Case Report

White sponge nevus: A case report of a rare keratinopathy and its novel treatment approach

Debasish Pramanick[1], Sandip Ghose[2], Piyali Polley[3], Rahul Patel[3]

From [1]Dental Surgeon, [2]Assistant Professor, [3]Ex-Dental Surgeon, Department of Oral Pathology, Dr. R. Ahmed Dental College and Hospital, Kolkata, West Bengal, India

ABSTRACT

White sponge nevus (WSN) is a hereditary mucocutaneous leukokeratosis due to an altered expression of *CK 4* and *CK 13* genes, thereby causing a defect in keratinization. We report the case of WSN in a 27-year-old who presented with a complaint of white, painless patches in both the cheek mucosa since childhood. The patient was examined and the biopsy was done. Based on the clinical findings, inheritance pattern, and histopathological features, a diagnosis of WSN was made. The patient responded well to our novel treatment approach with amoxicillin suspension (250 mg/5 ml). Regarding the treatment of WSN, no definite pharmacological therapy is available till date. We report this case to emphasize that amoxicillin suspension topical therapy may be used as a novel treatment measure with its unique advantages.

Key words: Amoxicillin suspension, Treatment, White sponge nevus

White sponge nevus (WSN) (OMIM ID # 193900), also designated as Cannon's disease, is a rare hereditary mucocutaneous leukokeratosis which is inherited as an autosomal dominant disorder and having a prevalence rate of about 1 in 200,000 [1]. Although most of the cases of WSN involves the oral mucosa, few cases have also been reported in the nasal, esophageal, laryngeal, vaginal, as well as rectal mucosa [2]. However, among all other types of genodermatoses, WSN has a sole preponderance for occurrence in the oral mucosa only. The first case of WSN was reported in 1909 by Hyde, and later in 1935, Cannon published a complete report and review on WSN [3,4]. Oral mucosal WSN, appearing either in early childhood or during adolescence, usually manifests as painless, symmetric, grayish-white thickened, and corrugated spongy plaque mostly involving the non-keratinizing mucosa. Pathogenesis of WSN may be attributed to altered expression and mutation of *CK 4* and *CK 13* genes, thereby causing a defect in maturation and keratinization of the epithelial cells of the stratum spinosum [5]. Hence, the designation of nevus may be considered as a misnomer.

Usually, WSN is refractory to any kind of treatment. In this report, we are going to describe a case of WSN in a 27-year-old, non-smoker Indian man who responded well to our novel treatment approach with amoxicillin suspension. Although very few international studies regarding the treatment of WSN with tetracycline and penicillin mouth rinse are available, the use of amoxicillin suspension in Indian patients of WSN is not reported yet.

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CASE REPORT

A 27-year-old man presented to the department of oral and maxillofacial pathology of a tertiary health-care center with a complaint of white, painless patches in both the cheek mucosa since childhood (Fig. 1). The personal history of the patient revealed no such deleterious oral habits such as tobacco, areca nut, and alcohol abuse. No history of local application of any chemicals was reported. Family history review unveiled that the patient's father and grandfather also had similar intraoral manifestations. Medical history was non-contributory.

A general survey of the patient was conducted and found to be within normal limits with a pulse rate of 77 beats per minute; blood pressure of 124/78 mm of Hg; a respiratory rate of 18/min, and axillary temperature of 97.6°F. There was the absence of any conjunctival and other mucosal lesions as examined by the ophthalmologist and dermatologist, respectively. During the extraoral examination, no deviation from normalcy was noted. No other cutaneous lesion was found elsewhere in the body. Regional lymph nodes were non-palpable. A thorough intraoral examination revealed the presence of velvety, white plaques without any ulceration on the entire labial mucosa, and the

Correspondence to: Dr. Debasish Pramanick, Department of Oral Pathology, Dr. R. Ahmed Dental College and Hospital, 114, A.J.C. Bose Road, Kolkata - 700 014, West Bengal, India. E-mail: dr.pramanick.debasish@gmail.com

bilateral buccal mucosa extending from the angle of the mouth up to the pterygomandibular raphe. The surface appeared folded. On palpation, the lesion was non-tender and spongy in appearance. Neither it was scrapable nor did it disappear on stretching the mucosa. The full complement of dentition was present with mild extrinsic stains and without any sharp cuspal edges.

Cytological smear preparation and periodic acid-Schiff staining from the lesion were done, but there was no evidence of fungal hyphae. Lesional incisional biopsy was carried out under local anesthesia.

Histopathological tissue section stained with hematoxylin and eosin revealed the presence of hyperplastic, hyperorthokeratinized, and stratified squamous epithelium backed by connective tissue stroma. The spinous layer showed acanthosis with intracytoplasmic vacuolation of epithelial cells. Perinuclear eosinophilic condensation of keratin was noted in the superficial cells of the stratum spinosum. Cells of stratum granulosum revealed the presence of increased keratohyalin granules. Cellular atypia was absent. The subepithelial connective tissue was fibrocollagenous in nature with a few blood vessels and a sprinkling of chronic inflammatory cells (Fig. 2).

Based on the clinical findings, inheritance pattern, and histopathological features, a diagnosis of WSN was made. Due to the financial constraints and institutional non-availability, any other investigations including genetic analysis could not be performed in this patient. As a treatment measure, the patient was advised to use amoxicillin suspension (250 mg/5 ml) topically by sluicing 5 ml of the same for 5 min twice daily for 1 month. After sluicing, the patient was instructed to spit out the suspension. Regular follow-up at weekly and monthly intervals was carried out and the patient showed complete remission without recurrence even after 6 months (Fig. 3).

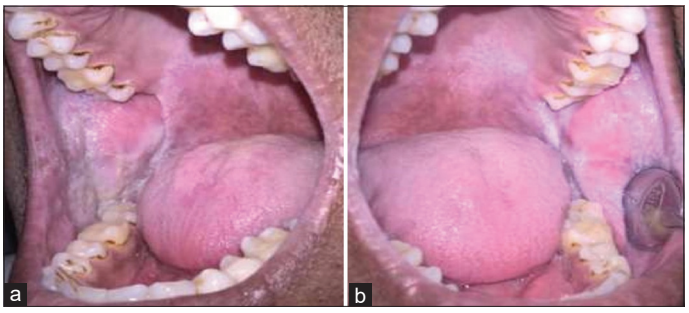

Figure 1: Intraoral clinical picture of white sponge nevus showing velvety white plaques

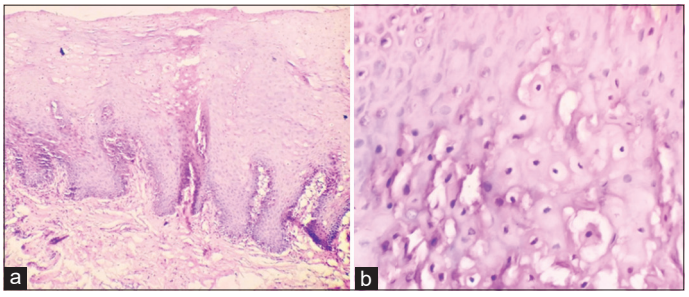

Figure 2: H and E stained section showing (a) hyperkeratosis, acanthosis, and intracytoplasmic vacuolation (×10 view); (b) perinuclear keratin condensation (×40 view)

DISCUSSION

WSN is a rare autosomal dominant disorder with variable penetrance and having a prevalence rate of about 1 in 200,000 [6]. The pathogenesis of WSN is attributed to the genetic mutation of *CK 4* and *CK13* genes [7]. Point mutation of 2B domain of *CK 4 gene* results in disruption and instability of keratin tonofilament [8]. Mutation in helix-binding motif (HBM) is considered as a hotspot in keratin disorder. This genetically altered HBM, which is reported to contribute in end-to-end linking of keratin subunit, causes cell fragility, cytolysis, and ultimately hyperkeratosis as compensatory overgrowth, thereby resulting in clinical manifestation of the lesion. Besides that, a relation between human papillomavirus type 16 with WSN was reported in a few literatures [3].

Based on the clinical appearance of the lesion, a wide range of differential diagnoses is possible, namely, fungal infection (candidiasis), leukoplakia, dyskeratosis congenita, hereditary benign intraepithelial dyskeratosis, pachyonychia congenita, lichen planus, and traumatic keratosis. Among the above-mentioned differential diagnoses, leukoplakia and lichen planus are the most important. Leukoplakia was excluded because the patient had the lesion since childhood which is unlikely in leukoplakia, the presence of positive family history is also uncommon in leukoplakia, an absence of oral deleterious habits is against the diagnosis of leukoplakia, and perinuclear condensation of keratin cannot be seen in the histopathology of leukoplakia.

Diagnosis of lichen planus was also discarded because the patient had the lesion since childhood which is unlikely in lichen planus, clinically, there was an absence of Wickham's striae and complaint of a burning sensation which are important features of lichen planus, unique histopathological features of lichen planus such as saw tooth rete pegs, basal cell degeneration, and juxtaepithelial band of inflammatory cells are absent in this case, and perinuclear condensation of keratin cannot be seen in the histopathology of lichen planus.

A biopsy is of utmost importance to confirm the diagnosis. WSN is an asymptomatic and benign lesion; hence, emphasis should be given to the early and correct diagnosis of these disorders to avoid unnecessary treatment.

Regarding the treatment of WSN, no definite pharmacological therapy is available till date. As it is a benign, asymptomatic, and

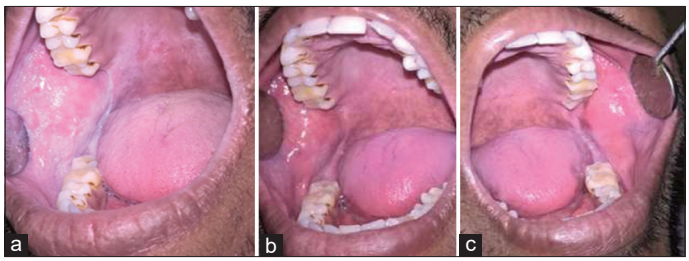

Figure 3: Clinical photo after (a) 5 days and (b) 6 months of treatment with amoxicillin suspension

harmless condition without having any potential for malignant conversion, explanation and reassurance may be all that is required. However, many trials with various drugs such as antihistaminics, antibiotics, beta-carotene, retinoic acid, and tetracycline mouth rinses have been done to reduce the clinical manifestation of the disease [9]. Surgical resection and laser ablation were also tried as a therapeutic measure, but recurrence within 2 years was noted [10].

In the present patient, we had used amoxicillin suspension (250 mg/5 ml) topically. The patient was asked to take 5 ml of the said suspension and sluice for 5 min twice daily for 1 month. After sluicing, the patient was instructed to spit out the suspension and not to take any solid or liquid food immediately. Partial healing was noted after 5 days of treatment followed by complete resolution of the lesion after 1 month. Hence, the treatment was discontinued after 1 month.

Regular follow-up of the patient revealed complete remission of the lesion without recurrence even after 6 months. As prolonged systemic use of tetracycline and amoxicillin can lead to serious side effects such as diarrhea, alteration of normal gut microflora, hepatotoxicity, nephrotoxicity, and photosensitivity, so, topical use of amoxicillin suspension may be used as a treatment measure for WSN. The main advantages of such therapy are (1) non-invasive procedure, (2) systemic antibiotic-induced adverse effects can be avoided, (3) good patient compliance, and (4) cost effective. The uniqueness of this case report lies in the use of amoxicillin suspension toward the treatment of WSN.

Few reports of WSN have been published in the recent past. Sanjeeta *et al*. reported cases of WSN in a patient along with her father and brother [11]. Another report was published by Hegde *et al*. in 2017 [12]. In 2020, Bezerra *et al*. reported cases of WSN demonstrating it as a condition that is not always clinically suspected [13].

CONCLUSION

WSN, being a rare hereditary condition, lacks a definite treatment protocol. Although WSN is asymptomatic and benign, no treatment is needed. However, after repeated counseling, it often becomes difficult to alleviate patients' anxiety. Hence, we have tried a safe drug like amoxicillin in a much safer mode, that is, topical application to treat the lesion. We report this case to emphasize that amoxicillin suspension topical therapy may be used as a novel treatment measure with its unique advantages. However, further studies on more number of patients are needed to establish the use of topical amoxicillin suspension as a first-line drug toward the management of WSN.

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