Medical Journal of the
Islamic Republic of Iran

Volume 11
Number 2
Summer 1376
August 1997

Case Reports

PAPILLON-LEFE'VRE SYNDROME: NEUTROPHIL MOTILITY AND KILLING DEFECT IN A CHILD WITH RECURRENT SEVERE INFECTIONS

M. MOIN, M.D., ABOLHASAN FARHOUDI, M.D., AND ATHAR MOIN, M.D.*

*From the Department of Clinical Immunology and Allergy, Children's Medical Center, Tehran University of Medical Sciences, Tehran, and the *Department of Dermatology, Shahed University, Tehran, Islamic Republic of Iran.*

ABSTRACT

A case of palmoplantar hyperkeratosis with periodontosis and a history of recurrent severe pyoderma, pneumonia and multiple liver abscesses is described in a 12 year old girl. The patient demonstrated neutrophil dysfunction characterized by decreased random migration and chemotaxis and defective bactericidal activity. The exact immunopathological mechanism for susceptibility to infections in Papillon-Lefe'vre syndrome patients still remains to be determined. However, the mode of clinical presentation, laboratory findings and response to retinoid treatment, all support the speculation of Papillon-Lefe'vre syndrome as a primary immunologic disease with a variable defect in neutrophil motility and bactericidal activity. The pattern of clinical presentations as skin and periodontal lesions alone or with susceptibility to infection in other sites will change accordingly.

Keywords: Keratosis, periodontosis, neutrophil, chemotaxis, chemiluminescense

MJIRI, Vol. 11, No. 2, 149-152, 1997.

INTRODUCTION

The association of palmoplantar hyperkeratosis with periodontopathy was first described by Papillon and Lefe'vre in 1924.[1] Papillon–Lefe'vre syndrome (PLS) is a rare recessively inherited[1] disorder of keratinization characterized by redness and thickening of the palms and soles and early loss of both primary and permanent dentition. There is a marked predisposition to different infections other than periodontal disease in about 20% of the patients.[2] The underlying mechanism for susceptibility to infections in PLS patients remains to be determined,[3] as the results of investigations have as yet been inconclusive. The reported polymorphonuclear leukocyte functional abnormalities[4-10] and impaired reactivity to T & B-cell mitogens[12,13] have not been observed in other studies.[3,14-16] A decreased total number of T-lymphocytes[10] or of memory T-lymphocytes[11] have been reported recently.

This is a report of an evaluation of neutrophil function

Correspondence: Mostafa Moin, MD, Department of Clinical Immunology and Allergy, Children's Medical Center, Tehran University of Medical Sciences, P.O. Box 14155-6386, Tehran, I.R. Iran.

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and the immunologic profile in a case of PLS with a history of recurrent pyogenic infections. The immunopathological possibilities for susceptibility to infections will also be discussed.

Case report

A 12 year old girl was referred to the Children's Medical Center for investigation because of palmoplantar hyperkeratosis associated with loss of teeth. The present illness started with erythema and pruritic scales appearing on the palms at the age of 4 years. She was treated by various ointments and medications to no avail. At about the same time, her deciduous teeth became loose and soon fell out. During the ensuing years, her permanent teeth were lost thereafter and the skin lesions gradually spread to the dorsa of hands, wrists and soles and flared up from time to time without seasonal variation or relation to other factors. She did not remember the circumstances preceding the loss of her teeth.

The patient is the first of six children, the pregnancy and delivery being normal. Her past medical history included on–and–off diarrhea, pyoderma and abscesses over the neck and pneumonia at the age of 2 years. One year ago she was admitted and operated for multiple liver abscesses and five months ago treated for pneumonia again.

There is consanguinity between the parents (second cousins). The second child which was mentally retarded, died recently due to pneumonia, hemoptysis and convulsions at the age of 11 years. The family and the other siblings were healthy.

Clinical examination showed a fair general condition but she looked somewhat thin and small for her age (height 141 cm, corresponding to the 50th percentile of 10.5 years of age; weight 33 kg, corresponding to the 50th percentile of 10 years of age. She was of normal intelligence. Scars of the previous skin infections and operation for liver abscesses were present.

Diffuse well-defined red hyperkeratotic lesions were present on the palms and fissured soles, with extension of the keratoses to the back of the hands and feet. A few erythematosquamous plaques were observed on both elbows. The hair and nails showed no abnormalities. Oral examination revealed premature loss of many of the teeth. There was no inflammation or active infection of the gingivae. A skin biopsy specimen from the hand disclosed severe hyperkeratosis and the epidemis showed acanthosis of rete ridges. There was no evidence of malignancy. Dental X-ray films disclosed resorption of alveolar bone. Roentgenograms of the skull were normal without any intracranial ectopic calcification. Results of laboratory studies, which included complete blood cell count, electrolytes, blood sugar, urea, creatinine, urinalysis and culture, and Wright and Widal agglutination tests were normal.

Neutrophil function and immunologic profile were evaluated which revealed defective neutrophil motility and killing activity.

Table I. Chemotaxis, serum immunoglobulins, chemiluminescense, complement levels and T & B-cell quantitation in patients compared to normal control levels.

Character	Patient	Control
Chemotaxis:		
Random motility (-CF)	25	40
Chemotaxis (+CF)	75	110
Chemiluminescense	755Mv/10min	1250Mv/15min
Serum Ig		
IgG	1900	600-1700
IgA	370	60-500
IgM	350	25-130
Serum complement		
C_3	107	55-120
C_4	70	20-50
CH_{50}	94%	90-94
T-cells		
CD_3	66.3	55-82
CD_4	47.7	27-57
CD_8	28.5	14-34
CD_4/CD_8	1.67	0.87-3.05
B-cells		
CD_{20}	10.3	9.22

In vivo leukocyte migration was studied according to the skin window method.[17] *In vitro* chemotaxis was examined by a modification of Boyden's method,[18] the details of which have been described.[19] Serum opsonic activity and phagocytosis of *Staphylococcus aureus* were studied as previously described.[20,21] The ability of granulocytes to reduce nitroblue tetrazolium dye after stimulation with phorbol myristate acetate (PMA) particles[22] was measured. Bactericidal activity of polymorphonuclear (PMN) leukocytes was studied by direct spectroscopic observation of singlet oxygen emission.[23] Serum immunoglobin G, A and M levels were measured by radial immunodiffusion.[24] C3 and C4 serum complement levels were measured by the same technique and total hemolytic complement (CH_{50}) levels were measured by the method of Kabat and Mayer.[25] Cell–mediated immunity was studied *in vivo* by delayed type hypersensitivity (DTH) skin tests including tuberculin (PPD), tetanus, candida and streptokinase-streptodornase (SK-SD), and *in vitro* phytohemagglutinin (PHA) lymphocyte stimulation as previously described.[26,27] T-cell (CD_3) and B-cell number (CD_{20}), subsets of T-cell (CD_4 and CD_8) and CD_4/CD_8 ratio were studied by a FACScan flowcytometer.[28] Skin window studies of chemotaxis showed a modest decrease in cell migration in the patient compared with normal subjects. The results of *in vitro* studies of chemotaxis are seen in Table I, where a defect in both random motility and chemotaxis is present. Activity of the patient's leukocytes in comparison with the control was

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normal. Reduction of nitroblue tetrazolium dye (NBT) after ingestion of PMA was shown by 91% of the patient's PMNs, compared with 96% of the control (patient's value within normal limits). The patient's phagocyte killing activity by chemiluminescense was low comparing with the control (Table I). The serum concentration of IgG and IgM was above the normal range (Table I). C3, C4 and CH_{50} levels were within normal limits. Intradermal skin test results were 5mm with commercial tuberculin, 6 mm to tetanus, 6 mm to candida and 10 mm to SK-SD. The lymphocyte response to PHA was within the normal range (patient: 04871; normal:>3000 CPM).The total number of T-cells (CD_3), B-cells (CD_{20}), subsets of T-cells (CD_4 & CD_8) and the CD_4/ CD_8 ratio as measured by an FACScan flow cytometer are seen in Table I.

DISCUSSION

The Papillon-Lefe'vre syndrome is an inherited defect (probably autosomal recessive) of keratinization presenting with diffuse palmoplantar hyperkeratosis and periodontosis with precocious loss of both primary and permanent dentitions.

The periodontal lesions are the most constant feature in PLS. In about 20% of the patients,[2] a marked susceptibility to different infectious diseases other than periodontal disease has been noted. The skin is the most common site of infection, furunculosis and pyoderma[1,2] being described most oftenly. Less frequently liver abscesses,[29] pneumonia and infections of the kidney and abdominal cavity[2,4,29] have been reported. In our patient there was a marked susceptibility to pyogenic infections involving the skin, lung and liver.

The exact underlying mechanism for this predisposition to infection still remains unknown. A high prevalence of PMN disorders and deficiencies in host defense mechanisms has been observed in patients with precocious periodontal disease[5,14] and recurrent pyoderma.[5-7] The immunologic status of these patients has been studied in different cases.[13] Defects in PMN motility and bacterial killing[4-6] or in bacterial killing alone[7,16] have been reported in some cases but other reports deny such defects.[14,15] A decreased myeloperoxidase content of neutrophils was found in some patients.[8,10] Still, in some studies, deficient lymphocyte stimulatory responses were found,[12,13,30] but not in others.[12,14,16] A decrease in the total number of T-lymphocytes[10] or of memory T-lymphocytes (CD_{45} Ro) needs further elucidation.

The case reported in this paper showed defects in both random motility and chemotaxis, and bacterial killing of the PMNs, while the other components of cellular and humoral immunity and the complement system showed normal activity. Increased levels of IgG and IgM could be due to the immune response to chronic and recurrent infections.

The benefical effects of synthetic retinoids in the treatment of keratinizing disorders[31] such as keratoderma in PLS patients[4,32-38] have been shown in different studies. On the other hand, retinoids have a diversity of effects on different components of the immune system.[39] Retinoids in low concentration can stimulate the production and release of superoxide by PMNs[40,41] and change their morphology.[41] Therefore, concerning the mode of clinical presentation, laboratory findings and response to retinoid treatment, we may speculate PLS to be a primary immunodeficiency disease with a variable defect in PMN motility and bactericidal activity. The pattern of clinical manifestations such as skin and periodontal lesions alone or along with susceptibility to infections in other sites will change accordingly.

ACKNOWLEDGEMENT

The authors wish to thank Mr. Abbaszadeh and Miss Shobeiri for excellent secretarial assistance.

REFERENCES

1. Gorlin RJ, Sedano H, Anderson VE: The syndrome of palmar-plantar hyperkeratosis and premature periodontal destruction of the teeth. J Pediat 65: 6, 1964.
2. Haneke E: The Papillon-Lefe'vre syndrome. Hum Genet 51: 1-35, 1979.
3. Bergman R, Fridman-Birnbaurn R: Papillon-Lefe'vre syndrome: long-term clinical course and the effects of etretinate treatment. Brit J Dermatol 119: 731-6, 1988.
4. Bravo-Piris J, Aparicio M, Moran M: Papillon-Lefe'vre syndrome: report of a case treated with oral retinoid. Dermatologica 166: 47-103, 1983.
5. Van Dyke TE, Taubman MA, Ebersole JL, et al: The Papillon–Lefe'vre syndrome: neutrophil dysfunction with severe periodontal disease. Clin Immunol Immunopathol 31: 419-29, 1984.
6. Stadler JF, Torres M, Taraud D, et al: Anomalies fonctionnelles des polynucle'ai -res dans la maladie de Papillon-Lefe'vre. Nour Presse Med 11: 2135-8, 1982.
7. Borroni G, Pagani A, Carcaterra A, et al: Immunological alterations in a case of Papillon-Lefe'vre. Dermatologica 170: 27-30, 1985.
8. D'Angelo M, Marigotta V, Ammatuna P, et al: Neutrophil dysfunction in Papillon-Lefe'vre syndrome. J Clin Periodontol 19(3): 214-9, 1992.
9. Bullon P, Pascual A, Fernandez Noyoa MC, et al: Late onset Papillon-Lefe'vre syndrome. J Clin Periodontol 20(9): 662-7, 1993.
10. D' Angelo M, Margiotta V, Franco V, et al: Treatment of prepubertal periodontitis: a case report and discussion. Minerva Stomatol 41(12): 591-6, 1992.
11. Gongora R, Corell A, Regueiro JR, et al: Peripheral blood reduction of memory T lymphocytes in Papillon-Lefe'vre syndrome. Hum Immunol 41(3): 186-92, 1994.

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12. Du Vivier A: Papillon-Lefe'vre syndrome. Proc R Soc Med 67: 440-1, 1974.
13. Levo Y, Wollner S, Hacham-Zadeh S: Immunological study of patients with the Papillon-Lefe'vre syndrome. Clin Exp Immunol 40: 407-10, 1980.
14. Lyberg TJ: Immunological studies in two siblings with Papillon-Lefe'vre syndrome. Periodont Res 17: 563-8, 1982.
15. Schroeder HE, Segar RA, Keller HU, Rateitschak-Pluss EM: Behaviour of neutrophilic granulocytes in a case of Papillon-Lefe'vre syndrome. J Clin Periodontol 10: 618-35, 1983.
16. Shams el Din A, Benton FR, Bottomley WK, et al: Hyperkeratosis, periodontosis and chronic pyogenic infections in a 15 year old boy. Ann Allergy 53: 11-14, 55-6, 1984.
17. Rebuck JW, Crowley JH: A method of studying leukocytic functions *in vivo*. Ann NY Acad Sci 59: 757-805, 1955.
18. Boyuden S: The chemotactic effect of mixtures of antibody and antigen on polymorphonuclear leukocytes. J Exp Med 115: 453-499, 1962.
19. Clark RA, Kimball HR: Defective granulocyte chemotaxis in the Chediak-Higashi syndrome. J Clin Inves 50: 2645-2652, 1971.
20. Mickenbery ID, Root RK, Wolff SM: Leukocyte function in hypogammaglobulinemia. J Clin Invest 49: 1528-1539, 1970.
21. Bujak JS, Root RK, West BC: Role of peroxidase in the bactericidal activity of blood eosinophils. Clin Res 20: 525, 1972.
22. Borregaard N, Cross AR, Herlin T, Jones OTG, Segal AW, Valerius WH: The human neutrophil: function and dysfunction. Eur J Hematol 41: 401, 1988.
23. Khan AU, Kasha M: Bactericidal activity of PMN and chemiluminescence. Natl Acad Sci (USA) 76: 6047-6049, 1979.
24. Mancini G, Carbonara AO, Heremans JF: Immunochemical quantitation of antigens by single radioimmunodiffusion. Immunochemistry 2: 235-254, 1965.
25. Kabat EA, Mayer MM: Experimental Immunochemistry. Second edition, Springfield, Illinois: Charles C. Thomas Publisher, p. 152, 1961.
26. Kirkpatrick CH, Rich RR, Smith IK: Effect of transfer factor on lymphocyte function in anergic patients. J Clin Invest 51: 1948-1958, 1972.
27. Rocklin RE, Meyers OL, David JR: An *in vitro* assay for cellular hypersensitivity in man. J Immunol 104: 95-112, 1970.
28. Ryan DH, Fallon MA, Horan PK: Flow cytometry in the clinical laboratory. Clin Chem Acta 171: 125, 1988.
29. Haim S, Munk J: Keratosis palmoplantaris congenita. Brit J Dermatol 77: 42, 1965.
30. Jawari D: Deficient phagocytic function in Papillon-Lefe'vre syndrome. Dermatologica 156: 189, 1978.
31. Orfanos CE: Retinoids in clinical dermatology: an update. In: Saurat JH(ed), Retinoids: New Trends in Research and Therapy. New York: S Karger AG, pp. 314-334, 1985.
32. Rufli T, Cajacob A, Schuppli R: Demonstrationen der Dermatologischen Universitatskinik Basel. Dermatologica 165: 296-321, 1981.
33. Driban NE, Jung JR, Papillon-Lefe'vre syndrome: a clinical and therapeutical contribution. Dermatologica 165: 296-321, 1981.
34. Daweke Pickardt G: Papillon-Lefe'vresyndrome (abst). Zeitschr Haut 58: 745, 1983.
35. Morishima T, Higaki M, Maeda T: A case of an infant with Papillon-Lefe'vre syndrome treated with etretinate. J Ped Dermatol 2: 834-8, 1983.
36. Wehrmann W, Traupe H, Happle R: Papillon-Lefe'vre syndrome. Hautarzt 36: 1735, 1985.
37. Nguyen TQ, Greet KE, Fisher GB Jr, et al: Papillon-Lefe'vre syndrome: report of two patients treated with isotretinoin. J Am Acad Dermatol 15: 46-9, 1986.
38. Blanchet -Bardon C, Nazzaro V, Rognin C, Geiger JM, Puissant A: Acitretin in the treatment of severe disorders of keratinization. Results of an open study. 24(6) 982-6, 1991.
39. Shapiro PE, Edelson RI: Effects of retinoids on the immune system. In: Saurat JH (ed.), Retinoids; New Trends in Research and Therapy. Basel: Karger, pp. 225-35, 1985.
40. Hemila H, Wikstrom M: Retinoids activate superoxide production by PMN leukocytes. Scand J Immunol 21: 227-34, 1985.
41. Badwey JA, Robinson JM, Curnulte JT, et al: Retinoids stimulate the release of superoxide by neutrophils and change their morphology. J Cell Physiol 127: 223-8, 1986.

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