An Autosomal Genetic Disease: White Sponge Nevus

Supriya Sharma[1], Kanchan Srivastava[2], Priyanka Gaur[3], Shalini Gupta[4]

ABSTRACT

White sponge nevus is a rare autosomal dominant genetic disease of the oral mucosa. The lesion is white or greyish, thickened, folded and spongy in nature. The genes related with WSN involve mutant cytokeratin keratin 4 (*KRT4)* and keratin 13 (*KRT13)*. It was also called as familial white folded dysplasia. The condition principally affects labial mucosa, ventral tongue, soft palate, alveolar mucosa, and floor of the mouth, and, less commonly, extra oral sites are the nasal, esophageal, laryngeal, and anogenital mucosa; but not the skin.

Key words: Dyskeratosis, white lesion, white sponge nevus

INTRODUCTION

White sponge nevus (WSN) is a disorder of skin inherited as autosomal dominant trait showing a changeable expressivity and great degree of penetrance.[1] It was first described by Hyde in 1909 and the term coined by Cannon in 1935.[2,3]

SYNONYMS OF THE DISEASE

Cannon's disease, familial white folded mucosal dysplasia, hereditary leukokeratosis, hereditary mucosal leukokeratosis, hereditary oral keratosis, congenital leukokeratosis mucosae oris, white folded gingivostomatosis, white gingivostomatitis, WSN, WSN of Cannon and WSN of mucosa.[4]

EPIDEMIOLOGY

The exact prevalence of is not clearly understood, but it is approximated to affect less than 1 in 200,000 individuals worldwide.[5] In one case report of oral white nevus, HPV 16 homologous DNA sequences have been detected in the biopsy specimen. The onset of this disease is often early in life and both genders are affected equally. It shows no gender or race predilection; however, because of this situation's autosomal dominant pattern of this transmission, various family members may reveal the disorder.[2,6]

ETIOLOGY

The defect in the normal keratinization of the oral mucosa leads to white sponge nevus. The pair of keratin 4 and keratin 13 is characteristically expressed in the spinous cell layer of mucosal epithelium. The alterations in the epithelial cells occur due to mutations in either of these keratin genes.[7,8]

GENETIC PATHOGENESIS

The tissue distribution and nature of the lesions in affected patients suggest that mutations in *KRT4* and/or *KRT13* might be responsible for this disorder. Moreover, defective *KRT* mutations, like *KRT4* and *KRT13*, are nearly linked to WSN. Type II *KRT4* and its type I partner, *KRT13* manifest in both the oral and anogenital mucosae. Furthermore, mutations of *KRT4* and *KRT13* were currently demonstrated to be the underlying source of this disease. These genes provide instructions for generating proteins called keratins. Keratins are a group of fibrous proteins that produce the constitutional framework of epithelial cells, which line the surfaces and cavities of the body and make up the various mucosae. The *keratin 4* protein (generated from the *KRT4* gene) and the *keratin 13* protein (generated from the *KRT13* gene) partner together to produce molecules called as intermediate filaments. These filaments form networks that provide flexibility and toughness to the diverse mucosae. Mutations in the *KRT4* or *KRT13* gene disturb the formation of the keratin protein. As a consequence, *keratin 4* and *keratin 13* are incompatible and do not fit well-organized properly, leading to the production of asymmetrical intermediate filaments that are simply injured with minor trauma or friction. During eating or brushing one's teeth, fragile intermediate filaments in the oral mucosa might be damaged. Meshwork of intermediate filaments protects the mucosae from different regular physical stresses or by friction. Injury to intermediate filaments promote inflammation and induces proliferation and the abnormal growth of epithelial cells, provoking the mucosae to thicken and resulting in WSN.[7,9,10,11]

CLINICAL FEATURES

The disease is characterized by: symmetric, thickened, white, corrugated or velvety, diffuse plaques affecting the buccal mucosa present bilaterally. The plaques were smooth with velvety texture and irregular, well-defined borders (Fig 1 and 2). The WSN plaques are considered benign because the lesions are asymptomatic and painless in many cases, although they may undergo alternate periods of remission and exacerbation due to infections. Common intraoral sites include ventral tongue, labial mucosa, soft palate, alveolar

[1]Senior Resident, Faculty of Dental Sciences, Department of Oral Pathology and Microbiology, [2]Women Scientist, Department of Respiratory Medicine, [3]Research Scholar, Department of Physiology, [4]Professor, Faculty of Dental Sciences, Department. of Oral Pathology and Microbiology, King George's Medical University (KGMU), UP, Lucknow, India

Corresponding author: Supriya Sharma, MDS, Senior Resident, Faculty of Dental Sciences, Department of Oral Pathology and Microbiology, King George's Medical University (KGMU), UP, Lucknow, India

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mucosa, and floor of the mouth, although the extent of involvement can vary from patient to patient. Extra oral mucosal sites are the nasal, esophageal, laryngeal, and anogenital mucosa appear to be less commonly affected. The white color does not diminish when the tissue is stretched in any mucosal site.[12,13]

HISTOLOGIC FEATURES

The microscopic features of WSN are characteristic but not necessarily pathgnomonic. Prominent hyperparakeratosis and marked acanthosis with clearing of the cytoplasm of the cells in the spinous layer are common features; however, similar microscopic findings may be associated with leukoedema and hereditary benign intraepithelial dyskeratosis. An eosinophilic condensation is recognized in the perinuclear area of the cells in the superficial layers of the epithelium in few instances, a feature that is unique to WSN (Fig 3a & 3b).[12,13,14,2,3]

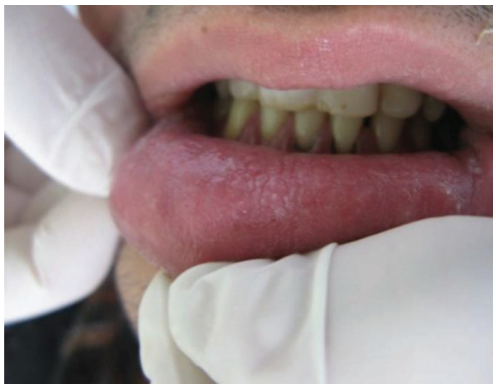

Figure-1: Bilateral, symmetrical and non-removable white plaques and patches on the labial mucosa. The plaques were smooth with velvety texture and irregular, well-defined borders with no elevation or erythema and clear margins.

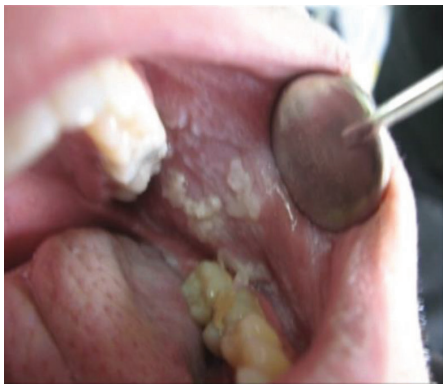

Figure-2: Bilateral, symmetrical white plaques and patches on the buccal mucosa, which could not be removed. The plaques were smooth with velvety texture and irregular, well-defined borders. There was no elevation or erythema. The margins were clear and no lymph nodes were noticeable.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

An identification of this disorder is crucial in that it must be discriminated from other familial or congenital disorders of more extensive clinical significance. The clinical manifestation is so characteristic that biopsy is usually not compulsory. The diagnosis is produce more definite if there is a supportive family history and other mucous membranes are influenced. In instance of any suspicion, biopsy should be recommended. The differential diagnosis of white sponge nevus comprises trauma, syphilis, tobacco and betel nut use, oral lesions of Leukoplakia and chemical burns. It may also be messed with Candidiasis, but inspection of fungus, the histology of biopsy samples, and the reaction to antifungal drugs will be the discriminating factors. Lupus erythematosus, cheek- biting, lichen planus, should also be rule out. The lesions of white sponge nevus may resemble lesions of panchyonychia congenita, Darier's disease, dyskeratosis congenita, and hereditary benign intraepithelial dyskeratosis. Not including lupus erythematosus, lichen planus which may be restricted to the oral cavity, these disorders can be notable clinically from white sponge nevus by their correlated extra oral lesions. Consequently, concurrent skin lesions rule out the diagnosis of white sponge nevus.[1,4]

TREATMENT

Although affected patients are asymptomatic, they often complain of a changed texture to their mucosa or discomfort with the manifestation of the lesions. Many affected patients undergo curative treatments with Nystatin, antihistamines, vitamins and mouth rinses. Azithromycin, tetracycline and penicillin have presented few clinical effects.[15] Following penicillin administration, Victoria A acid and tetracycline mouth rinse a significant improvement has been reported in a case.[16,17,18] Long-term small dose systemic antibiotic

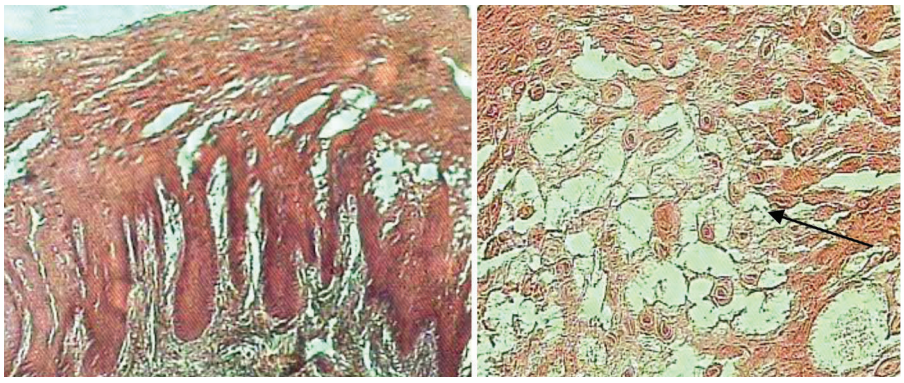

Figure-3: 3 (a) Hematoxylin and Eosin section (×10); 3(b) Hematoxylin and Eosin section shows perinuclear condensation of keratin tonofilaments (black arrow) (×40).

treatment maintained the exemption of WSN.[19,20] However, there is no excellence management protocol for WSN to date. Meanwhile, affected patients should maintain proper oral hygiene to reduce infection in the oral cavity. The suitable diagnosis and treatment of this rare disease will demand the combination of clinical history, clinical examination and histopathologic findings.[6]

CONCLUSION

This condition is benign, but this lesions persist through life on mucous membranes. This lesion arised early in life without any described transition throughout the patient's life, but diffuse widening of the lesion apears to be a dangerous factor. Biopsy in such cases is mandatory for treatment planning and exclude of other lesions.

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