REACTIVE PLASMACYTOSIS ASSOCIATED WITH CHRONIC GENERALIZED PERIODONTITIS – A CASE REPORT

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ABSTRACT: Plasmacytosis is a condition in which there are an unusually large proportion of plasma cells in tissues, exudates, or blood. Reactive plasmacytosis is a diagnosis of exclusion, to be differentiated from other autoimmune, allergic and neoplastic disorders with plasma cell infiltrates. This paper describes a rare case of 73-year-old male patient diagnosed as plasmocytosis depending upon the clinical and histological findings. There was chronic inflammatory enlargement of the gingiva and palate with severe periodontitis. Histopathological examination revealed a stratified squamous orthokeratinized epithelium with underlying fibrocellular connective tissue stroma. The connective tissue showed intense infiltrate of small round cells of plasmacytoid type with eccentrically placed nucleus suggestive of reactive plasmacytosis. The diagnostic and management challenges encountered are described in this case report.

KEYWORDS: Plasmacytosis, chronic inflammatory enlargement, neoplastic disorder.

INTRODUCTION

Plasmacytosis, a benign inflammatory disease, is rarely found in the oral cavity. Plasmacytosis is a condition in which there is an unusually large proportion of plasma cells in tissues, exudates, or blood. It is microscopically characterized with intensive subepithelial plasmacyte infiltrate and capillary formation and edema and necrosis of the epithelium. The reactive plasma cell proliferation represents a heterogeneous spectrum of mucocutaneous disorders manifesting clinically with intense hyperemia, erosions or lobulated warty lesions affecting mostly mucosal/orificial areas. These have been considered to be benign immunologic inflammatory reactions to known (subclinical infection, friction, poor hygiene, trauma, etc.) or unknown stimuli. However, its etiology largely remains speculative.

Cases of plasma cell infiltrate of gums, tongue, oral and labial mucosa have been described mostly under atypical gingivostomatitis, plasma cell gingivostomatitis, plasma cell gingivitis or plasmacytosis mucosae in dental literature. Herein we report an unusual case of reactive plasmacytosis associated with chronic generalized periodontitis.

Case report

A 73-year old male patient presented with a chief complaint of enlarged swollen gums in upper and lower teeth region since 1 year. The condition initially started as swelling of gums in lower front teeth region and gradually involved the lower back and upper teeth regions. The swellings gradually increased in size and were accompanied by bleeding during brushing. The patient had no other associated symptoms like pain, difficulty in chewing, speech or deglutition.

The patient is a known hypertensive since 10 years and has been on amlodipine 5mg per day for 5 years. Clinical examination revealed diffuse gingival enlargement in both the arches, with erythematous epithelium (Fig.1, Fig.2 and Fig.3). Generalised gingival recession and bleeding on probing were present. The enlargement was reddish pink in color, soft and edematous in consistency, with rounded gingival margins. The enlargement involved only the marginal and attached gingiva and did not progress beyond the mucogingival junction. A mean pocket probing depth of 5-7 mm was recorded.
Grade 2 mobility of the mandibular and maxillary second and third molars and Grade 1 mobility of mandibular and maxillary premolars and central incisors was noted. Patient had a poor oral hygiene and had discontinued oral hygiene measures since 3 months due to pain and bleeding while brushing. Palatal mucosa over the enlargement appeared pale and ulcerated in maxillary anterior and left posterior region with associated pus discharge.

Orthopantamograph showed generalized horizontal loss of alveolar bone upto middle third of roots with the alveolar crest at the apical third of roots in relation to 16, 26, 27, 28, 41. Lower border of the mandible was intact. An ill defined radiolucent lesion was seen in between the roots of 47 and 48. Trabecular pattern was asymmetrical with sparse trabeculae in relation to 43, 44, 45, 46 (Fig.4). Blood investigations were performed in order to rule out leukemia or other blood dyscrasias. No abnormality was detected. It was provisionally diagnosed as drug induced gingival enlargement associated with chronic generalized periodontitis.

Incisional biopsy was performed in maxillary anterior palatal region. The hematoxylin & eosin stained soft tissue section showed stratified squamous orthokeratinized epithelium with underlying fibrocellular connective tissue stroma (Fig.5). The connective tissue showed intense infiltrate of neoplastic small round cells along with some bizarre cells (Fig.6). The neoplastic round cells were of plasmacytoid type with eccentrically placed nucleus and fragmented chromatin, giving the appearance of clock face nucleus and with some cells showing eccentrically placed nucleus (Fig.7). Connective tissue also showed islands of eosinophilic areas suggestive of Russell bodies (eosinophilic cells with eccentrically placed nucleus) and immunoglobulin pooling. Histopathological features were suggestive of small round cell tumor – probably extramedullary plasmacytoma.

Differential diagnosis of peripheral giant cell granuloma, peripheral ossifying fibroma, soft tissue plasmacytoma and multiple myeloma were considered. For confirmation, further investigations were advised. Urine analysis was negative for Bence Jones proteins. Lateral view of skull and radiographs of long bones did not reveal any abnormality. Immunohistochemical staining of the tissue showed focal positivity for lambda and diffuse positivity for kappa light chains in the ratio of 1:4 indicative of polyclonal proliferation, hence suggestive of reactive cell lesion (Fig.8). The plasma cells were immunopositive for CD138/CD38 and there was no evidence of malignancy (Fig.9). Overall clinical, radiographical, histopathological, immunohistochemical investigations was suggestive of reactive plasmacytosis.
Treatment included initial periodontal therapy comprising of scaling and root planning and oral hygiene instructions were given. Patient was advised to use a mouthrinse of 0.2% chlorhexidine twice daily along with the use of an ultrasonic toothbrush and dental floss. Teeth with poor periodontal prognosis were extracted. Proper home care and the use of chlorhexidine mouthwash reduced inflammation after four weeks. However, complete resolution of enlargement was not accomplished.

The patient was prescribed topical corticosteroids - triamcinolone acetonide gel 0.1% for application 3 times daily. Prednisolone 20mg per day was prescribed for 2 weeks and gradually tapered. The patient was followed-up weekly. At 5 months follow-up, there was significant reduction in the clinical appearance of the gingival and palatal lesions (Fig.10).

Discussion

The phenomenon of plasma-cell infiltrate was first described by Zoon in 1952 when he described balantitis plasma cellularis. Since then plasma-cell infiltrates have been found on the vulva, buccal mucosa, palate, nasal aperture, gingival, lips, tongue, larynx and other orofacial surfaces. During the late 1960s and early 1970s, cases of plasma-cell infiltrates of the lips, gums and tongue were described primarily in the dental literature under the names atypical gingivostomatitis, idiopathic gingivostomatitis and allergic gingivostomatitis.1

Sherman and Luders simplified the nomenclature by grouping the infiltrates by anatomy under the titles plasmacytosis circumorificialis and plasmacytosis mucosae. However, additional terms have been used in the literature to describe plasma-cell infiltrates of the aerodigestive tract, such as plasma cell-gingivitis, plasmacytosis of the gingiva and plasma-cell cheilitis. In 1986, White et al grouped all plasma-cell infiltrates of the aerodigestive tract under the name plasma-cell orificial mucositis because of the fact that all the cases reported had clinical and histological findings indistinguishable from one another.2 Clinically, the lesions of plasmacytosis when appearing on the lips and gums reveal a well-circumscribed, soft, slightly elevated, edematous mass with red and glistening surface.3

It is very important to investigate the benign/neoplastic nature of the plasma cell infiltrate, as the management and prognosis of plasma cell neoplasms are very different from benign conditions. Gene rearrangement studies can be done when results of immunohistochemistry are inconclusive.4

Plasma cell tumors are neoplastic proliferation of B cells that may appear in disseminated form (multiple myeloma), or solitary bone lesions (solitary bone plasmacytoma) or in soft tissues (extramedullary plasmacytoma).5 Extramedullary plasmacytoma (EMP) comprises about 3% of all plasma cell tumors. They are more commonly seen in the 5th-6th decades of life and more commonly in men. 80-90% of EMP arises from the mucosa associated lymphoid tissue in the aerodigestive tract like the nasal cavity, nasopharynx, paranasal sinuses and tonsils. They can also be seen in the oral cavity as painful tumor masses involving the alveolus causing discomfort and loosening of teeth.6 Plasmacytic tumors are characterized by monoclonal proliferation of plasma cells that produce a single immunoglobulin molecule unlike plasmacytosis which shows polyclonal proliferation of plasma cells.

Multiple myeloma is a systemic disease and is characterized by neoplastic proliferation of monoclonal immunoglobulins (M protein). It is a disseminated disease
Figure 5: 2x view - The Hematoxylin & Eosin stained soft tissue section shows hyperplastic stratified squamous surface epithelium with fibrocellular connective tissue.

Figure 6: 20x view - The Hematoxylin & Eosin stained soft tissue section shows fibrocellular connective tissue with infiltration of inflammatory cells predominantly lymphocytes.

Figure 7: 40x view - The Hematoxylin & Eosin stained soft tissue section shows infiltration of plasma cells with cart-wheel nucleus and some cells with eccentrically placed nucleus.

Figure 8: Immunohistochemical staining of the tissue shows focal positivity for lambda and diffuse positivity for kappa light chains in the ratio of 1:4 indicative of polyclonal proliferation.

Figure 9: Plasma cells immunopositive for CD 138/CD38.
involving many bones. The classic triad in the diagnosis of multiple myeloma is the detection of M protein in the serum or urine (Bence-Jones proteins), greater than 10% plasmacytosis in the bone marrow, and the presence of osteolytic lesions by radiography.\textsuperscript{5} Urine analysis of the patient was negative for Bence-Jones protein and absence of clinical and radiological evidence of skeletal lesions distinguished the present case from multiple myeloma.

An immunohistological study by Wei et al determined the ratio of cytoplasmic $\kappa$ to $\lambda$ light chains in plasma cells to be 0.4–3.5 in reactive plasmacytosis, 0.2–3.0 in monoclonal gammopathy of unknown significance (MGUS), and < 0.2 or > 11.1 in multiple myeloma.\textsuperscript{6} The immunohistochemical staining of present case reported a ratio of 4 suggestive of reactive plasmacytosis.

Plasma cell gingivitis is a rare benign condition of the gingiva characterized by sharply demarcated erythematous and edematous gingivitis often extending to the mucogingival junction. Plasma cell gingivitis is considered a hypersensitive reaction to some antigen, often to chewing gum, toothpaste, and other foreign substances. The antigens identified were mostly cinnamaldehyde and cinnamon, used as flavoring agents in chewing gums and dentifrices.\textsuperscript{7} In the present case, patient had not revealed any history of exposure to allergens.

Amlodipine is a dihydropyridine calcium channel blocker that is used in the management of both hypertension and angina. Ellis et al. first reported amlodipine-induced gingival overgrowth. Since then, very few cases of amlodipine-induced gingival hyperplasia have been reported, although there are numerous reports of nifedipine-induced gingival overgrowth till date. There are less data on reports of hyperplasia with amlodipine at a dose of 5 mg, even after taking it for more than 6 months.\textsuperscript{8} Drug induced gingival enlargement is more fibrotic in nature but the present case demonstrated soft and edematous gingival enlargement.

Plasma cells are common in chronically inflamed sites, including periodontal lesions. Accumulation of plasma cells in inflamed sites is promoted by chronic inflammation, activators of microbial origin, and specific antigen. Periodontitis is an example of a chronic inflammatory disease in which the predominant cells infiltrating the lesion are of B-cell lineage. Development of periodontitis typically depends on the accumulation of certain oral bacteria in gingival crevices. Studies with gingival crevicular fluids show that local specific humoral responses may be mounted against antigens from certain periodontitis-associated bacteria. In addition to bacterium-specific antigens, these bacteria are known to contain potent polyclonal B-cell activators. The mechanisms are unknown, but either antigen or nonspecific activators of microbial origin may markedly increase the total plasma...
cell population in chronically inflamed sites. In the present case, investigations done excluded all the conditions considered in the differential diagnosis.

Immunohistochemical staining also revealed no evidence of malignancy. The presence of plasma cells, plasmacytoid lymphocytes and immunoblasts in the peripheral blood smear is usually suggestive of a reactive process. These include bacterial or viral infections. Reactive plasmacytosis is a diagnosis of exclusion, to be differentiated from other autoimmune, allergic and neoplastic disorders with plasma cell infiltrates. Hence the present case was diagnosed as an idiopathic condition like reactive plasmacytosis with plasma cell infiltrates in the submucosa. It is treated by removing the underlying cause. In this case inflammatory periodontal condition may be the cause for plasmacytosis.

Management of plasmacytosis is mostly symptomatic and underlying cause should be treated. Corticosteroids (topical, intralesional, systemic) have been tried with some success. Other topical immunosuppressants like tacrolimus and cyclosporine and oral antibiotics are alternative therapeutic options. Plasmacytosis is more common in the elderly age group where other co-existing systemic conditions like diabetes, hypertension, hyperacidity and osteoporosis can further complicate the management with long term systemic corticosteroids.

CONCLUSION

The exact etiology of reactive plasmacytosis is not known, but it may be the result of hypersensitivity reaction to other unidentified environmental antigens. Even with the treatment- both periodontal and medical done, the enlargement did not regress completely. Long-term follow-up and new treatment strategies are therefore required.

References


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