

Multifocal Epithelial Hyperplasia: A Case Report and Review of Literature

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INTRODUCTION.

Multifocal epithelial hyperplasia (MEH) is considered as a rare, benign, contagious condition of the oral mucosa commonly found among young individuals.¹ It was formally known as focal epithelial hyperplasia and other synonyms include Heck's disease or multifocal papilloma.

It was first described by Heck's in 1965 from the observation of isolated or multiple soft papular or nodular eruptions in the oral cavity hence, the name

ABSTRACT

Objective: Multifocal epithelial hyperplasia (MEH) or Heck's disease is a rare benign disorder caused by Human Papilloma Virus (HPV). It is characterized by multiple soft well demarcated nodules of the oral mucosa. They are commonly seen in buccal, labial and lingual mucosa. However, tonsillar and gingival lesions have also been reported. A detailed clinical history, examination and histopathological review is needed to arrive at a diagnosis. The aim of this report is to show the successful treatment of MEH using Salicylic acid and Zinc supplement.

Case Report. Two cases of a 5 year old Hausa girl and 7-year-old Hausa boy with a widespread oral lesion of 8 months and 1-year duration respectively. The diagnosis of the case reported were based on clinical evaluation and histopathological investigation. The presence of multiple painless pink nodules and papules on the lips, buccal mucosa and the gingiva as well as histological presence of koilocytes and mitosis seen on hematoxylin and eosin slide led to the diagnosis of Multifocal Epithelial Hyperplasia.

Conclusion: We reported 2 cases of MEH, a rare benign oral mucosa lesion in a 5-year-old Hausa female and a 7 year old Hausa male in North-West Nigeria who presented with 8 months and 1-year history of widespread oral mucosa lesion respectively and was treated successfully using salicylic acid and zinc supplement.

Keywords: Multifocal Epithelial Hyperplasia, Salicylic acid, Zinc supplement.

Heck's disease². Subsequently, Witkop et al.³ reported similar diagnosis in Navajo Xavante Indian and Alaska Eskimo children³. It was initially reported mostly among Native Americans, Eskimos and South Africans but now wider worldwide reports are seen including in Nigeria⁴, Polynesia⁵, Puerto Rico⁶, in an adult female Caucasian⁷, and in small cultural groups in Bolivia⁸, Paraguay, Peru⁹, Colombia¹⁰ and Mexico¹¹ and other ethnic groups. Incidence is asymmetrically distributed worldwide. No prevalence has been given

for this disease condition. It however occurs between a wide age range 3-69 years with the disease occurring the most in the first decade of life¹². Some studies found no gender difference while a study by Ledesma-Montes et al.¹³ reported a female preponderance.

Low socioeconomic status (SES), poverty and poor oral hygiene has been strongly linked with the disease¹². Roman and Sedano¹⁴ reported a correlation between low SES and Heck's disease and did not find a single case among children in high SES group schools studied. Moreover, a systematic review by Bascones-Martinez¹² showed a clearly skewed predominance among low SES.

The aetiology of Heck's disease has been strongly linked to Human Papilloma Virus (HPV) presence. HPV infection is the most popular sexually transmitted disease, although it is usually cured by the immune system.¹⁵ HPV is from the *papilloma viridae* family and it displays tropism towards epithelial basal layers which house the mature epithelial basal stem cells responsible for refilling the epithelium with daughter cells.¹⁶

Pfiser¹⁷ was the first to relate the disease to HPV-13 subtype after examining a sample in a Turkish patient, However, samples from 10 individual scattered around the world showed a correlation with HPV -32¹² while other studies identify association with HPV-1, HPV-6, HPV-11 and HPV-16.¹⁸⁻²¹

The familiar nature of the disease has been reported in literature, Gomez et al¹⁰ in 1969 first highlighted the role of genetics involvement. This familial tendency may be related to either genetic susceptibility or HPV transmission between family members²²

The role of immunosuppression has been suggested as an aetiology in the development of Heck's disease. Galanakis *et al.*²³ reported a case of young girl who was HIV positive and Marvan *et al.*¹⁵ concluded that there was correlation between immune state and HPV infection. Suppression of the immune system leaves the patient vulnerable to opportunistic infections, including HPV infections.²⁴

Heck's primarily occur in children and many of the cases seen in Nigeria has been exclusively seen in children with an average age of 5.8years and a slight male predilection (M: F, 1.7:1)²⁵ but no gender predilection was recorded in another study.⁴ The condition present as occurrences of multiple unique whitish pink to normal mucosa color, small papules or nodules usually about 5-10mm sometimes forming a cobblestone appearance in the oral cavity⁴.

The site of presentation is usually on the buccal and labial mucosa but can be found in any other site in the oral cavity. They coalesce to form a larger lesion sometimes. The lower lip has been found to be the most affected site^{1, 4, 25} biopsy pathological report using hematoxylin and eosin-stained slides showed the presence of squamous, parakeratinized epithelium with marked acanthosis showing long and deep rete ridges.¹⁵ Immunohistochemistry showed basal epithelial cells having positivity in few of the reviewed cases, spinous layer showed wide variation in positivity, and in the superficial layers it varied from slight to strong.²⁶

Treatment of Heck's disease has evolved over time. The use of surgery has been the mainstay of treatment before the introduction of cryotherapy, electrocautery, CO₂ laser therapy, chemical agents (such as nitric acid, podophylline). Immunosuppressant like interferon, 5% Salicylic acid and Zinc sulfate tablet are recent addition to the treatment option which is the treatment we are reporting in this case report.¹⁷ On the other hand, patients with across the board sores are up-and-comers for foundational treatments like aminopterin, acitretin, etretinate, levamisole, interferon, and methotrexate²⁷

This case report is aimed at reporting the successful management of a rare disease (Heck's disease) in two patients using topical Salicylic acid and Zinc supplementation.

Case Report

First case Report:

A 5-year-old Hausa female from North West Nigeria presented to the Oral Medicine clinic of Ahmadu Bello University Teaching Hospital (ABUTH), Zaria, Kaduna State Nigeria, with widespread multiple oral mucosa lesion of 8 months duration. The lesions were painless, soft in consistency spreading through the upper lip, buccal mucosa, lower lip and the gingiva (Figure1). No similar lesions were seen in any part of her body. Past medical and dental history was not contributory. Extra oral examination reveals no abnormality, however intra oral examination reveals widespread multiple soft pinkish papules and nodules located in upper lip, buccal mucosa, lower lip and the gingiva. The following investigations were done: Retroviral Screening which came out negative; full blood count with normal range; and punch biopsy of the lesion was sent for histology which reveals keratinized squamous epithelium exhibiting marked acanthosis with fairly sequential maturation, occasional koilocyte and some structure akin to

Multifocal Epithelial Hyperplasia

mitotic figures (mitosoid). Based on the clinical evaluation and histological report, a diagnosis of Multifocal Epithelial Hyperplasia (Heck's Disease) was made.

Parents of patient were counseled and reassured, and the following treatment was instituted-topical application of 5% Salicylic acid and Zinc sulphate

tablet 10mg daily for 2 weeks. Patient was reevaluated after two weeks, and topical application of 5% Salicylic acid was continue for another 2 weeks. At the next visit all lesions have completely disappeared (Figure 2a and 2b). Patient has been followed up for 3 months with no relapse.



Figure 1. Patient at presentation.



Figure 2a: Patient following treatment with salicylic and zinc supplement (upper view)



Figure 2b: Patient following treatment with salicylic acid and zinc supplement (lower view)

Second Case Report

The second patient is a 7-year-old Hausa male patient who presented to the same clinic on account

of a widespread oral mucosa lesion of a year duration. The lesions were painless, soft in consistency spreading through the upper lip, buccal mucosa, lower lip and the gingiva (Figure 3). No similar lesions were seen in any part of her body however, family history revealed a similar lesion in his siblings aged 8 and 10 years of same sex. The lesions were noticed at the same time but his siblings lesion resolve over time and his was persistent hence necessitating presentation at the clinic. Past medical and dental history was not significant. Extra oral examination reveals no abnormality, however intra oral examination reveals widespread multiple soft



Figure 3. Patient at presentation

DISCUSSION

Multifocal epithelial hyperplasia (Heck's disease) is a rare, benign, familial disorder caused by the Human Papilloma Virus subtype 13 and 32²⁸. There is no sex predilection. It usually affects children as reported in this case report. It is commonly seen in the buccal, labial, lingual mucosa as seen in this report. However, tonsillar and gingival areas have also been reported²⁹.

Diagnosis of MEH is usually based on clinical, histological and cytological features of the lesions. This can also be supported by immunohistochemistry assay, insitu hybridization, southern blot and polymerase chain reaction (PCR)⁴. The histological features of MEH include, epidermal acanthosis, parakeratosis, thickening and extension of the rete ridges, koilocytes and characteristic mitosoid^{30,31} as seen in the histological report of our

pinkish papules and nodules. The following investigations were done- Retroviral Screening which came out negative and full blood count with normal range. Parents of patient were counseled and reassured, and the following treatment was instituted topical application of 5% Salicylic acid and Zinc sulphate tablet 10mg daily for 2 weeks. Patient was reevaluated after two weeks and topical application of 5% Salicylic acid was continued for another 2 weeks. At the next visit all lesions has completely disappeared (Figure 4). Patient has been followed up for 2 months with no relapse.

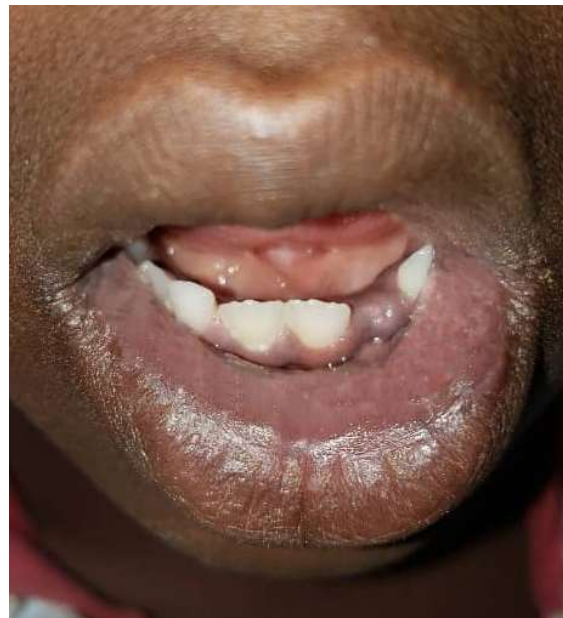


Figure 4: Patient following treatment with Salicylic acid and zinc supplement.

first case. Studies have also shown that MEH have genetic and familial predisposition^{30,31}. This was seen in our second case, where 3 siblings had the same lesion at the same time.

MEH, may be associated with immunodeficiency, suppressed immunity and malnutrition. Both cases showed no evidences of immunosuppression and malnutrition²⁸ as there retroviral screening were negative and full blood count values were within normal physiological range.

They are two major approaches to the management of MEH i.e. the medical (topical or systemic) or a surgical (destructive method) or a combination of both³².

As regards to the medical management, salicylic acid is a first line therapy and has reported a cure rate of 70 -80%.³² This was used in the management of our patients. Different studies have reported the

Multifocal Epithelial Hyperplasia

successful management of MEH using imiquimoid³³ and β interferon.³⁴ Other topical agents such as podophyllum, podophylin, trichloroacetic acid, 5-fluorouracil are effective in treating cutaneous wart, but a high evidence of being toxic and therefore not recommended for oral use.³¹

Zinc supplementation has been used to treat recalcitrant oral wart³⁵, this was added to our patient treatment in form of zinc sulphate 10mg daily for 2 weeks. Cryotherapy using liquid nitrogen (-196°C) is often used as first line surgical technique for wart management. It is equally as effective as topical salicylic acid therapy.^{36,37} Other surgical techniques include electrocautery and laser therapy.³¹

CONCLUSION

We report 2 cases of MEH, managed successfully with salicylic acid and zinc supplement on follow up with no relapse. This case report showed a non-invasive method of management of MEH which was successful.

Consent for Publication

Informed consent was obtained from the patients' parents for publication of this case report and accompanying images.

Source of Support

Nil.

Conflict of Interest

None declared.

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