Papillon Lefevre syndrome: Treatment of two cases with a clinical microbiological and histopathological investigation

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Papillon Lefevre syndrome is presented in the cases of two female patients of the ages of 7 and 9, who exhibited all typical symptoms of the disease. Microbiological and histopathological studies were done and treatment provided.

Actinobacillus actinomycetemcomitans, *which is suspected as a pathogenic factor in the disease was identified as well as some other gram negative microorganisms and an antibiogram was performed in which amoxycillin plus clavulanic acid was most effective. Histopathological investigation also confirmed the presence of gram negative bacteria. Granular cell infiltration was predominant in the surface epithelium.*

Prosthetic appliances were provided for the patients after mechanical and chemical plaque control. In addition to this, antibiotics (amoxycillin plus clavulanic acid) were prescribed every six months. No tooth loss was observed in both patients after more than two years follow-up period. At the moment only one patient is under review and because she is uncooperative, mild periodontal inflammation is still present around the teeth which erupted before the antibiotic regime, but not in the other teeth.

Introduction

The syndrome palmarplantar hyperkeratosis was first described by Papillon and Lefevre in 1924. It is mainly characterized by (1) hyperkeratosis of the palms and soles (2) extensive periodontal destruction, which causes early loss of the primary and permanent teeth. Although it is said to be inherited as an autosomal recessive character the etiology of the disease is not clear. Hyperkeratotic lesions are also found in the toes, elbows, heels and knees. The syndrome is estimated to have a frequency of 1 to 4 per million. More than 130 patients have been reported up to the present time.[3,4,5,10,13]

Clinically periodontal inflammation can be seen both in the primary and permanent dentition soon after the eruption of the teeth, followed by mobility of the teeth. Excessive alveolar bone loss can be detected on radiographic examination. Generally loss of teeth is inevitable.

In recent years, two main factors are suggested to be responsible for tooth loss in Papillon LeFevre Syndrome (PLS); Firstly, the presence of gram negative microorganisms in the periodontal pockets of the patients. This finding promoted microbiological studies and gram negative bacteria such as *Bacterioides gingivalis*, Capnocytophage and Spirochaetes have been found in periodontal pockets of patients with PLS[9,11,13] Preus[12] and Tinanoff[18] reported a possible relationship between *Actinobacillus actinomycetemcomitans* (A a) and PLS Baer,[1] Preus and Gjermo[11] suggested that this syndrome might be bacteriological mediated and therefore could be treated with antibiotics. The other factor suggested in the etiology is cellular deficiency in chemotaxic and phagocytic function of neutrophylic granulocytes.[15,18] A genetic component is suggested to be responsible for deficiency of neutrophylic lymphocyte function.[7,18]

Until recently it was believed that treatment of the syndrome is usually unsuccessful. However Baer,[1] Preus and Gjermo[11] reported successfully treated cases with the extraction of primary teeth by 3 years of age and the prescription of tetracycline with the construction of prosthesis followed by another therapeutic dose of antibiotics given at the eruption of first molars and incisors.

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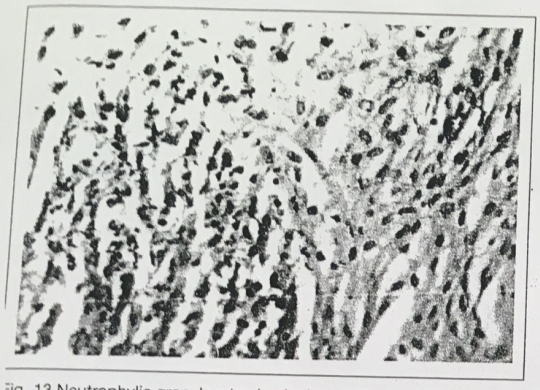


Fig. 13 Neutrophylic granulocytes in gingival epithelium (40X)(case 2)

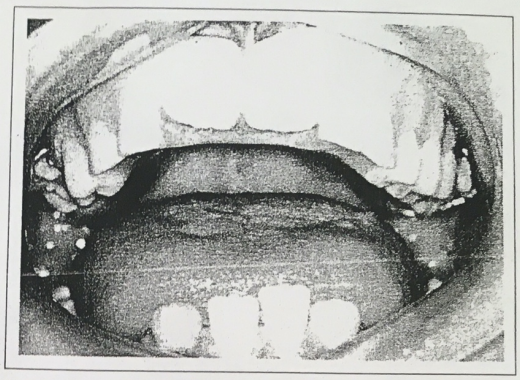
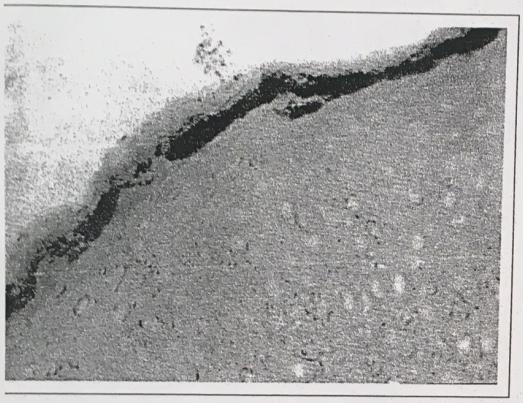


Fig. 16 Prosthetic rehabilitation of patient in case 1.



14 Gram negative bacteria in the surface layer of epithelium (20X)
2).

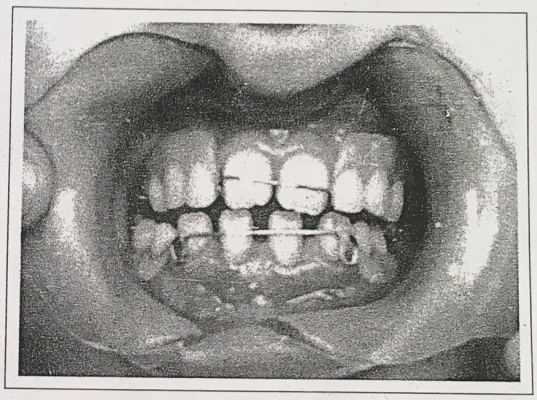
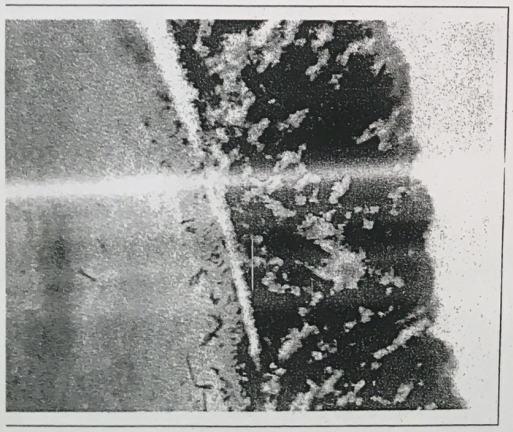


Fig. 17 Prosthetic rehabilitation of patient in case 2.



ram negative bacteria in the plaque attached to the root sur-

antibiotics with an agar disc diffusion method, but in anaerobic conditions diffusion of antibiotics in agar may give wrong results as reported by Bailey and Scott.[2]

The results of the antibiogram were evaluated according to Sutter.[2] The most effective antibiotics were found to be amoxycillin + clavulanic acid (Augmentin). Cephtriaksom (Rocephin) and Erythromycin were found to be moderately effective and penicillin, tetracycline and chloramphenicol were less effective. Metronidozole and Ornidazole was found to be ineffective.

Gingival biopsies of the extracted teeth and subgingival plaque samples were processed for histopathologic investigation and 5-8 μm sections were taken. Some sections including extracted teeth were stained with Hematoxylene-Eosin and some selected sections were stained with gram stain for bacteriological investigation.

In histopathological investigation granular cell infiltra-

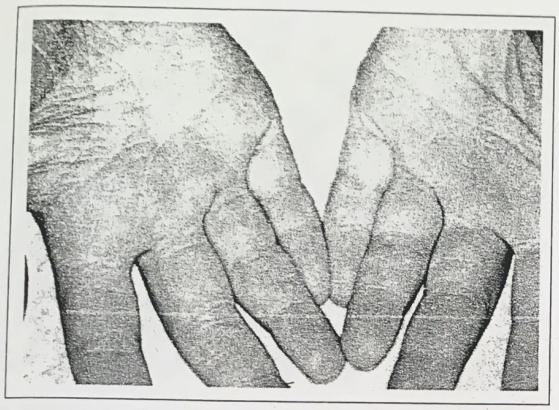


Fig. 1 Palms of patient in case 1.



Fig. 4 Soles of the feet of patient in case 1

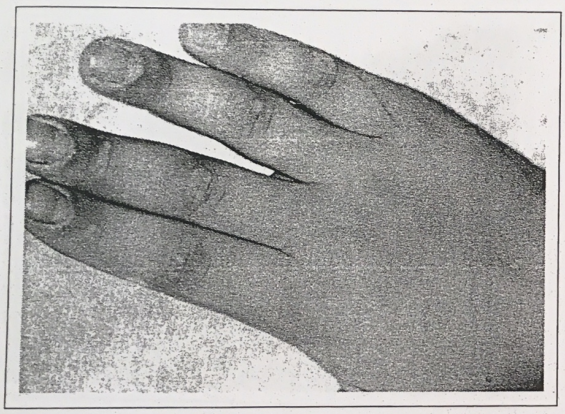


Fig. 2 Dorsal aspects of the fingers of patient in case 1.

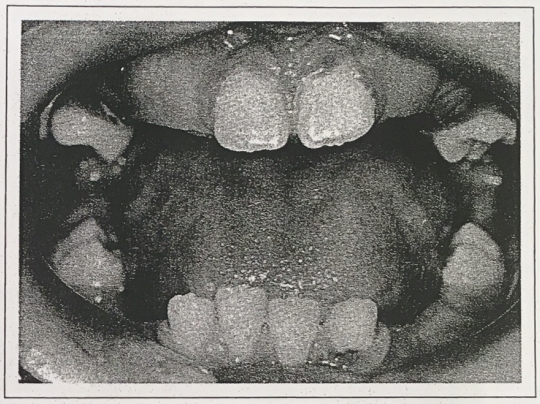


Fig. 5 General view of the oral cavity of patient in case 1.

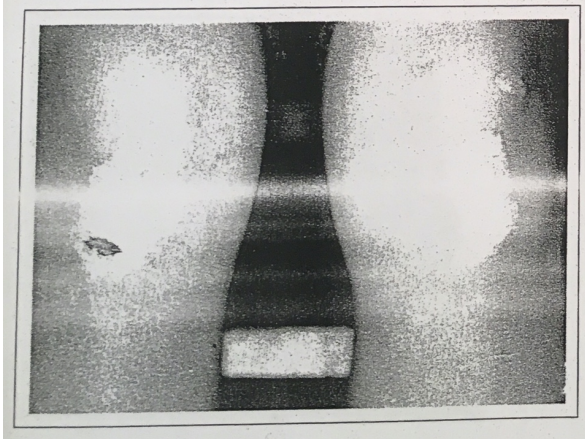


Fig. 3 Knees of patient in case 1.

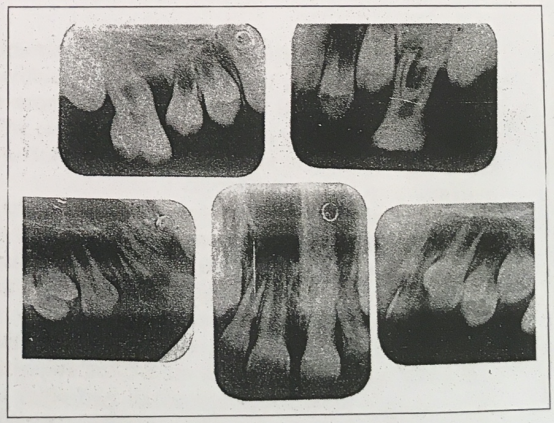


Fig. 6 Serial radiography of upper arch of patient in case 1.

Nazarro and co-workers[7] treated three siblings with Acitrecin (Vitamin A analogs) and reported successful results, but toxic effects of the drug are not yet known.

Case Reports

Case 1: A 7-year-old patient, M.S. was first examined on 13.5.1988 by us at the E.U. Department of Pedodontics because she complained of mobility of the teeth. She was the third child of a couple without a history of consanguinity. Their second child had died soon after birth of an unknown disease. Both parents and the eldest daughter have been and are free of similar cutaneous and periodontal abnormalities.

Keratotic skin lesions were seen on the palms, dorsal aspects of the fingers, knees, elbows and soles.These lesions were painful during the cold winter months (Figs. 1, 2, 3, 4).

Total blood count and urine analysis, and serum calcium phosphate and alkaline phosphate levels showed normal values. Hand-wrist radiographs showed normal features.

The patient's parents reported that mobility of the primary teeth started at the age of four. In the oral examination the following teeth were seen: 16, 11, 21, 26 and 36, 32, 31, 41, 42, 46. The gingivae around the erupted teeth were inflamed and there were abscesses and gross mobility of the teeth with pathological gingival pockets (Fig 5). There was a strong foeter ex ore. On radiographic examination, alveolar bone loss was detected around the erupted teeth (Fig 6, 7). All erupted teeth had supragingival plaque, but not calculus.

Case 2: A 9-year-old female patient, C.C. was referred to our clinic on February 1990 on account of mobility of her teeth and red gums. She was the third child of parents without a history of consanguinity. The first child and parents were free of the cutaneous and periodontal lesions. The second child of the family had died because of an unknown disease 2.5 months after birth.

The mobility of the teeth was first realized when the patient was four-years-old by her physician. Hand and wrist radiographs revealed a relatively slow growth rate and there were low levels of iron and calcium the blood at that time and medical therapy was prescribed. When the patient was examined by us hand and wrist radiographs revealed normal features. Blood count and urine analysis and serum calcium phosphate and alkaline phosphate levels showed normal values. There were less severe cutaneous lesions compared with case 1, and these were localized around the nails and on the soles.

The following teeth were seen on clinical examination (Fig 8): 16, 11, 21, 25, 26 and 36, 32, 31, 41, 42, 46. There was excessive mobility of the incisors and first permanent molars and red gingival hypertrophy which was characterized by abscess formation. There were deep periodontal pockets around the first molars and mandibular incisors. Foetor ex ore was also present. Radiographs revealed extensive alveolar bone destruction around all erupted teeth (Fig 9, 10).

Microbiological and Histopathological Investigation

In both patients extraction of 16,26 was planned as there was severe periodontal involvement. One molar tooth was put into incubation media for microbiological investigation and the other molar tooth was put into 10% formaldehyde for histopathological investigation immediately after extraction. For microbiological investigation as well as gingival biopsies, subgingival plaque samples taken with sterile paper points from those two teeth were collected in aerobic and anaerobic conditions. The patient was asked not to take antibiotics for three months before extraction to prevent interference.

The microbiological samples were taken from the gingival sulcus with sterile paper points before extracting the two molar teeth. The paper points were put into thioglycollate broth as well as the extracted teeth immediately. The microorganisms investigated were microaerophylic *Actinobacillus actinomycetemcomitans* (A.a) and strict anaerobic microorganisms; Capnocytophage, Bacterioides, Veilonella, Fusobacterium, Anaerobic Streptococcus species and some other gram negative bacilli. Selective media were prepared for each genus for isolating them from the sample found in thioglycollate broth. For A.a. tryptic soy agar was prepared and blood serum was added as described by Slot.[17] For the other genus brain heart infusion agar, VL medium, Fusobacterium medium. Reinforced clostridia medium (RCM) were used as selective medium for isolating.[6,14] After 72 hours incubation samples from isolated colonies for A.a. were inoculated on TSBV (Tryptic soy-serum - bacitracin-vancomycin) which is a selective medium for A.a. using streak plate technique. For the other genus inoculated cultures were incubated in selective media with gas-pak anaerobic jar method for 72 hours. Incubated colonies were investigated microscopically, cultural, morphologically and biochemically. When investigating the colonies in TSBV agar, A.a. agar colonies were seen macroscopically as star-like, transparent and attached to the media (Fig 11). In microscopically investigation A.a. was seen as round or rod-shaped with 0.1-0.7 µm length and 0.4-1 µm wide and non-motile and gram negative. The biochemical characteristics were; hydrolyze in blood agar(-), lactose (-), saline (-), mellibiose(-), trehalose (-), catalase (+), oxidase(+), phosphatase(+), gelatinase (-), H_2S (-), glycerol (-), maltose(+), sucrose(-) which were differentiating findings for A.a. from the other species. Fusobocterium, Capnocytophage Bacterioides, anaerobic Streptococcus and Veilonella genus were other bacteria observed.

An antibiogram was performed using an agar dilution method in order to select the antibiotics effective against A.a. which is suggested to be responsible in etiology of the disease. In fact it is easier to select the effectiv