

HAIM MUNK SYNDROME: TWO SIBLINGS OF SOUTHERN PAKISTAN TREATED WITH ACITRETIN

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ABSTRACT

Haim Munk Syndrome (HMS) is an extremely rare autosomal recessive disorder with the allelic mutation of exon 6 codon in cathepsin C gene. It is characterized clinically by palmo-plantar keratoderma (PPK), aggressive early onset of periodontitis, onychogryphosis, arachnodactyly, acro-osteolysis and pes planus. This study presents two cases of the same family with HMS having almost all the cardinal features of this rare disorder. Both the siblings were treated with acitretin, co-trimoxazole and topical keratolytics and followed up for 6 months.

Key words: Aggressive periodontitis; Palmo-plantar keratoderma, Papillon Lefeuvre syndrome

INTRODUCTION

In 1965, Dr Haim (Dermatologist) and Dr Munk (Radiologist) reported a rare congenital type of genodermatosis called Cochin Jewish disorder in four siblings of a Jewish religious isolate from Cochin India on the Malabar Coast, later known as Haim Munk Syndrome.^{1,2}

Initially some researchers^{3,4} considered HMS a variant of Papillon Lefeuvre syndrome (PLS) on the basis of common clinical features such as palmo-plantar keratoderma (abnormal hyperkeratosis of the palms and soles) and aggressive periodontitis.⁵

Although both HMS and PLS share the common pathogenomic features of PPK and severe periodontitis^{6,7} and are allelic variants of cathepsin C gene mutations^{6,8}, a number of additional findings are reported in HMS including onychogryphosis (curved nails), arachnodactyly (spider fingers/elongated and slender shaped fingers and toes), acro-osteolysis (tapered pointed distal phalangeal ends due to osteolysis), pes planus (flat foot), occasionally hyperkeratotic psoriasisiform

lesions with an erythematous background on the extensor surfaces of elbows and knees^{9,10,11,12} and rarely destructive arthritis of the wrists and shoulder joints.¹³ Similarly among other differences, gingivitis is more severe in HMS than PLS and periodontitis is a bit less aggressive in HMS than PLS, but still periodontitis in HMS is sufficient enough to cause early exfoliation of primary dentition at the age of 4 and secondary dentition at the age of 14.

Parental consanguinity is characteristic of many cases of both disorders.¹⁰ The etiological factor as reported by Hart et al is the allelic mutations in the lysosomal protease cathepsin C (CTSC) gene located on the chromosome 11q14.1-q143 resulting in phagocytic particularly macrophage dysfunction thus reducing individual's immunity towards micro-organisms residing/flourishing in periodontal pockets causing aggressive periodontitis. Once all the teeth are exfoliated the process of gingivitis and bone loss in the form of periodontitis stops. The cathepsin C gene is expressed in the epithelial regions such as palms, soles, knees, elbows and keratinized oral gingiva.⁶

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This case report illustrates 2 siblings (11 years child and 18 years adult) of a Pakistani Muslim family with HMS whose severe palmo-plantar keratoderma and periodontal disease responded well to treatment with acitretin, co-trimoxazole and topical keratolytics.

CASE REPORT

An 11 years old boy reported to the Oral Medicine Department of Fatima Memorial Hospital College of Dentistry, Lahore, Pakistan complaining of loose teeth. The patient also complained of peeling of the skin, white scales and cuts on his hands and feet. Family history revealed that his elder brother (18 years old) had the same problem who was then called after 2 days for thorough history, examination and investigations. Parental consanguinity was found as the parents were first cousins and the family had been strictly following the "cousin marriage tradition" for long.

Proband (11 years old)

Intra oral examination of the younger sibling revealed aggressive periodontitis and moderate gingivitis with gingival recession (Fig 1). The upper incisors had grade III mobility with bone level only at the apical most portions of the incisors (Fig 2). The upper remaining teeth excluding the 1st permanent molars had grade II mobility. The maxillary and mandibular permanent 1st molars and mandibular permanent incisors were already exfoliated at the time of patient's initial acquaintance (Fig 2). His entire primary dentition also had shown premature shedding as a result of periodontitis at the age of 4 years.

Extra oral examination revealed abnormality of the skin in the form of keratoderma on the palmo plantar aspects of hands and feet (Fig 3), keratosis of the dorsal surface of hands and feet (Fig 4) and erythematous psoriasisform keratotic lesions on the extensor surfaces of both elbows and knees (Fig 5), both of which appeared first when he was 2 years old; nail abnormalities in the form of onychogryphosis (curved nails) (Fig 6) and transverse grooves (Fig 7); finger abnormalities in the form of arachnodactyly (elongated fingers/ spider fingers). Other features such as acro-osteolysis and pes planus were absent in proband but present in the elder sibling.

Sibling (18 years old)

Intra oral examination of the sibling revealed only 3rd molars in the oral cavity (Fig 8). The rest of the teeth were exfoliated when he was 15 years old. As already described that once all or almost all of the teeth are exfoliated, the process of gingivitis and periodontitis stops, hence no gingival or periodontal inflammation was found in the sibling. He was using a denture (U/L) when seen during his first visit. Extra oral examination revealed similar features as that of his younger brother in the form of palmo-plantar keratoderma (PPK) (Fig 9), keratosis of the dorsal surface of hands and feet (Fig 10) and erythematous keratotic psoriasisform lesions on the extensor surfaces of both elbows and knees (Fig 11) (The patient started developing the above mentioned extra oral features at the age of 2-3 years), onychogryphosis and transverse grooving of the nails (Fig 12), arachnodactyly (Fig 13) plus additional features of acro-osteolysis (Fig 14) and pes planus. Pes planus though present was not distinctive.

The patients parents were unaffected and no abnormal signs were present on physical examination.

Both patients were treated with 25mg of acitretin (Cap Neotret 25 mg) orally taken as a bolus dose in the morning once every 3rd day in order to prevent its side effects which includes osteoporosis, periosteal plucking and premature epiphyseal closure; Co-trimoxazole (200:40) (Septrozone suspension 450ml) orally 3 times daily; Chlorhexidine gluconate + Benzylamine HCL mouth wash

(Enzichlor) 2 times daily for 8 weeks; topical keratolytics such as isotretinoin (Isotrex gel) and salicylic acid (Betasalic ointment 15gm) 2-3 times daily and additional methods such as dietary modifications by encouraging patients to use carrots, sweet potatoes, pumpkin and spinach more in their diet as these are rich in natural retinoids (b-carotene). Patients were given extensive oral hygiene instructions including proper methods of tooth brushing. They were asked to use Dove soap as it is more moisturizing and use petroleum jelly (Vaseline) on their skin quite often.

The proband's maxillary incisors were extracted as they were very mobile and there were negligible chances of their survival. Gingival and sub-gingival ultra sonic scaling was done in both the patients and was planned to be repeated every 6 months.



Fig 1: Shows aggressive periodontitis and gingival recession

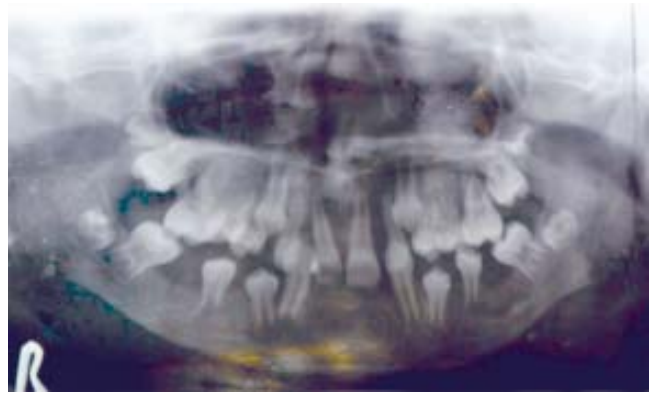


Fig 2: Bone present only at the apical portions of most of the teeth



Fig 3: Keratoderma on the palmpoantar aspects of hands and feet



Fig 4: Keratosis of the dorsal surface of hands and feet

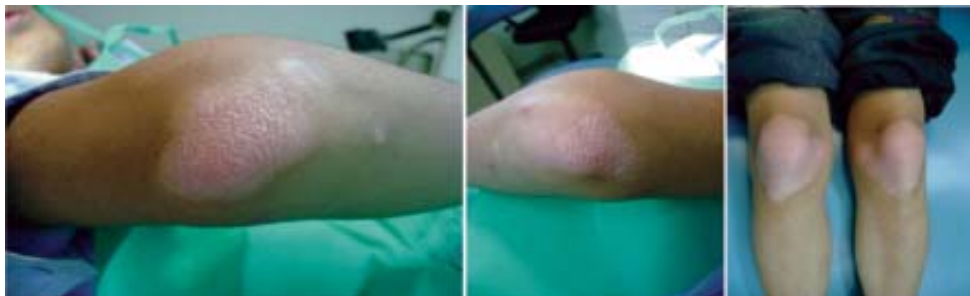


Fig 5: Erythematous psoriasisiform keratotic lesions on the extensor surface of both elbows and knees



Fig 6: Nails abnormalities in the form of curved nails (onychogryphosis)



Fig 7: Nails abnormalities in the form of transverse grooves Sibling (18 years old)

A follow up was taken after 2 months that showed dramatic improvements (shown in the comparison of



Fig 8: Only third molars present

pre-op and post-op pictures). The periodontitis of the proband was diminished and neither of the teeth had any mobility in them. There was a mild sign of localized gingivitis. Upper and lower partial dentures were being made for the proband with no clasps in the upper denture (retention was obtained by using deep undercuts-well developed labial flange) and a few clasps in the lower denture keeping in mind the equal distribution of load (As unequal non-uniform stresses would have made the teeth mobile again). There was marked regression of the palmo-plantar keratoderma and erythematous psoriasisiform keratotic lesions in both siblings. Both the patients were followed on the same maintenance dose for the next 4 months and reviewed 2 monthly and were planned to be followed for at least 5 years with 6 monthly follow up visits. During these follow-ups it was planned to under go 6 monthly routine investigations including complete blood count (CBC), liver function tests (LFT's), CD4 count, serum electrolytes and radiographic investigations including OPG, hand wrist radiographs and yearly DEXA scans.

TABLE 1: COMPARISON OF FEATURES BETWEEN THE TWO SIBLINGS

	Gingi- vitis	Aggres- sive perio- dontitis	PPK	Psorisi- form lesions	Onycho- grypho- sis	Arach- noda- ctyly	Radio- graphic evalua- tion of arachno- dactyly	Acro- osteo- sis	Pes planus
Proband 11 years old	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No
Sibling 18 years old	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes



Fig 9: Shows palmo-planter keratoderma (PPK)



Fig 10: Keratosis of the dorsal surface of the hands and feet



Fig 11: Erythematous keratotic psoriasisiform lesions on the extensor surface of both elbows and knees



Fig 12: Transverse grooving and curving of the nails



Fig 13: Arachnodactyly



Fig 14: Acro-osteolysis plus additional feature of arachnodactyly

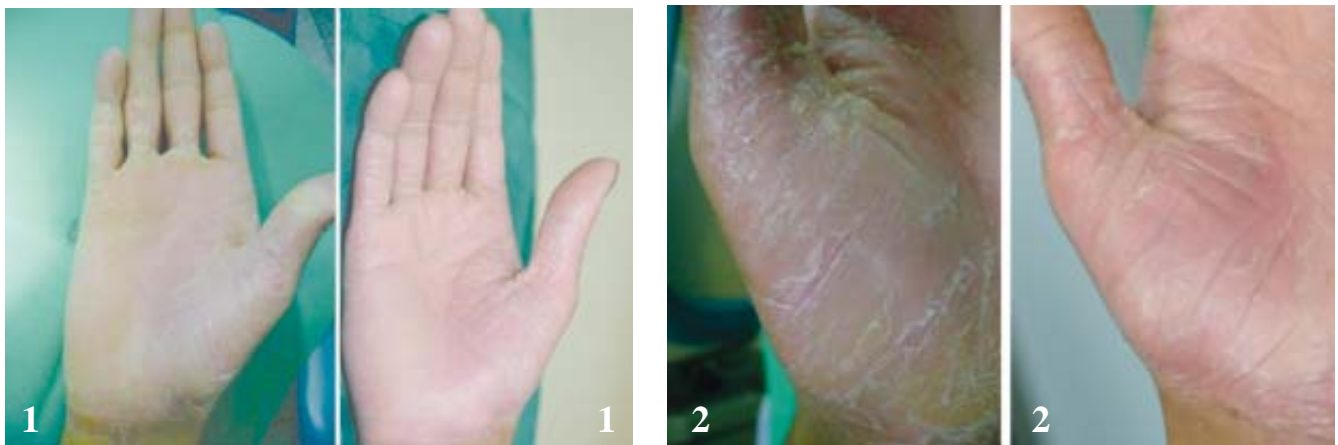
Comparison of (Pre-op and Post-op) pictures of the 2 siblings (Improvement in 2 months)

Proband



(1) pre-tr aggressive periodontitis and gingivitis, (1) post-tr restored dentition with no periodontitis and gingivitis, (2) pre-tr PPK, (2) post-tr improvement of PPK, (3,4,5) pre-tr psoriasisiform lesions of the elbows and knees, (3,4,5) post-tr improvement of psoriasisiform lesions of elbows and knees.

Sibling





(1,2) pre-tr PPK, (1,2) post-tr improvement of PPK, (3) pre-tr keratosis of dorsal surface of the foot, (3) post-tr improvement of keratosis of dorsal surface of the foot, (4,5) pre-tr psoriasisiform lesions of knees and elbows, (4,5) post-tr improvement of psoriasisiform lesions of knees and elbows, (6) Oral cavity with exfoliated teeth, (6) Restored dentition.

DISCUSSION

HMS is a rare disorder which is inherited in a mendelian recessive fashion that was first reported in

migrant Jews of Israel in 1965. Later on some researchers considered HMS as a variant of PLS on the basis of common features such as hyperkeratosis of the palms and soles and aggressive periodontitis.

Parental consanguinity was seen in our case study as parents were first cousins. HMS and PLS locus is mapped to chromosome 11q 14-q21. This is the region where cathepsin C gene maps. The cathepsin gene consists of seven exons. Two mutations are reported in CTSC gene in families affected by HMS.

Because of the lack of the facility of genetic testing in FMH College of Dentistry, genetic analysis for cathepsin C gene could not be performed, though the diagnostic criteria of HMS globally is based on history, clinical examination and radiological evaluation. Lack of functional cathepsin causes defective enzyme production which has been implicated in variety of inflammatory and immune processes including phagocyte destruction of bacteria. Leukocytic functions are depressed due to lack of cathepsin C gene activity. The cathepsin gene is expressed in the epithelial regions of palms, soles, knees and keratinized oral gingiva as well as in osteoclasts.

Hence hyperkeratosis of palms, soles, knees and gingivitis shows the presence of defective gene in these areas. Both periodontitis and gingivitis are present in HMS and PLS but periodontitis is somewhat more severe in PLS as compared to HMS. In addition to these common oro-cutaneous features; other features like acro-osteolysis, onychogryphosis, arachnodactyly, pes planus and acro-osteolysis are only present in HMS.

Radiographic evaluation of arachnodactyly can be done by measuring the metacarpal index (MI). MI can be taken by dividing length by width of a metacarpal preferably the first metacarpal. MI of the hands of males and females are different having standard normal mean values. Similarly metacarpal index (MI) of the left and right hand of an adult male individual is also different and the same is true for females.¹⁴ MI of the right hand of a healthy adult male individual has a mean value of 6.86 (range 5.9-8.1).¹⁴ So any value higher than 8.1 (max normal) depicts long metacarpals meaning arachnodactyly.¹¹ Such patients have elongated phalanges with pointed tapered distal ends pertaining to arachnodactyly/acromatia and acro-osteolysis respectively.¹¹ Arachnodactyly is clearly evident from the hand wrist radiograph of the elder sibling having metacarpal index of 8.8 in the right hand. Arachnodactyly can't be seen radiographically in younger patients because the mean values of MI corresponds to the normal values of an adult and

because the proband was only 11 years old at the time of diagnosis of HMS therefore arachnodactyly could not be radiologically evaluated.

Acro-osteolysis can be seen in hand wrist radiograph of the elder sibling (pointed by white arrows) shown in Fig 14, which was absent in the proband as this feature along with arachnodactyly becomes evident in adult life.

Liver abscess could be a systemic complication associated with PLS. No liver abnormality was found in both the patients. Similarly sometimes PLS patients show a radio-opaque lateral skull view which was again absent in both patients.

Complications related to HMS include arthritis. But appropriate therapy and early diagnosis makes it less vulnerable to this complication.

CONCLUSION

Differential diagnosis of HMS includes Papillon Lefèvre syndrome and to some extent Juvenile periodontitis (pre-pubertal periodontitis). Though palmo-plantar keratoderma is absent in Juvenile periodontitis but it shows aggressive periodontitis and if associated secondarily with other skin disorders such as psoriasis and eczema, can still be confused with HMS.

Along with proper antibiotic against actinomycetem-comitans, excellent oral hygiene is required to minimize growth of pathologic microbial flora. Cotrimoxazole is the first line therapy against Actinomycetem-comitans. Retinoids besides some uncommon side effects can be very helpful in inherited hyperkeratotic skin disorders and inherited periodontitis. They may be used as topical as well as in oral forms.

Treatment methodology for HMS should include the involvement of a team of Oral Physicians, Dermatologists, Radiologists, Paediatricians and Dentists.

Before wrapping up it needs to be emphasized that further research needs to be done on the genetic basis, anomalies and complications of this rare genodermatosis in order to gain deeper insight on the cause, inheritance, symptomatology, improvements on current treatment modalities and possibly more revolutionary treatment approaches.

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