Pyogenic Liver Abscess and Papillon-Lefèvre Syndrome: Not a Rare Association

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ABSTRACT. Papillon-Lefèvre syndrome is a rare, autosomal recessive disease comprising palmoplantar keratoderma and periodontitis. Pyogenic liver abscess is an increasingly recognized complication. We report a new case of this association and review the current literature. ***Pediatrics*** **2003;111:e85–e88. URL: http://www.pediatrics.org/cgi/content/full/111/1/e85;** ***Papillon-Lefèvre syndrome, liver abscess.***

ABBREVIATIONS. PLS, Papillon-Lefèvre syndrome; PPK, palmoplantar keratoderma; CT, computed tomography.

Papillon-Lefèvre syndrome (PLS) is a rare, autosomal recessive disease characterized by palmoplantar keratoderma (PPK) and juvenile periodontitis. The syndrome is believed to affect 1 to 4 persons per million. More than 200 cases have been reported.[1,2]

Pyogenic liver abscess is an uncommon surgical problem among children.[3] Patients typically have an underlying disease associated with functional or quantitative neutrophil abnormalities, and 50% will be immunocompromised.[4]

Patients with PLS seem to be particularly predisposed to develop pyogenic liver abscess. The first report of this occurrence was published in 1988.[5,6] We report a patient who presented with fever of unknown origin in whom pyogenic liver abscess was diagnosed. He was later proved to have PLS.

CASE REPORT

A 10-year-old Saudi boy presented with fever of 2 months duration. The fever was intermittent until 2 weeks before admission when it became persistent, high-grade, and associated with chills and night sweats. Decreased activity and poor appetite were progressing with time. The initial workup by a private physician included a complete blood count with differentials, liver function test, coagulation profile, urinalysis, and blood chemistry. All were normal. The patient received 2 courses of oral antibiotics for presumed tonsillitis without resolution of the fever. A few days before admission, the mother noted an abdominal mass associated with right upper quadrant pain. The pain, which was dull, achy, intermittent, but not radiating, was not associated with vomiting, diarrhea, or jaundice.

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On physical examination, the child was well developed and well nourished. He was febrile with a temperature of 40°C, but other vital signs were normal. There was diffuse gingival redness and swelling with loss of many teeth. He had a diffuse erythematous PPK with transgrediens to the dorsae of the hands and feet (Fig 1). He also had multiple, sharply defined, scaly hyperkeratotic plaques over the elbows and knees. The liver was tender and palpable 4 cm below the right costal margin. The spleen was not palpable. Complete blood count, blood chemistry profile, and liver function tests were normal. Blood, urine, and stool cultures were all negative. Abdominal ultrasound and subsequent computed tomography (CT) of the abdomen with contrast showed a solitary liver abscess measuring 6 × 6 cm (Fig 2). Initial differential diagnosis included a pyogenic liver abscess, amebic liver abscess, and *Echinococcus granulosus* (hydatid cyst); however, the CT scan was not consistent with the characteristics of hydatid cyst. Serum antibody test for *Entamoeba histolytica* and *E granulosus* was negative, as well as stool for ova and parasite. Ultrasound-guided drainage was performed, and 100 mL of thick, yellowish exudate was obtained. *Staphylococcus aureus*, sensitive to cloxacillin and vancomycin and resistant to penicillin, was isolated from the liver abscess culture. Because of the rarity of liver abscess in immunocompetent children, the loss of teeth, and the presence skin lesions, a dermatology consultation was requested, which established the diagnosis of PLS.

Immunologic studies on the patient revealed a normal neutrophil burst test, a low T-lymphocyte (CD_3^+ CD_4^+) count, and a slight elevation of natural killer cell population (CD_3^+ [1820] 55%, CD_3^+ CD_4^+ [720] 22%, CD_3^+ CD_8^+ [1046] 32%, CD_3^- CD_{56}^+ [390] 12%, and CD_{19} [960] 29%).

The patient's medical history was significant for recurrent skin infections, and he was followed up infrequently for his skin eruption. His parents were consanguineous and divorced. Half-siblings from both parents were alive and well.

After complete drainage of the abscess, the patient was treated with cloxacillin intravenously for 4 weeks, followed by oral therapy for another 2 weeks. The patient recovered dramatically and was discharged in a good condition. Kerotolytic preparations containing 20% salicylic acid were prescribed for the skin lesions, and a dental appointment was arranged.

DISCUSSION

PLS was first described by Papillon and Lefèvre[7] in 1924. The disease is characterized by diffuse PPK and juvenile periodontitis.[5,8,9]

PPK usually arises during the first 4 years of life with sharply demarcated erythematous hyperkeratosis more pronounced on the soles and possibly extending to the dorsa of the hands and feet.[10] In winter, PPK may worsen, causing painful fissures that limit ambulation.[10] Erythematous hyperkeratotic plaques may also affect the elbows, knees, and trunk.[10] The second major feature of PLS is severe periodontitis, which starts at age 3 or 4 years and affects the deciduous and permanent teeth.[10] The teeth erupt normally but are soon lost, and by the age of 14 years, patients with PLS are usually edentulous.[10] The underlying cause of the juvenile peri-

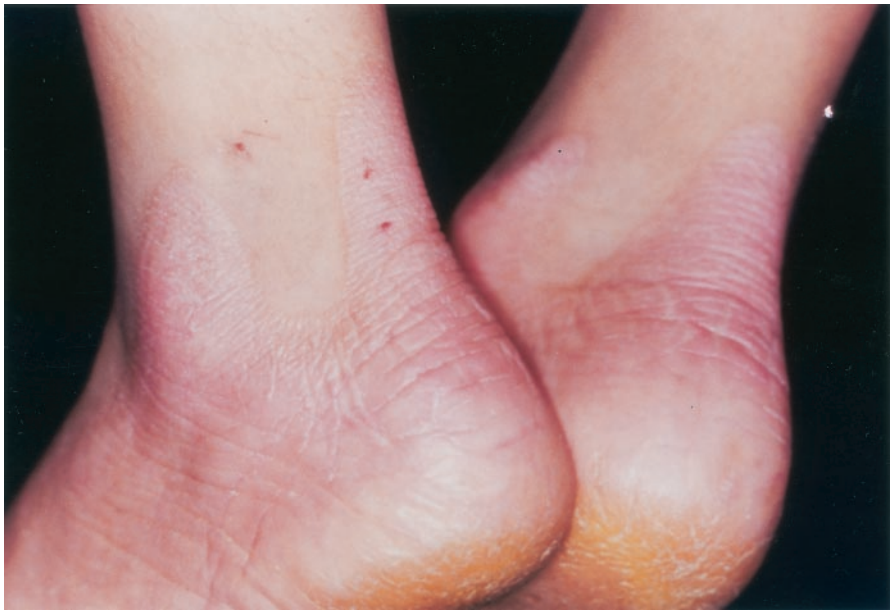

Fig 1. Plantar keratoderma with transgrediens.

odontitis is not well understood but is now thought to be related to an abnormal immune system and to invading bacteria in the cementum of the teeth.[11,12] A possible role of *Actinobacillus actinomycetemcomitans* has been reported.[13–15]

Recurrent infections are relatively common in PLS.[14] An estimated 17% of patients present with marked predisposition to a variety of usually mild infections like skin pyodermas.[14,16] Occasionally, fatal infections like multiple abdominal abscesses have been reported.[16–18] Other minor features of PLS include calcification of the dura, falx cerebri, tentorium cerebelli, and choroids plexus.[1,19]

On presentation, our patient had the 2 major features of PLS. He had severe active periodontitis and PPK. In addition, the mother related a history of recurrent skin infections in the patient's first few months of life.

Liver abscesses may be particularly common in patients with PLS.[5,8] In 1 study of 16 patients with pyogenic liver abscess, 2 patients were found retrospectively to have PLS.[8] To date, 4 reports of 5 patients with PLS who developed pyogenic liver abscess have appeared in the English literature.[5,6,8,20] Pyogenic liver abscess usually results from the seeding of the liver by pathogenic bacteria through a hematogenous route.[21] The most common etiologic agent is *S aureus*, and most often a solitary abscess is found.[21] Liver abscess may also result from contiguous spread of infection from within the liver or from an adjacent inflamed organ. In this setting, the infection is usually polymicrobial with Gram-negative enterics and anaerobes forming multiple liver abscesses.[21] Unexplained or cryptogenic hepatic abscess accounts for ~20% of cases.[21] Bacteremia occurs in normal and immunocompromised hosts;

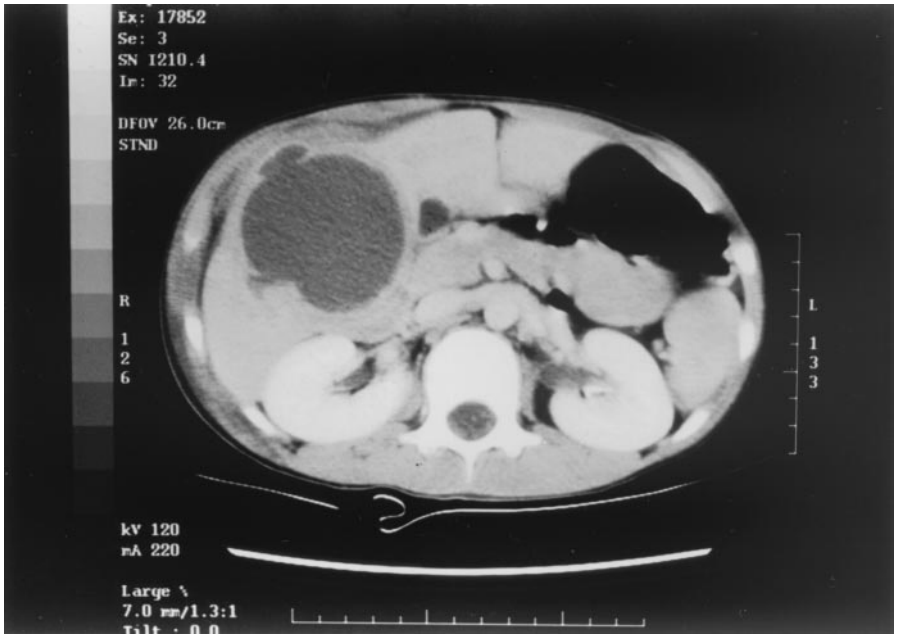

Fig 2. Axial image of CT of the abdomen demonstrates large liver abscess measuring 6 × 6 cm.

however, it is usually transient and rarely seeds the liver in immunocompetent individuals.

Bacteremia during periods of extensive periodontal inflammation associated with the abnormal polymorphonuclear chemotaxis and oxygen consumption are known to occur in PLS patients.[22] These 2 factors likely contribute to the development of the liver abscess.[8] In our patient, the inflamed gingiva was the likely point of entry of *S aureus* that led to bacteremia and subsequently the liver abscess. Different immunologic defects have been described in patients with PLS. A decreased peripheral T-lymphocyte subpopulation, which was noted in our patient, was described in a previous report.[13]

Although our patient had a normal production of superoxide radicals by polymorphonuclear leukocyte (burst test), this defect has also been described in PLS patients.[14] Impairments in chemotaxis of polymorphonuclear leukocytes, which is commonly described in PLS patients, was not tested in our patient.[14]

A multidisciplinary approach is important for the care of patients with PLS. PPK is usually treated topically with emollients.[10] Salicylic acid and urea can be added to enhance their effects. Systemic retinoids, including isotretinoin, etretinate, and acitretin, have proven to be effective in PPK of PLS as well as in other PPKs.[6,19,23–26] There has been some concern that retinoid treatment in PLS may increase the risk of pyogenic liver abscess.[5] This is probably unfounded, as this complication may occur in patients not receiving retinoids.[8] In fact, among 5 patients who developed this complication, only 1 was receiving retinoid treatment.[5,6,8] The periodontitis in PLS is usually difficult to control. Reported effective treatment for the periodontitis includes extraction of the primary teeth combined with oral antibiotics and professional teeth cleaning.[15,27,28]

Moreover, etretinate and acitretin have been claimed to modulate the course of periodontitis and preserve the teeth.[9,26,29,30] However, frequently these treatments do not succeed in preserving the permanent teeth.[28] Prophylactic antibiotics use has not been studied, and there has been no clear indication of what to use and when. Because of the sparse number of PLS patients with pyogenic liver abscess, it is difficult to make any suggestions regarding prophylactic antibiotic use. Stronger evidence is needed to support the use of prophylactic antibiotics in these populations in the future; however, we believe that a course of antibiotics should be tried to control the active periodontitis in an effort to preserve the teeth and to prevent bacteremia and subsequently pyogenic liver abscess. The risk of pyogenic liver abscess should be kept in mind in evaluating these patients when they present with fever of unknown origin.

Recently, the gene for PLS has been mapped to 11q14-q21.[31,32] In 1999, Hart et al[33] identified a germline missense and truncating mutations in the gene encoding cathepsin C (or dipeptidyl aminopeptidase I), a lysosomal cysteine proteinase that plays an important role in intracellular degradation of proteins in families with PLS. Cathepsin C is an enzyme that processes and activates several granule serine proteases critical to immune and inflammatory responses of myeloid and lymphoid cells.[34] Interestingly, cathepsin C gene mutations were also identified in familial prepubertal periodontitis.[35] Another related syndrome, Haim-Munk syndrome, was also found to have a mutation in the same gene and is now considered to be an allelic variant of PLS.[36]

CONCLUSION

Pyogenic liver abscess is increasingly recognized as a complication of PLS because of impairment of the immune system.

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