion, characterized by blood-filled spaces of varying size associated with a fibroblastic stroma containing multinucleated giant cells, osteoid and woven bone.

Clinical features
2% of aneurysmal bone cysts are found in the head and neck, with 66% of these being located in the mandible.

Histopathological features
The histopathology of the surgical specimen showed a stroma containing sinusoidal spaces. These spaces contain red blood cells lined by fibroblastic tissue with areas of granulation tissue. Some giant cells were present. New bone formation with osteoblastic rimming and some osteoclasts were evident.

Treatment
There is no uniform treatment and management of ABC due to its varied nature. The usual treatment of choice is curettage as it is a benign lesion. The failure to remove the lesion completely has been associated with a recurrence.

4. METABOLIC LESIONS
HYPERPARATHYROIDISM
Hyperparathyroidism (HPT) is characterized by hypersecretion of parathyroid hormone. HPT is divided into primary, secondary and tertiary categories. Classic skeletal lesions, which are bone resorption, bone cysts, brown tumours and generalized osteopenia, occur in less than 5% of cases.

Clinical features
The most characteristic jaw lesion associated with hyperparathyroidism is a brown tumor, so named because its gross appearance is characterized by a red-brown color. It may be seen in patients with either primary or secondary hyperparathyroidism.
Histopathological features
Histologically, HPT is characterized by an abundant stroma, consisting of bundles of spindle or oval cells, and several multinucleated osteoclast-like giant cells. Calcified material can be found, as well as areas with extravasation of red blood cells and pigmentation by haemosiderin.\textsuperscript{[31]}

Treatment
Spontaneous resolution of a brown tumor may occur after treatment of the underlying source of the lesion.\textsuperscript{[71]} However, several cases of brown tumor that did not disappear or even grew after normalization of HPT level have been reported. In these cases brown tumor resection should be the preferred treatment.\textsuperscript{[31]}

5. MISCELLANEOUS LESIONS
PAGET’S DISEASE
Sir James Paget, after whom this disease is known, first gave a clear account of its main features in 1876 at the age of 62, but it was Professor Czerny of Freiburg in 1873 who suggested the term osteitis deformans, meaning an enlargement and disfigurement of bones resulting from some inflammatory process.\textsuperscript{[32]}

Clinical features
In a study it is reported that PDB is characterized by increased bone turnover, which can affect a single bone (monostotic) or multiple bones (polyostotic). According to the literature, skull involvement in Paget’s disease occurs in 65–70\% of advanced polyostotic cases.\textsuperscript{[6]}

Histopathological features
Irregularly shaped trabeculae of woven bone are scattered throughout the stroma. The bone often is lined by osteoblasts and osteoclasts, indicating simultaneous resorption and formation of the bone. Characteristically, numerous basophilic reversal lines are noted throughout many of the bony trabeculae. The lines may give the pagetoid bone somewhat of a jigsaw or mosaic pattern.\textsuperscript{[33]}

Treatment
Slowly evolving PDB or in asymptomatic patients, treatment often is unnecessary or is delayed until the level of alkaline phosphatase is more than 25\% to 50\% above normal.
Parathyroid hormone antagonists, including calcitonin and bisphosphonates, usually are used to reduce the rate of bone turnover. Surgery is not usually indicated.\[33\]

**FIBROUS DYSPLASIA**

It is a rare localised disease often associated with bony deformities caused by the abnormal proliferation of fibrous tissue.\[90\] It frequently affects the jawbones. The lesion is classified into two forms: monostotic (75–80%) and polyostotic types (20–25%).\[34\]

**Clinical features**

Overall, 25% of all fibrous dysplasias and 35% of patients with McCune-Albright syndrome exhibit maxillary or mandibular involvement. Although mandibular lesions may be monostotic. Although multiple bones are affected, the contiguous distribution of the lesions precludes the classification of craniofacial fibrous dysplasia as polyostotic disease.\[33\]

**Histopathological features**

There is considerable microscopic in cases of monostotic fibrous dysplasia of the jaws. The lesion is essentially a fibrous one made up of proliferating fibroblasts in a compact stroma of interlacing collagen fibers. Irregular trabeculae of bone are scattered throughout the lesion with no definite pattern of arrangement. Characteristically, some of these trabeculae are C-shaped or as described by one author, Chinese character-shaped. These trabeculae are usually coarse woven bone but may be lamellar.\[17\]

**Treatment**

The surgical management of a small, monostotic mandibular lesion is much less problematic than treatment of larger, more diffuse lesions or of craniofacial fibrous dysplasia. Conversely, spontaneous regression of fibrous dysplasia also has been reported. If treatment is necessary, especially in young patients with significant cosmetic or functional deformity, therapy should be limited to a contouring procedure, without complete resection, to minimize morbidity. However, it has been estimated that 25% to 50% of patients will exhibit subsequent regrowth of the lesion and, thus, may require multiple shave-down procedures. Radiation therapy is contraindicated owing to the increased risk of malignant transformation. Long-term clinical and radiographic follow-up is recommended for any patient with fibrous dysplasia.\[33\]

**REFERENCE**

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