Asian Journal of Medical Research Case Report

Acute graft-versus-host-disease masquerading as oral early squamous cell carcinoma: a case report

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Abstract

Graft-versus-host disease is an altered immune response of host. Various oral manifestations have been reported in literature; however, any associated malignant changes have been rarely reported. This paper highlights early carcinomatous changes developing in an individual following blood transfusion.

Key Words: Graft-Versus-Host Disease, Malignant, Immunology.

INTRODUCTION

Graft-versus-host disease showing oral manifestations is a rare finding. Most commonly, it manifests as Lichenoid reaction in form of white striations or as white patches. Rarely, it presents as malignant or potentially malignant lesions. This case report highlights upon a rare finding of graft-versus-host disease clinically appearing as early invasive squamous cell carcinoma.

CASE REPORT

A 41-year old patient reported to a private dental clinic with chief complaint of discomfort in mouth. Intra-oral examination showed bilateral keratotic, multiple non-homogenous white patches extending from commissure of mouth to retromolar area. An ulcerated lesion was observed on left buccal mucosa. Ventral surface of tongue showed extensive whitish corrugated lesion. Patient gave a history of blood transfusion due to low hemoglobin content (4.5 gm/dl) four months back following which oral manifestations appeared.

Patient also gave a habit history of gutkha chewing for four to five months and occasionally, drinking locally made liquor. Patient was tested for HIV and Hepatitis B cross-reactivity and was found to be negative . Incisional biopsy was done and histopathological diagnosis was suggestive of early invasive squamous cell carcinoma.

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DISCUSSION

Graft-versus-host-disease can be divided into two forms: acute and chronic graft-versus-host disease (GVHD). Acute GVHD develops after three months; is of short duration; involves only the epithelia and is induced by recognition of host-specific antigens. In contrast, chronic GVHD manifests via relapsing episodes, has multiple targets and its pathophysiology is poorly understood. The frequency of acute GVHD varies between 6% to 90% of graft recipients as a function of patient age, HLA type etc.[1,2].

Chronic graft - versus - host disease has heterogeneous manifestations. Several diagnostic features relatively commonly seen are sclerosis, lichen planus-like lesions, poikiloderma and esophageal webs. The distinctive features of chronic GVHD are oral ulcers, epithelial atrophy, onchodystrophy and sicca syndrome. Early clinical signs include lichen planus-like or dry papulosquamous lesions. Late signs are fibrosis of buccal mucosa and decreased jaw movements. In acute GVHD, the oral lesions are often painful, erythematous, ulcerative and desquamative while in chronic GVHD, they appear as lichenoid lesions associated with erythema and ulceration in association with Sicca syndrome characterized by xerostomia and progressive salivary gland atrophy.

MHC gene is located on the short arm of chromosome 6 and is responsible for encoding cell-surface proteins called HLAs. The HLAs are subdivided into class I and II MHC antigens. Class I antigens (HLA-A, -B, -C) are expressed on all nucleated cells in the body and allow the immune system to recognize cells as “self” or “non-self”. Class II antigens (HLA-DR, -DP, -DQ) are found on antigen-presenting cells and effector cells and

Table 1 Grading of chronic GVHD

Limited:	Localized skin involvement, liver dysfunction of both.
Extensive:	Generalized skin involvement. Localized skin involvement or liver dysfunction plus one of the following: 1. Chronic aggressive hepatitis, bridging necrosis or cirrhosis. 2. Eye involvement (Result of Schirmer's test, <5 mm). 3. Involvement of salivary glands. 4. Mucosal involvement (on lip biopsy). 5. Involvement of other target organs).

Table 2 Grading of acute GVHD

Stage	Skin	Liver	Gastro-intestinal
0	No	No	No involvement.
1	<25%	tbili 2.0-2.9 mg/dl	500-1000 cc stools/day, nausea, anorexia.
2	25%-50%	tbili 3.0-5.9 mg/dl	1000-1500 cc stools/day, histologic diagnosis of gastrointestinal involvement.
3	Generalized erythema	tbili 6.0-14.9 mg/dl	1500-2000 cc stools/day.
4	Bullae, desquamation	tbili >15.9 mg/dl	>2000 cc stools/day, ileus, severe pain.

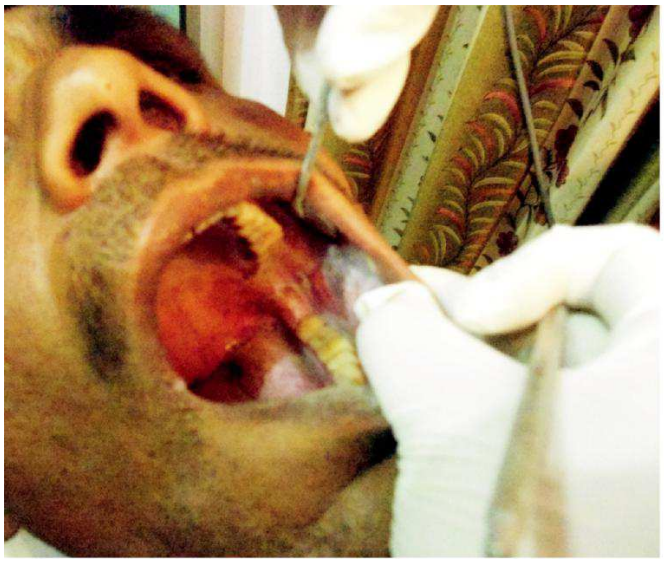

Figure 1: A heterogenous leukoplakic patch seen on left buccal mucosa

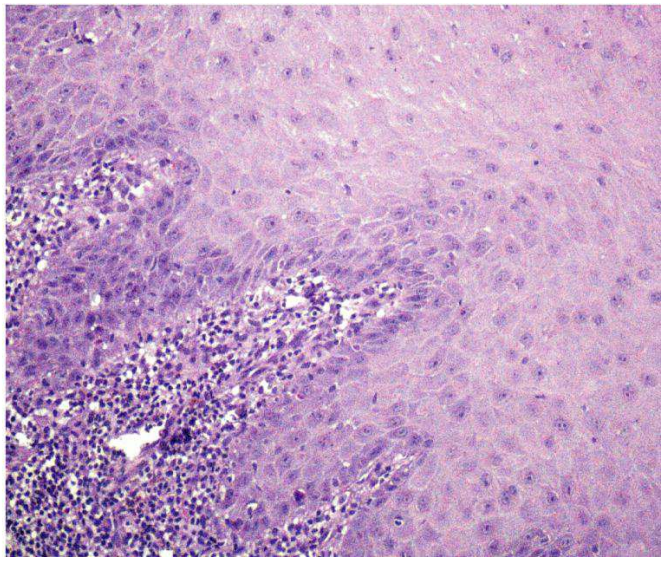

Figure 2: Photomicrograph showing dysplastic epithelial island in lamina propria. Overlying epithelium is also showing malignant changes. Dense inflammatory infiltrate is seen (40X).

help to regulate immune reaction by facilitating recognition of foreign antigens and activation of antigen presenting cells as well as effector cells. Non-compatible HLA antigens on a graft elicit both humoral and cell-mediated host responses that eventually lead to destruction of the graft. Genetic disparity at non-MHC loci encoding "minor histocompatibility antigens" also play a role in recognition of graft as "foreign". There are three conditions for GVHD development. First, the graft must contain immunologically competent cells (T cells). Second, the recipient must express tissue antigens sufficiently different from those of thus aiding the donor cells in identification of host tissues as "foreign". Third, the recipient is incapable of rejecting the graft because of tolerance, lack of recognition or immunosuppression.

Chronic GVHD is defined as occurring more than 100 days post-bone marrow transfusion either as GVHD progression (progressive onset) or following quiescent

acute GVHD or de novo. Predisposing factors for chronic GVHD include HLA disparity, prior acute GVHD and older age. Oral presentations of chronic GVHD include- erythema, mucosal atrophy and lichenoid changes (Table 1).[3]

Approximately 60%-70% of patients with grade III to grade IV acute GVHD have oral signs. Acute oral GVHD signs include- painful desquamative and ulcerative lesions, white popular eruptions and/or reticular and lichenoid lesions involving the entire oral cavity. Hsiao et al in their study on 55 allogenic transplant recipients found that mucosal erythema, atrophy and ulceration predominate in early acute GVHD, while hyperkeratotic and lichenoid changes appear later (Table 2).[4]

Present case represents a rare manifestation of acute GVHD masquerading as epithelial malignancy. It is hence, very important for a dental practitioner to have a sound knowledge of the pathogenic mechanisms that underlie leukoplakic or Erythroplakic patches so as to plan patient management.(Figure 1&2).

CONCLUSION

A practicing clinician should be aware of various systemic factors involved behind a potentially malignant disorder apart from a history of habit or trauma. This paper highlights upon such a case that had developed a malignant state after blood transfusion. The preexisting habit added as a existing risk factor thus, highlighting the role of immunity against development of such a lesion.

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