CASE REPORT
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Papillon Lefevre Syndrome and Footprints of Mycobacterium Tuberculosis

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ABSTRACT

Papillon-Lefevre syndrome (PLS) is a very rare genetic syndrome, and fewer than 500 cases have been reported in the world. Patients exhibit typical cutaneous involvement with hyperkeratosis, especially on the soles and palms, and early shedding of primary teeth. Internal organ involvements, such as liver abscesses, have been described in case reports. This communication represents the first time that genetically documented PLS with footprints of mycobacterium tuberculosis in liver and kidney is reported. T-Lymphocyte transformation Test with PHA was abnormal in this patient.

Key words: Mycobacterium tuberculosis; Papillon-Lefevre syndrome

INTRODUCTION

In 1924, two French physicians, Papillon and Lefevre, described a brother and sister with a condition characterized by palmoplantar hyperkeratosis associated with severe, early-onset periodontitis and premature loss of primary and permanent teeth.[1] To date, fewer than 500 cases have been reported, and almost half showed a familiar pattern.

The inheritance is autosomal recessive, and consanguinity is a notable feature in many patients. There is no racial predominance, but most reports have been from Turkey. The prevalence of the condition is estimated to be 1 to 4 per million in the general population, with a carrier rate of 2 to 4 per 1000.[2] This disease usually has its onset in early childhood. Common cutaneous changes include well-demarcated erythematous hyperkeratotic lesions on the palms, soles, dorsum of the hands, and interphalangeal joints. These plaques may occur focally but usually involve the entire surface of the palms and soles, sometimes extending onto the dorsal surfaces of the hands and feet. Other features of the syndrome that have been reported less frequently include psoriasiform plaques of the elbows and knees, nail changes, calcification of the dura, and recurrent pyogenic skin infections.[3]

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Herein, we present the case of a 15-year-old boy with footprints of mycobacterium tuberculosis and granulomatous changes in the liver and his lost left kidney. This is the first report of a genetically documented case of Papillon-Lefevre syndrome (PLS), particularly with respect to an unusual manifestation of liver and kidney mycobacterium involvement.

CASE REPORT

A 15-year-old boy presented to our center (Bahrami Children's Hospital) with a history of nocturnal fever, chills, malaise, weight reduction, sweating, and sensation of right flank pain that became worse with coughing and extended to the right shoulder. These problems began two weeks prior to presentation, and the patient was not able to attend school in the previous week. The boy's parents are consanguineous (first cousins). The patient has had a previous history of such fevers and right flank pain dating back to approximately two years ago and a liver abscess was revealed on abdominal sonography, which led to his hospitalization and prolonged intravenous antibiotic therapy. When the patient was one year old, physicians found a mass in his left kidney and suspected Wilms' tumor; thus, he underwent a left nephrectomy. In the pathologist's report on the removed organ, there was no evidence of Wilms' tumor, but "xanthogranulomatous pyelonephritis" was reported. The parents also indicated a history of early shedding of primary teeth when the patient was two years of age. On the physical examination, the patient's core temperature was 39ºC and he had normal permanent teeth without any gingivitis or any inflammation in the oral cavity. The patient had well-demarcated erythematous hyperkeratotic lesions on the palms, soles, dorsum of the hands, and the interphalangeal joints, with extension to the dorsal surfaces of the hands, feet, elbows, and knees and some pitting and deformities of the nails of the hands and feet (Figure 1). These cutaneous changes had begun in early childhood.

The patient had abdominal tenderness; especially over the right upper quadrant. The vital signs were normal except for a high-grade fever. Biochemical studies, liver and kidney function tests, and leukocyte enumeration and differentiation yielded results within normal limits, but an elevated ESR (86 mm/1st hour) and positive CRP were detected. Abdominal CT imaging with contrast revealed a 4 x 4.5 cm abscess in the 6th liver segment (Figure 2). Due to the extensive history of abscess formation, we requested immunologic studies. Initial assessments of the patient's immune system, such as serum immunoglobulins, complement system, phagocytic system (NBT, DHR, chemotaxis assays), and flow cytometry for B-cells, T-cells, and NK cells, all yielded normal results, but the results of a lymphocyte transformation test with PHA and BCG for the assessment of T-cell function were abnormal. Based on an open-liver biopsy, the pathological changes were compatible with a caseating granulomatous lesion. The culture for mycobacterium tuberculosis was negative, but the PCR was positive. Due to the high suspicion of tuberculosis, standard therapy with isoniazid, rifampin, and azithromycin was initiated. After approximately two weeks, the previously intractable fevers resolved, and the patient showed general improvement.

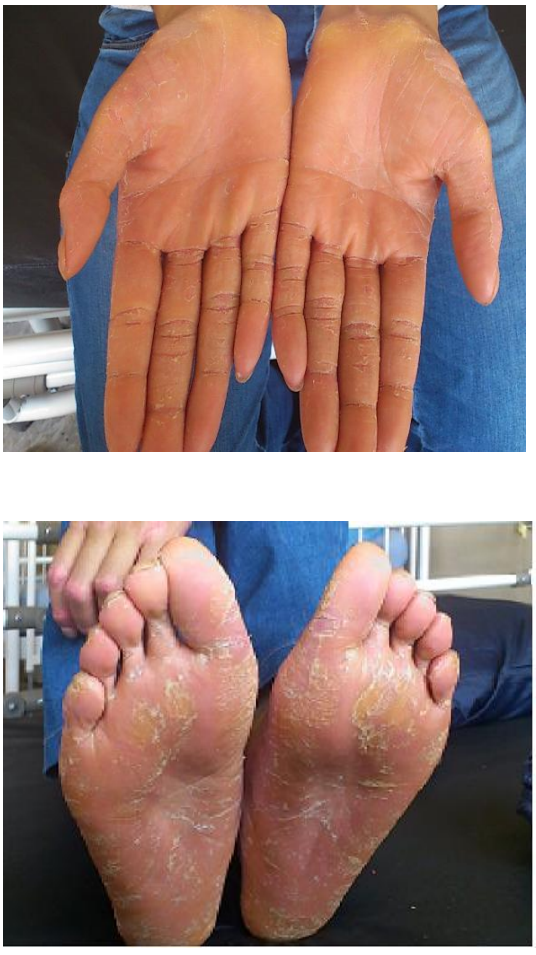

Figure 1. Hyperkeratosis of palms and soles

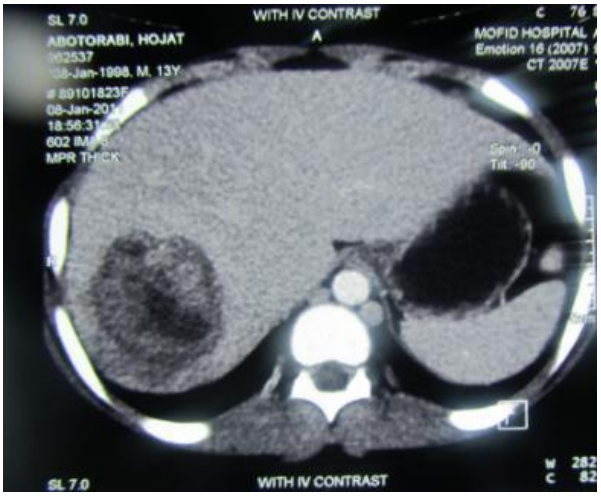

Figure 2. Abdominal CT scan with contrast could demarcate an abscess with dimensions of 4 x 4.5 cm in the 6th liver segment

DISCUSSION

PLS studies are very rare, and our knowledge about this syndrome is very limited. What is common to all reported cases is hyperkeratotic changes, especially on the soles and palms, but dental shedding, particularly of primary teeth, is the second most common symptom but is not always exhibited in this syndrome. Internal organ involvement has previously been reported in unusual and rare cases. SV Dhadke and colleagues reported an 18-year-old boy who presented with a history of right-sided chest pain, dyspnea, recurrent skin infections, and two admissions for liver abscesses in 2006.[4] There was no report of tuberculosis in these patients. Almost all of these patients show some compromised immunity. First, an impairment of neutrophil chemotaxis, phagocytosis, and bactericidal activities accompanied by a decrease in cell migration was noted in previous reported cases, but we could not find any apparent abnormality in the phagocytic system in our case. Second, a defect in cell-mediated mechanisms, including reduced lymphocyte response to pathogens and depression of the helper/suppressor T-cells ratio, were identified.[5,6] In our case, T-cell flow-cytometric enumeration was normal, but the results of a lymphocyte transformation test with PHA and BCG for the assessment of T-cell functions were abnormal. Humoral and complement system exhibited normal function.

Recently, genetic examinations have revealed the Papillon-Lefevre syndrome gene locus in these patients. The gene responsible for PLS has been localized to chromosome 11q14-21, where the cathepsin C gene encodes a lysosomal protease, in the interval between D11S4082 and D11S931. Inactivating mutations have been identified in this gene, and an almost complete loss of cathepsin C activity was observed in these patients. An interesting feature of the cathepsin C gene is that mutations in this gene also result in two other closely related conditions: Haim-Munk syndrome and prepubertal periodontitis. A common clinical manifestation in all three syndromes is severe, early-onset periodontitis. We were able to perform a genetic study on our patient with the help of medical faculty from the Department of Medical Genetics at Istanbul University. DNA sequencing was used for this analysis, and we discovered that the patient is homozygous for p.Arg272pro in exon 6 of the cathepsin C gene.

Retinoid administration has been suggested to be the most effective treatment for the skin condition associated with PLS. The concern that retinoid treatment in PLS may increase the risk of pyogenic liver abscess is probably unfounded because this may occur in patients not receiving retinoids. We began anti-tuberculosis therapy and also administered topical emollients such as urea and Eucerin with very significant improvement in the fevers and skin hyperkeratosis after approximately two weeks.

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