

White sponge nevus: Report of three cases in a single family

Ngairangbam Sanjeeta, DB Nandini, Takhellambam Premlata¹, Sumita Banerjee

Departments of Oral Pathology and Microbiology and ¹Conservative Dentistry and Endodontics, Dental College, Regional Institute of Medical Sciences, Imphal, Manipur, India

Abstract

White sponge nevus (WSN) is an interesting hereditary oral mucosal disorder that commonly manifests as bilaterally symmetrical, thickened white, corrugated or velvety, diffuse plaques that predominantly affects the buccal mucosa. The lesions may develop at birth or later in childhood or adolescence. Because it is asymptomatic and benign, WSN requires no treatment. Recognition of this disorder is important due to its potential confusion with other lesions that may be found in the oral cavity. Emphasis should be given to the early and correct diagnosis of this disorder to avoid unnecessary treatment. This report presents three affected members of a single family.

Key Words: Cannon disease, genodermatosis, CK 4, CK 13, spongiosis, white plaque, white sponge nevus

Address for correspondence:

Dr. Ngairangbam Sanjeeta, Department of Oral Pathology and Microbiology, Dental College, Regional Institute of Medical Sciences, Imphal, Manipur, India.
E-mail: dr.sanjeeta.ng@gmail.com

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INTRODUCTION

White sponge nevus (WSN) is a rare autosomal dominant genodermatosis affecting the oral mucosa in the majority of the cases. Other less frequently affected sites include the nasal, esophageal, rectal and vaginal mucosa.^[1,2] WSN was first reported by Hyde in 1909,^[3] and Cannon coined the term “white sponge nevus” in 1935.^[4] A defect in the normal keratinization process of the oral mucosal epithelium results in this disorder. The genes responsible for production of cytokeratins (CKs) 4 and 13, which are specifically expressed in the spinous cell layer of oral mucosal epithelium, have been found to be mutated in this disorder.^[2,5,6] This genetic disorder affects about one in 200,000 people, and the condition often shows variable expressivity and irregular penetrance.^[7]

CASE REPORT

A 13-year-old female child reported to the Outpatient Department of the Dental College, with a chief complaint

of pain in her mandibular right posterior region. Intraoral examination revealed grossly carious tooth #46, which was tender on percussion and had periapical radiolucency, consistent with periapical inflammatory disease.

A striking incidental finding that was also noted upon performing her intraoral examination was the presence of diffuse, soft, thickened white plaques with a corrugated surface affecting the buccal mucosa bilaterally. The plaques extended from the retro-commissural area anteriorly to retromolar region posteriorly and also involved the soft palate [Figure 1]. Lesions were also noticed on the dorsal surface of the tongue [Figure 2], lower labial mucosa and even the mucosa of the hard palate. The lesions could not be removed by scraping and were asymptomatic. The patient was referred to the Departments of Ophthalmology and Obstetrics/Gynecology to rule out the presence of any conjunctival and genital lesion, respectively. No other sites were identified. A cytologic preparation from the lesion failed to reveal any fungal hyphae when stained with

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periodic acid-Schiff (PAS) method. No other contributing factors, such as tobacco use or chemical burn, could be elicited. A biopsy was advised to rule out other lesions.

The patient's past history revealed that the lesions were present since early childhood. Information as to whether the lesions were present since birth could not be confirmed. The family history revealed that similar lesions were present in the father (aged 56 years) and the eldest brother (aged 31 years) of the four siblings. The father had bilateral lesions on buccal mucosa [Figure 3] while the brother had scattered lesions on the buccal mucosa bilaterally [Figure 4].

Histopathologic examination of the lesional tissue revealed hyperplastic keratinized squamous epithelium, with prominent hyperparakeratosis, marked acanthosis and spongiosis [Figure 5]. Cells showing clearing of the cytoplasm with perinuclear eosinophilic condensation, a characteristic feature of WSN, were noticed [Figures 6 and 7]. Based on the clinical features, past history, family history and the characteristic histopathological findings, the lesions were diagnosed as WSN.

DISCUSSION

WSN is a rare hereditary disease that is transmitted as an autosomal dominant disorder. In the present case, the disease was transmitted from the affected father to two of his four children, consistent with an autosomal dominant mode of inheritance. Historically, this condition has also appeared in the medical literature under a variety of names, including Cannon disease, familial white folded hypertrophy of the mucous membranes, hereditary leukokeratosis, white gingivostomatitis and exfoliative leukoedema.^[8,9]

Point mutations for genes coding for CK 4 and/or 13 are responsible for this entity.^[2] Both of CK 4 and CK 13 may be affected, or no abnormalities may be detected in the CK 4 gene as reported by Martelli *et al.*^[10] Terrinoni *et al.* described a new mutation in CK 4 genes and an amino acid insertion in 1A alpha helical domain of CK 4 that was responsible for the condition in some individuals.^[6]

Disruption of the stability of the keratin filament as a result of mutation in the 2B domain of CK 4 gene has also been described in an affected Taiwanese patient by Chao *et al.*^[11] Several similar investigations have been carried out to ascertain the specific genetic mutation in CK 4 and CK 13 which is responsible for the development of WSN. Recently, Cai *et al.* found a point mutation in the CK 13 gene that may cause abnormal degradation of CK 13 protein which could probably be associated with abnormal ubiquitination process.^[12]



Figure 1: Clinical image showing diffuse, soft and thickened white plaque with corrugated surface on left buccal mucosa



Figure 2: Clinical image showing lesions on the dorsal surface tongue, right buccal mucosa and parts of the palatal mucosa



Figure 3: Clinical image showing lesions on right buccal mucosa of the father

The lesions of WSN usually appear at birth or in early childhood; however, sometimes, the condition develops during



Figure 4: Clinical image showing scattered lesions on right buccal mucosa of the brother

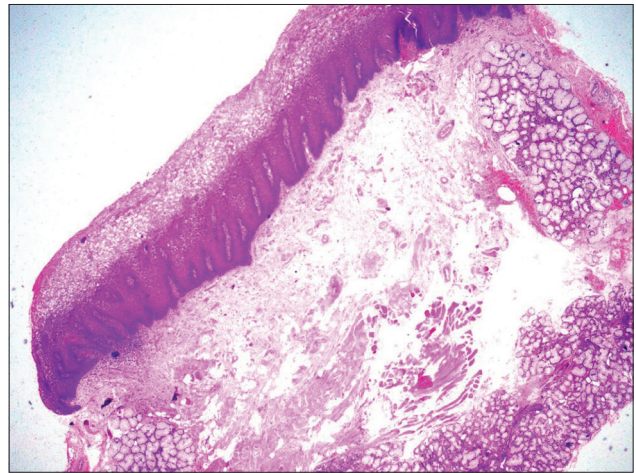


Figure 5: Histopathological picture showing hyperplastic keratinized squamous epithelium with prominent hyperparakeratosis, marked acanthosis and spongiosis (H&E stain, x50)

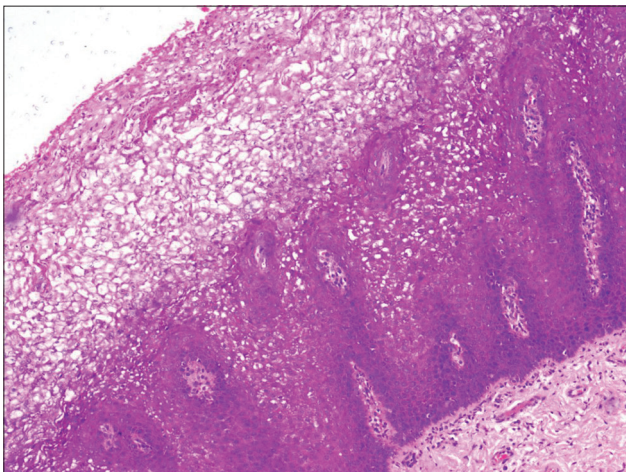


Figure 6: Histopathological picture showing cells with clearing of the cytoplasm and perinuclear eosinophilic condensation (H&E stain, x200)

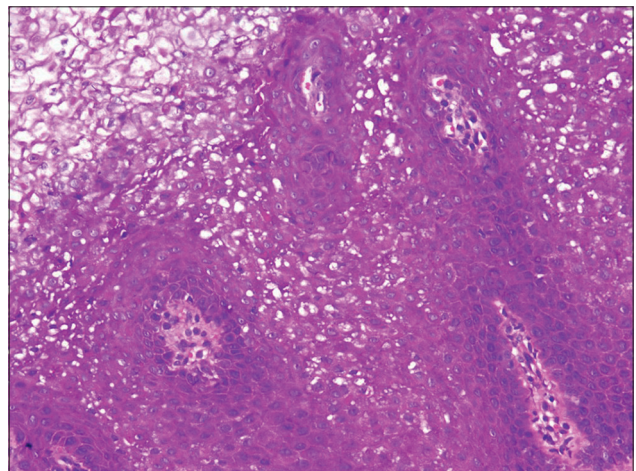


Figure 7: High power view of the section shows cells with clearing of the cytoplasm and perinuclear eosinophilic condensation (H&E stain, x400)

adolescence.^[8] In most instances, the lesions are seen bilaterally as symmetrical, thickened, white, corrugated or velvety, diffuse plaques that affect the buccal mucosa as observed in the present case. The affected mucosa appears folded with a soft or spongy texture and a peculiar white opalescent hue.^[9] Ragged white areas may also be present that can be removed sometimes by gentle rubbing, without any associated bleeding.^[9]

The other less common intraoral sites of involvement include the tongue, labial mucosa, soft palate, alveolar mucosa and floor of the mouth. The clinical expression of the lesions, such as size of the plaques, the affected areas and their distribution, may change with the time.^[8,10] All the three cases in the present report had bilateral lesions of the buccal mucosa. Extraoral mucosal sites, such as the nasal, esophageal, laryngeal and anogenital mucosa, also may be affected in some cases though less common. The plaques in our patient were confined to the oral mucosa and were not found to occur elsewhere.

The histopathological findings of WSN are characteristic but not necessarily pathognomonic. Similar findings may be seen in leukoedema and hereditary benign intraepithelial dyskeratosis. Prominent hyperparakeratosis and marked acanthosis with clearing of the cytoplasm of the cells in the spinous layer are common features. An eosinophilic perinuclear condensation of the cells in the superficial layers of the epithelium may be seen as observed in the present case. This feature is unique to WSN, and this eosinophilic material has been ultrastructurally identified as tangled masses of keratin tonofilaments. In many cases, an exfoliative cytologic preparation that is stained with the Papanicolaou method will show the eosinophilic perinuclear condensations more readily than histopathological sections will.

WSN may superficially appear clinically similar to several other oral white lesions that have varied clinical behaviors

and treatment protocols. It is important that the condition is distinguished from the other entities to avoid unnecessary treatment. The diagnosis of WSN is usually based on its distinctive clinical appearance and history. However, exfoliative cytologic preparations or biopsy can aid in the diagnosis and may be performed to rule out other lesions. A positive family history and histopathological or cytopathological features can distinguish WSN from the other lesions.

WSN may resemble a wide spectrum of oral disorders that may present as diffuse white plaques. Hereditary benign intraepithelial dyskeratosis should be considered in the differential diagnosis which can be excluded from the absence of bilateral limbal conjunctival plaques.

Leukoplakia though not a reasonable consideration has been discussed by some reports in differential diagnosis of WSN. However, leukoplakia particularly, verrucous leukoplakia and proliferative verrucous leukoplakia, will have sharply defined margins in at least some areas compared to diffuse and blending margins of WSN. Further, a negative history of tobacco use, age of onset of the lesions and histopathological features rule out leukoplakia. Hyperplastic candidiasis, plaque type lichen planus and lupus erythematosus can be considered if WSN lesions are mild and not diffuse as in case 2 and 3. However, the latter two lesions typically have a few areas of striae formation at the periphery of the white plaques. WSN on the tongue rarely can be mistaken for syphilitic glossitis which can be ruled out by history and symptoms. Pachyonychia congenita, Darier's disease and dyskeratosis congenita can be ruled out by characteristic nail and skin lesions. Oral lesions are more cobblestone than plaque-like in Darier's disease. Rare differentials include chronic cheek biting, tobacco pouch keratosis, verrucous carcinoma and squamous cell carcinoma which can be excluded from the history and unilateral clinical presentation as well as characteristic histopathological features.^[2,10,13] In case of suspicion of infection by *Candida albicans*, PAS-stained cytologic preparations could be done. WSN can have superimposed candida infection, which may cause it to be symptomatic at times.

No treatment is required since WSN is a harmless condition with no potential for malignant transformation. No treatment was done for the cases as none of them had any symptoms or clinical complaints. Various attempts to reduce the clinical presentation of WSN have been made but without any success. These include vitamins (beta-carotene, local applications of retinoic acid), antihistamines, tetracycline mouth rinses, antibiotics (penicillin, azithromycin) and laser ablation.^[2,10,14] Surgical

resection has also been tried with no recurrence even after 2 years.^[14] Recently, with the report of new cases of WSN with associated mutations, gene-based diagnosis and gene therapy for WSN may become available in the near future and could provide a reference and instruction for the treatment of other keratin-associated diseases.^[15]

In conclusion, this case report is presented for its rarity and also for the striking resemblance of the lesions to other lesions that present themselves more commonly in the oral cavity. It is necessary that the condition is correctly diagnosed early to avoid unnecessary treatment.

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Conflicts of interest

There are no conflicts of interest.

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