

PULMONARY HEMOSIDEROSIS IN AN INFANT WITH PSORIASIS

M. Alshehri, MBBS, FRCPC

Generalized pustular psoriasis (GPP) is an acute inflammatory dermatosis typically associated with systemic features, such as fever, arthralgia, leukocytosis, diarrhea, and altered liver function. It is relatively rare, although onset in infancy has been described.¹⁻² GPP has also been reported in association with chronic, recurrent, multifocal osteomyelitis (CRMO) in the first few months of life.³ Cardiorespiratory failure is reported as the most common cause of death in patients with erythrodermic dermatoses, including GPP, where mortality approaches 70%.⁴ We describe an infant who developed lytic bone lesions, GPP and pulmonary involvement in the form of pulmonary hemosiderosis.

Case Report

A 21-month-old male was born at 36 weeks' gestation to a 28-year-old gravida two para one mother. He presented at our hospital with a stormy clinical course that included chronic skin rash, lytic bone lesions, chronic respiratory symptoms and a past history of birth asphyxia and hypotonia.

A generalized skin rash, involving the scalp, trunk, and limbs and associated with nail pitting and swelling over his joints, appeared in the first few months of life. The patient subsequently developed chronic respiratory symptoms, including tachypnea, wheeze, cough, and chest indrawing. The relevant physical findings included tachypnea, intercostal and subcostal retraction, decreased air entry at the lung bases with crackles and occasional wheeze, hepatomegaly, and generalized pustular rash (see before and after photographs, Figure 1). His chest x-ray revealed both air space and interstitial patterns. Feeding study revealed a lack of swallowing coordination and aspiration of liquids, and skeletal survey revealed soft tissue swelling and lytic lesions over the distal femora, proximal and distal tibia, and over the ribs and vertebrae (Figure 2). Later, x-rays showed healing of some of these

lesions. Abdominal ultrasound showed coarse liver appearance without focal changes, a normal spleen and no adenopathy. Infectious work-up, including bone samples for fungi, tuberculosis and other bacteria, were all negative. Mantoux and VDRL tests were negative. The immunological work-up showed normal immunoglobulin levels, T- and B-cell populations, and normal day 3 and day 6 lymphocyte proliferation studies. Neutrophil studies showed impaired chemotaxis but normal phagocytosis, killing test, nitroblue tetrazolium reduction, and skin window.

Other laboratory investigations, including repeated CBC, liver function enzymes, BUN, creatinine, and electrolytes, did not reveal major abnormalities, apart from chronic normocytic anemia.

The patient's clinical course was complicated mainly by skin rash exacerbation, occasionally associated with skin infection. He also continued to have frequent exacerbation of his respiratory symptoms, which led to several hospital admissions, including the Intensive Care Unit, resulting in several episodes of intubation. He was initially treated with salbutamol, ipatropium promide, pulmicort and antibiotics, mainly at the time of respiratory exacerbation. His skin condition was treated initially with

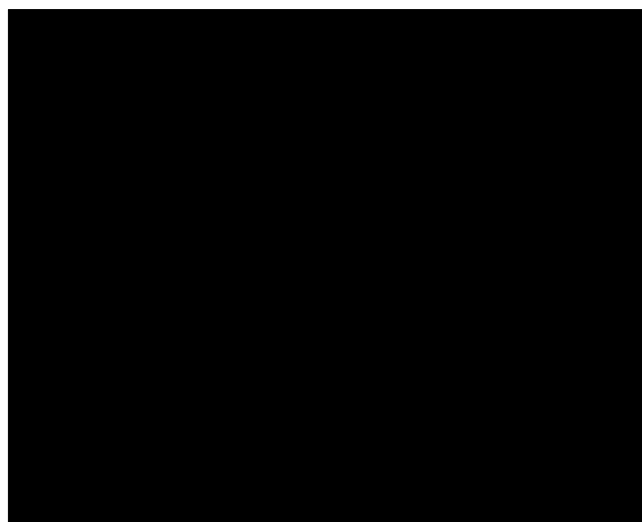


FIGURE 1. Patient photo showing skin involvement: Left: before, and, right, after treatment.

From the Department of Pediatrics, College of Medicine, King Saud University, Abha Branch, Abha, Saudi Arabia.

Address reprint requests and correspondence to Dr. Alshehri: Department of Pediatrics, College of Medicine, King Saud University, Abha Branch, P.O. Box 641, Abha, Saudi Arabia.

Accepted for publication 23 August 1998. Received 22 March 1998.

topical steroids and systemic antibiotics at times of skin infection. Skin histology excluded histiocytosis X, and favored pustular psoriasis, with aseptic subcorneal pustules and mild acanthosis (Figure 3). The patient was then treated more aggressively with systemic steroids, improving both his skin rash and respiratory status with decreased oxygen requirement and less frequent exacerbation of the generalized pustular rash.

To determine the nature of his lung involvement, the patient underwent open lung biopsy, which showed some pleural and septal fibrosis, type 2 pneumocyte hyperplasia, and prominent alveolar exudate of hemosiderin-laden macrophages. No vasculitis was present and immunofluorescence staining for immunoglobulins and C3 complement were negative, and no organisms were identified. He was then maintained on a regimen of steroids and cyclosporin, which led to control of his skin lesions and less frequent respiratory exacerbations. Other maintenance treatment included Fer-In-Sol, cisapride, gastrostomy tube feedings, and 0.250 L/min. oxygen.

At the age of 28 months, the patient refused to be seated upright. CT scan and magnetic resonance imaging of the spine revealed a prevertebral mass at the level of the 7th and 8th thoracic vertebrae. The CT scan-guided biopsy was inconclusive, and he underwent an open biopsy that showed aseptic osteomyelitis with periosteal fibrosis and new bone formation.

Discussion

Pulmonary hemosiderosis has been reported in some cases with an immune etiology⁵ associated with collagen vascular diseases, or as an early manifestation of a systemic vasculitis.⁶

Previous reports of pulmonary inflammation coincident with generalized pustular psoriasis^{7,8} were diagnosed as sterile pneumonitis or unexplained alveolar shadowing on x-ray. Recently, three adult cases of GPP complicated by profoundly increased pulmonary capillary permeability (capillary leak syndrome) have been described.^{9,10} It has been proposed that pulmonary inflammation coincident with extensive cutaneous disease might result from the action of epidermal cell-derived inflammatory mediators on the pulmonary vasculature.⁹

Psoriasis is a chronic skin disease characterized histologically by prominent keratinocyte (KC) hyperplasia and an early inflammatory-cell infiltrate that predominantly includes T-lymphocytes and macrophages.¹¹ In vivo studies¹² have shown an important coordinated interaction between tumor necrosis factor-alpha-producing dermal dendrocytes and overlying KCs, which have increased expression of interleukin 8 (IL-8), intercellular adhesion molecule 1 (ICAM-1), and transforming growth factor-alpha (TGF- α). Furthermore,

increased serum levels of tumor necrosis factor-alpha (TNF- α) were found in a patient with psoriasis,¹³ suggesting that cytokines synthesized by KCs are released into the circulation during cutaneous inflammation. Cytokines are important mediators of pulmonary inflammation.¹⁴ This immune-mediated mechanism was proposed by McGregor and colleagues⁹ to be the probable cause of the development of increased pulmonary vascular permeability in their two patients. We speculate that this immune-mediated mechanism might also account for alveolar hemorrhage in our case. The hemorrhage appeared coincident with exacerbations of GPP, leading to recurrent respiratory symptoms in our patient. Glucocorticosteroids are efficacious in a wide variety of

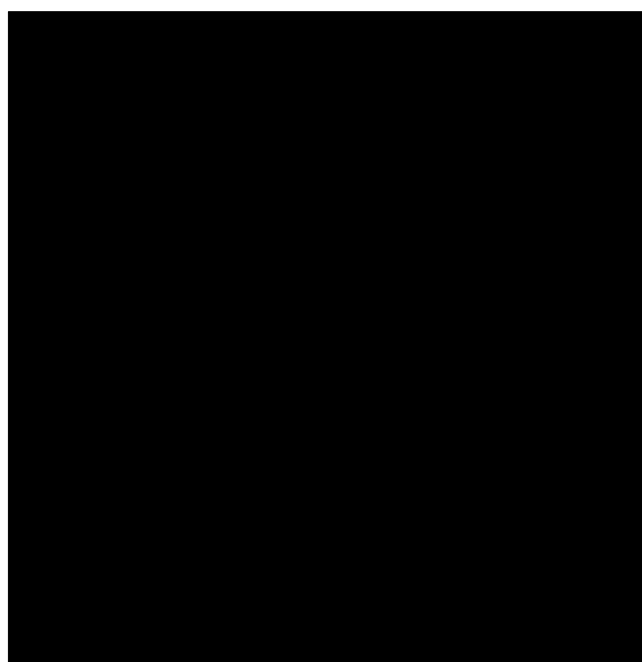


FIGURE 2. Bone x-ray showing lytic lesions.

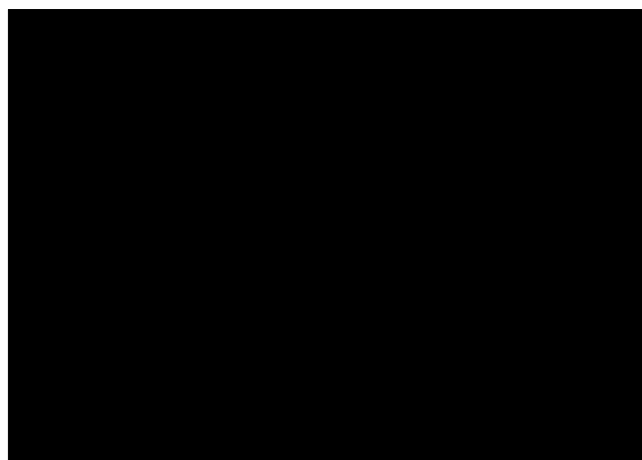


FIGURE 3. Skin biopsy showing subcorneal pustule (H&E, 250x).

inflammatory skin diseases with multiple etiologies. The suggested logical explanation for their action is that they block production of pro-inflammatory cytokines, adhesion molecules and chemotoxins by KCs and immunocytes.¹⁵

The patient's respiratory symptoms and chest x-ray findings, as well as his skin disease, improved with steroid treatment. Unfortunately, the patient developed systemic steroid side effects, requiring substitution with cyclosporine. This regimen also led to control of both his respiratory symptoms and skin disease. Cyclosporine A can improve psoriasis¹⁶ because this compound has been shown to inhibit TNF- α production.¹⁷

Interestingly, in the long-term follow-up of our patient, the pulmonary disease paralleled that of the GPP. Respiratory symptoms would appear at the times of flare-ups of the pustular psoriasis. The patient is maintained mainly on cyclosporine and a short course of steroids is added at the time of exacerbations.

Acknowledgements

We thank Dr. G. Taylor from the Pathology Department and Dr. M. Grouhi from the Immunology Department for their critical review of this paper. This paper was prepared with the assistance of Editorial Services, The Hospital for Sick Children, Toronto, Ontario, Canada.

References

1. Baker H, Ryan T. Generalized pustular psoriasis: a clinical and epidemiological study of 104 cases. *Br J Dermatol* 1968;80:771-93.
2. Van de Kerkhof PCM. Generalized pustular psoriasis in a child. *Dermatologica* 1985;170:244-8.
3. Ivker RA, Grin-Jorgensen CM, Vega VK, Hoss DM, Grant-Kels JM. Infantile generalized pustular psoriasis associated with lytic lesions of the bone. *Pediatr Dermatol* 1993;10:277-82.
4. Marks J. Erythroderma and its management. *Clin Exp Dermatol* 1982;7:415-22.
5. Leatherman JW, Davies SF, Hoidal JR. Alveolar hemorrhage syndromes: diffuse microvascular lung hemorrhage in immune and idiopathic disorders. *Medicine* 1984;63:343-61.
6. Byrd RB, Trunk G. Systemic lupus erythematosus presenting as pulmonary hemosiderosis. *Chest* 1973;64:128-9.
7. Landry M, Muller S. Generalized pustular psoriasis: observations on the course of the disease in a familial occurrence. *Arch Dermatol* 1972;105:711-6.
8. Reed WB. Pustular psoriasis of Zumbusch, generalized. *Arch Dermatol* 1973;107:621.
9. McGregor JM, Barker JNWN, MacDonald DM. Pulmonary capillary leak syndrome complicating generalized pustular psoriasis: possible role of cytokines. *Br J Dermatol* 1991;125:472-4.
10. Handfield-Jones SE, Garvey M, McGibbon DH, Black MM. Capillary leak syndrome in generalized pustular psoriasis. *Br J Dermatol* 1992;127:64.
11. Fry L. Psoriasis. *Br J Dermatol* 1988;119:445-61.
12. Nickoloff BJ, Karabin GD, Barker JNWN, et al. Cellular localization of interleukin-8 and its inducer, tumor necrosis factor-alpha in psoriasis. *Am J Pathol* 1991;138:129-37.
13. Murdoch M, Navaseria H, Balkwell F, Trousdale J, Leigh I. Tumor necrosis factor and psoriasis. *Br J Dermatol* 1989;119(Suppl 33):46.
14. Kelley J. Cytokines of the lung. *Am Rev Respir Dis* 1990;141:765-87.
15. Barker JNWN, Mitra RS, Griffiths CEM, et al. Keratinocytes as initiators of inflammation. *Lancet* 1991;337:211-4.
16. Bos JD. The pathomechanisms of psoriasis: the skin immune system and cyclosporine. *Br J Dermatol* 1988;118:141-55.
17. Remick DG, Nguyen DT, Eskandari ME, Streiter RM, Kunkel SL. Cyclosporine A inhibits TNF production without decreasing TNF mRNA levels. *Biochem Biophys Res Comm* 1989;161:551-5.