Commentary

Of palms, soles, and gums

Of not quite venerable status, Papillon-Lefèvre syndrome was first described in 1924. That was a year after I was born and one never likes to think of oneself as venerable. However, as a graduate fellow in pathology at Columbia Presbyterian Hospital, New York, USA in the late 1940s, my initial exposure to the general concept of syndromes had only just occurred (acanthosis nigricans and gastric adenocarcinoma). Although I had high hopes that other oral syndromes existed for me to identify (the idea of discovering a new one did not enter my mind at the time), I remember talking about my new found interest to almost everyone I encountered at Columbia University Dental School, my hope being that they would show me a new one. In late 1949, Dr Sam Rosenthal, Chair of Pediatric Dentistry, knowing of my interests, asked me to see a child who was experiencing exfoliation of his entire dentition. The child clearly did not have mercury intoxication.

I noticed that his palms and soles were thick and calloused. Not finding an obvious explanation, I wondered whether this patient had one of those syndromes. Knowing nothing about binary combinations, I set out to do my first search, hampered by my inchoate knowledge of German and French. Pure chance led me to a very brief library search, leading perhaps 30%, these findings might have public health implications.

Our dentists and dental hygienists have always preached to us that periodontal disease is a result of microbial onslaught and poor oral hygiene. The genetic aetiology of Papillon-Lefèvre syndrome, Haim-Munk syndrome, prepubertal periodontosis, and other syndromes have suggested that there is a genetic basis for susceptibility to these microbes. The susceptibility gene for Papillon-Lefèvre syndrome, Haim-Munk syndrome, and prepubertal periodontosis is cathepsin C. Cathepsin C is an enzyme which processes and activates several granule serine proteases critical to immune and inflammatory responses of myeloid and lymphoid cells. Loss of function mutations in the gene in these three disorders should, therefore, result in an altered immune response to infection. This would explain both the oral and dermatological phenotypic spectrum of the three syndromes. The series of groundbreaking work done by Hart and colleagues lends new meaning to the much used adage “by the skin of one’s teeth”!

For me, it has been a long 50 year voyage, but a fascinating one.

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7 Haim S, Munk J. Keratosis palmo-plantaris congenita, with periodontosis, arachnodactyly, and peculiar deformity of the terminal phalanges. Br J Dermatol 1965;77:42-54.

1997-98, three independent groups mapped the gene for Papillon-Lefèvre syndrome to 11q14-q21. Last year, Hart et al. identified germline missense and truncating mutations in the gene encoding cathepsin C (or dipetidyl aminopeptidase I), a lysosomal cysteine proteinase which plays an important role in intracellular degradation of proteins, in families with Papillon-Lefèvre syndrome. These results were also found by an independent group.

In this issue, Hart et al. show that Haim-Munk syndrome is allelic to Papillon-Lefèvre syndrome. More tantalising, however, is the identification of a germline missense mutation in a highly conserved residue in the cathepsin C gene in familial prepubertal site specific periodontitis. Since periodontitis is a common problem among the general population, affecting perhaps 30%, these findings might have public health implications.


