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CASE REPORT

White sponge nevus in a 14-year-old female: case report with exfoliative cytology and oral biopsy findings

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Abstract:

White Sponge Nevus (WSN) is a rare autosomal dominant genodermatosis, affecting approximately 1 in 200,000 individuals. Clinically, WSN presents as asymptomatic, diffuse white plaques that are thickened and corrugated, with most lesions appearing in early childhood. Diagnosis of WSN is confirmed through microscopic examination following an oral biopsy. However, exfoliative cytology is also an effective diagnostic tool, offering a simple and non-invasive alternative that may be more acceptable for younger patients Herein, we report a case of a 14-year-old female presenting asymptomatic, bilateral, diffuse, non-removable white plaques with a corrugated surface on the buccal and alveolar mucosa. The clinical diagnosis was WSN, and both an incisional biopsy and exfoliative cytology were performed under local anesthesia. The cytological and histological features confirmed the diagnosis of WSN and the patient was oriented about the condition and scheduled for regular follow-up. Therefore, clinicians should consider using exfoliative cytology when assessing suspected cases of WSN.

Keywords: Oral mucosa; White lesions; White sponge nevus; Cytology.

INTRODUCTION

White Sponge Nevus (WSN) is a rare autosomal dominant genodermatosis, affecting approximately 1 in 200,000 individuals. The condition results from mutations in the KRT4 and KRT13 genes, which encode keratin-4 and keratin-13, respectively. These proteins are essential for the assembly of keratin filaments specific to mucosal tissues. WSN exhibits irregular penetrance and variable expressivity, even among family members, with some familial cases[1-4].

Clinically, WSN presents as asymptomatic, diffuse white plaques that are thickened and corrugated. These plaques do not disappear when the tissue is stretched and are primarily located on the oral mucosa. The condition shows no gender preference, with most lesions appearing in early childhood. Typically, WSN affects the buccal mucosa bilaterally, though less common sites such as the floor of the mouth, alveolar ridge, and lips can also be involved[2]. The lesions can resemble various other oral white lesions, including proliferative verrucous leukoplakia, lichen planus, frictional keratosis, and pseudomembranous candidiasis, among others[4]. Furthermore, lesions may extend to nasal, esophageal, rectal, or vaginal mucosa.

Statement of Clinical Significance
The white sponge nevus — a rare hereditary disease — although well described in the literature, still presents as a diagnostic challenge for many clinicians. Therefore, the present study illustrates two forms of diagnosis, through biopsy and exfoliative cytology, which will help in the diagnosis of this lesion.

The diagnosis of WSN is typically confirmed through histopathological examination of an oral biopsy, which commonly reveals pronounced hyperkeratosis and acanthosis. Cells within the spinous layer characteristically display clear cytoplasm, while superficial epithelial cells show perinuclear eosinophilic condensation — features considered hallmark findings of the condition. Nonetheless, exfoliative cytology also represents an effective diagnostic modality, capable of detecting perinuclear eosinophilic condensation and offering a non-invasive, well-tolerated alternative, particularly suitable for pediatric patients. Although it provides less detail regarding tissue architecture and lacks the ability

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to definitively exclude dysplasia, exfoliative cytology remains a valuable adjunct — especially in scenarios where biopsy is contraindicated or not feasible.

In this report, we present a case of WSN diagnosed in a 14-year-old female using both biopsy and exfoliative cytology techniques, highlighting the features of each exam.

CASE REPORT

A 14-year-old female was referred to an oral and maxillofacial surgeon for evaluation of a class III dentofacial deformity. Her medical history was non-contributory, and she reported no use of tobacco or alcohol. The extraoral clinical examination showed no abnormalities. Intraoral examination showed asymptomatic, bilateral, diffuse, non-removable white plaques with a corrugated surface on the buccal and alveolar mucosa (Figure 1A-C). Familial history did not reveal any other affected member, and the patient's mother stated that she had noticed similar lesions on the patient's vaginal mucosa since she was 11 years old.

The clinical differential diagnosis included WSN, frictional keratosis, proliferative verrucous leukoplakia, and other genodermatosis. In order to establish the diagnosis, both exfoliative cytology and incisional biopsy under local anesthesia were performed. Microscopic analysis of the surgical specimen showed hyperkeratosis and marked acanthosis, with cells in the spinous layer exhibiting clear cytoplasm, as well as some cells in the superficial layer displaying perinuclear eosinophilic condensation (Figure 2A–D). Cytopathological evaluation

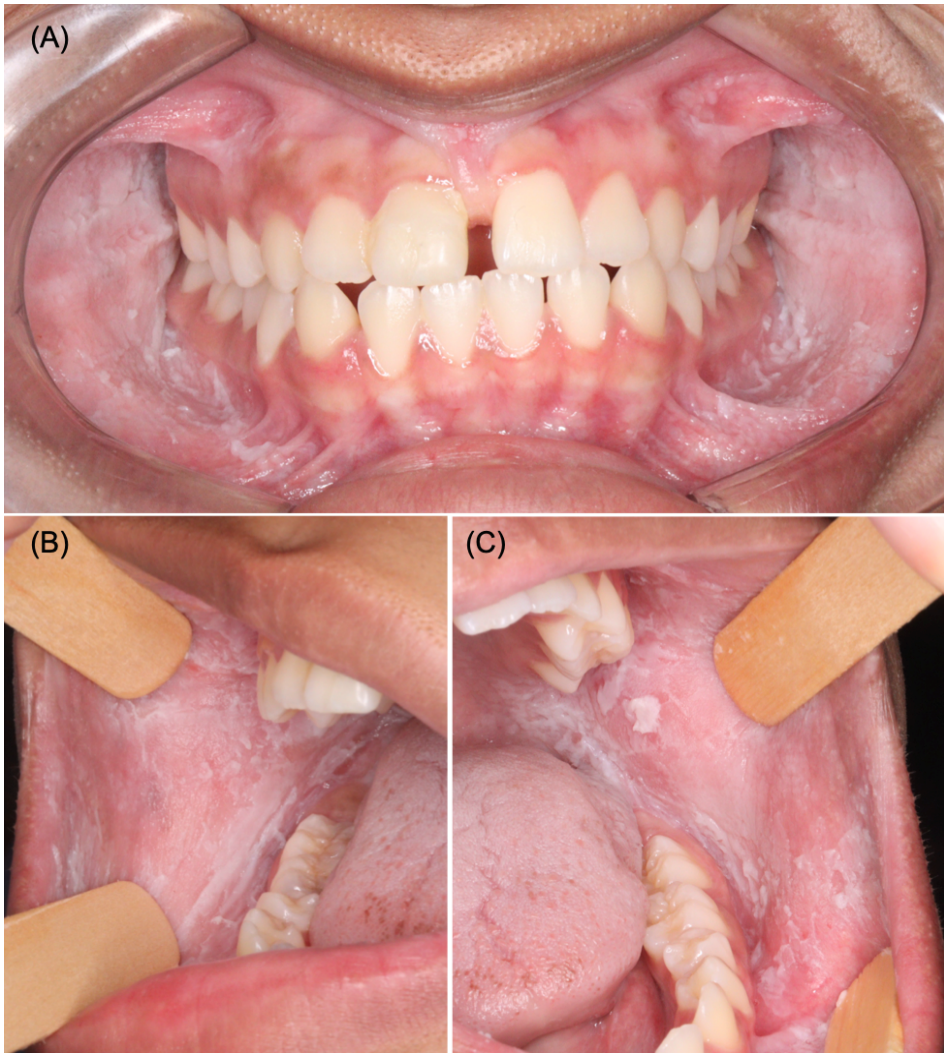

Figure 1. White Sponge Nevus clinical features. A-C, bilateral, diffuse, non-removable white plaques with a corrugated surface were observed on the buccal and alveolar mucosa.

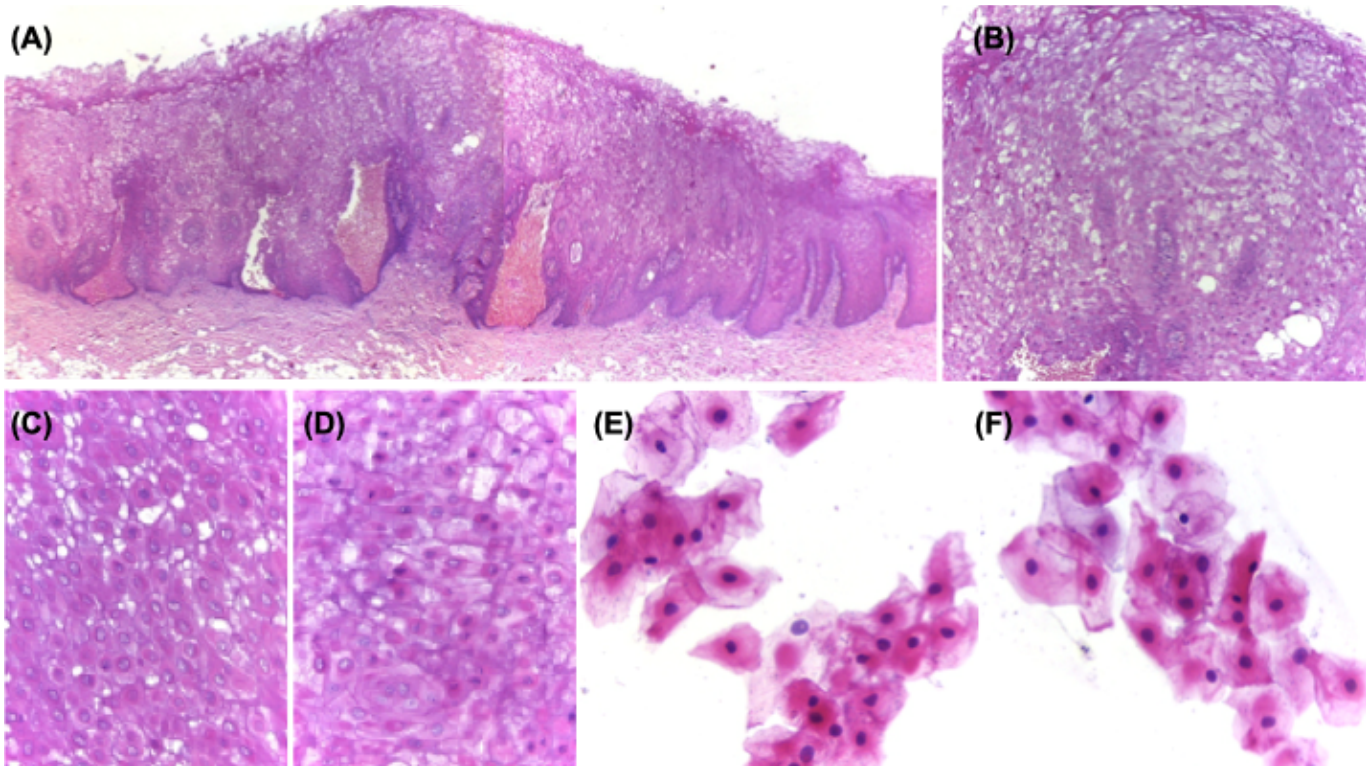

Figure 2. Histological and cytological aspects of White Sponge Nevus. **A-B.** Acanthosis and hyperparakeratosis on the stratified squamous epithelium (hematoxylin-eosin, original magnification **A** 40x, **B** 100x). **C-D**. Perinuclear eosinophilic condensation is also observed (hematoxylin-eosin, original magnification **C** and **D** 400x). **E-F**. Squamous cells with no nuclear atypia and perinuclear eosinophilic condensation (hematoxylin-eosin, original magnification **E** and **F** 400x).

revealed no cellular/nuclear atypia and the presence of a perinuclear eosinophilic condensation on several cells (Figure 2E–F). Both histology and cytology confirmed the diagnosis of WSN. The patient and her family were informed about the nature of the condition, and, as no additional treatment was deemed necessary, she was placed under routine clinical follow-up. Additionally, she was referred to a gynecologist for further evaluation of the associated vaginal lesions.

DISCUSSION

WSN is an autosomal-inherited genodermatosis, mentioned for the first time by Hide in 1909. However, it was Canon[1] in 1935 that defined WSN as a rare, benign genetic condition characterized by the appearance of white, spongy lesions primarily on the oral mucosa. The disease shows no gender predilection and most patients observe the first signs of the condition during childhood[5]. Clinically, affected individuals commonly exhibit soft or corrugated, white or gray plaques distributed throughout the oral cavity, with the buccal and labial mucosa representing the most frequently involved sites. Palatal involvement, however, is rarely observed. Bilateral manifestation on the buccal mucosa is a characteristic finding in the majority of cases[1-10]. Furthermore, mucous membranes from other sites such as the upper airway and vaginal tract may be affected[2-6]. Therefore, the present case is consistent with previously reported cases in the literature with regard to its clinical presentation, anatomical location, and age of onset.

The lesions are usually asymptomatic and do not require any therapy, as observed in the present case. However, the associated alterations in mucosal texture and oral aesthetics often lead to patient dissatisfaction. A range of therapeutic modalities has been proposed, including vitamin-based interventions (e.g., β-carotene and topical retinoic acid), antihistamines, tetracycline mouth rinses, systemic antibiotics such as penicillin and azithromycin, as well as laser ablation. Despite a high likelihood of recurrence across these approaches, both partial and complete clinical responses have been documented — particularly in cases managed with topical tetracyclines[2,6,7].

Accurate diagnosis of WSN through histopathological analysis is indispensable for distinguishing it from other lesions that may present with greater

severity and even premalignant potential, as well as from other genodermatoses. These include conditions such as candidiasis, hereditary benign epithelial dyskeratosis, lichen planus, lichenoid reactions, pemphigus, pemphigoid, lupus erythematosus, and verrucous proliferative leukoplakia[2,3,5-11]. For example, pseudomembranous candidiasis is characterized by diffuse, easily scrapable whitish plaques that respond favorably to antifungal treatment[2]. Hereditary benign epithelial dyskeratosis is less common than WSN and is often associated with bilateral conjunctival plaques[2,4]. Moreover, lichen planus frequently shows a striated pattern; pemphigus, pemphigoid, and lupus erythematosus typically involve cutaneous manifestations[2-4]; and lichenoid reactions are associated to an offending agent[2]. Finally, proliferative verrucous leukoplakia is classified as a potentially malignant disorder, typically diagnosed from the fifth decade of life onward[4]. Although these clinical distinctions are useful in differentiating WSN from other white lesions, a definitive diagnosis can only be established through microscopic evaluation. Therefore, exfoliative cytology represents an interesting non-invasive diagnostic method for WSN, characteristically demonstrating perinuclear eosinophilic condensation[9]. When combined with the lesion's onset and clinical presentation, this cytological finding is considered pathognomonic for the condition.

Biopsy remains the most accurate diagnostic tool for WSN, as it enables detailed assessment of the characteristic tissue architecture of the condition[1-10]. Histologically, it reveals pronounced epithelial hyperplasia accompanied by hyperparakeratosis, along with focal accumulation of keratohyalin granules within the suprabasal epithelial cells[2]. However, it is an invasive procedure and may be contraindicated in certain cases — such as in systemically compromised patients, individuals with high anxiety levels, or those at the extremes of age. Histopathological examination in the present case revealed the classical features of WSN, as previously described[2-9]. Additionally, exfoliative cytology was performed, yielding the same diagnosis. As a low-cost, minimally invasive, and accurate approach, exfoliative cytology microscopically shows perinuclear eosinophilic condensation and has proved beneficial, particularly for younger patients who may harbor anxieties regarding oral biopsy or for those whom such procedures are contraindicated[9]. Recent advancements in cytopathology in the context of oral medicine have highlighted its usefulness in oral cancer screening and the diagnosis of various oral conditions, including WSN[12]. Other non-invasive diagnostic modalities for WSN involve genetic analysis to identify mutations in the KRT13 and KRT4 genes[10]. However, these genetic investigations can be costly and are often not readily accessible, particularly within public health systems — as was the case in the present report.

CONCLUSION

WSN is a rare genetic disorder that primarily affects the oral mucosa as well as other mucous membranes. Its clinical presentation may closely resemble other whitish lesions in the oral cavity, which inherently increases the risk of misdiagnosis. Thus, the role of microscopic examination becomes indispensable in ensuring diagnostic accuracy. Moreover, since some patients may be uneasy or unsuitable for an oral biopsy, exfoliative cytology is a reliable, cost-effective, simple, and non-invasive diagnostic alternative. Therefore, clinicians should consider using exfoliative cytology when assessing suspected cases of WSN.

AUTHORS' CONTRIBUTIONS

BTGR: data curation, formal analysis, writing – review & editing. **FRP:** data curation, investigation, writing – original draft, writing – review & editing. **TCRBS:** data curation, investigation, writing – original draft, writing – review & editing. **HMS:** data curation, writing – original draft, writing – review & editing.

CONFLICT OF INTEREST STATEMENT

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Ethics approval: Data from the patients here included were treated anonymously and a statement of informed consent was signed by all patients allowing the use of their dental records.

REFERENCES

1. Cannon AB. White sponge nevus of the mucosa (nevus spongiosus albus mucosa). Arch Derm Syphilol. 1935;31(3):365-70. https://doi.org/10.1001/archderm.1935.01460210076008
2. Bezerra KT, Leite TC, Roza ALOC, Araújo R, Israel MS, Canedo NHS, et al. White sponge nevus: a condition not always

clinically suspected. J Cutan Pathol. 2020;47(1):22-6. https://doi.org/10.1111/cup.13581
3. Zhang J, Quan J, Ren Y, Chen M, Yang J, Zhang X. Keratin 4 regulates the development of human white sponge nevus. J Oral Pathol Med. 2018;47(6):598-605. https://doi.org/10.1111/jop.12728
4. Kürklü E, Öztürk □, Cassidy AJ, Ak G, Koray M, Çefle K, et al. Clinical features and molecular genetic analysis in a Turkish family with oral white sponge nevus. Med Oral Patol Oral Cir Bucal. 2018;23(2):e144-e150. https://doi.org/10.4317/medoral.21437
5. Sanjeeta N, Nandini DB, Premlata T, Banerjee S. White sponge nevus: report of three cases in a single family. J Oral Maxillofac Pathol. 2016;20(2):300-3. https://doi.org/10.4103/0973-029X.185915
6. Martelli Jr H, Pereira SM, Rocha TM, Santos PLAN, Paula AMB, Bonan PRF. White sponge nevus: report of a three-generation family. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2007;103(1):43-7. https://doi.org/10.1016/j.tripleo.2006.05.029
7. Richard G, De Laurenzi V, Didona B, Bale SJ, Compton JG. Keratin 13 point mutation underlies the hereditary mucosal epithelial disorder white sponge nevus. Nat Genet. 1995;11(4):453-5. https://doi.org/10.1038/ng1295-453
8. Rugg EL, McLean WH, Allison WE, Lunny DP, Macleod RI, Felix DH, et al. A mutation in the mucosal keratin K4 is associated with oral white sponge nevus. Nat Genet. 1995;11(4):450-2. https://doi.org/10.1038/ng1295-450
9. Lajolo C, Cafiero C, Stigliano E, Grippaudo FR, Chiurazzi P, Grippaudo C. Exfoliative cytology and genetic analysis for a non-invasive approach to the diagnosis of white sponge nevus: case series. Bioengineering (Basel). 2023;23;10(2):154. https://doi.org/10.3390/bioengineering10020154
10. Westin M, Rekabdar E, Blomstrand L, Klintberg P, Jontell M, Robledo-Sierra J. Mutations in the genes for keratin-4 and keratin-13 in Swedish patients with white sponge nevus. J Oral Pathol Med. 2018;47(2):152-7. https://doi.org/10.1111/jop.12652
11. Akeel S, AlFarabi S, Binsaad S, Almazroa S, Binmadi N. A case report on familial white sponge nevus in Saudi Arabia. Cureus. 2022;18;14(12):e32674. https://doi.org/10.7759/cureus.32674
12. Perez-de-Oliveira ME, Wagner VP, do Amaral-Silva GK, Leite AA, Lopes MA, Santos-Silva AR, et al. An audit of cytopathology in the oral and maxillofacial region: 18 years of experience. Cytopathology. 2020;31(6):555-63. https://doi.org/10.1111/cyt.12891