Generalized Pustular Psoriasis in Two Children: Acitretin Therapy: Case Report

Asitretin Tedavisiine Yanıtlı
Jeneralize Püstüler Psöriyazisli İki Çocuk Olgu

ABSTRACT

Von Zumbusch type pustular psoriasis is rarely seen in pediatric patients. Attacks of pustular psoriasis are characterized by fever that lasts several days, followed by sudden onset of pustules. The pustules are disseminated over the trunk and extremities, including the nail beds, palms, and soles. Acitretin, alone, or combined with oral corticosteroids, is the first-line treatment method. Methotrexate or cyclosporine may also be used. Acitretin is a second generation aromatic retinoid. It takes effect by regulating keratinocyte proliferation and differentiation. A two-year-old girl and a three-year-old boy, presented with widespread pustules on an erythematous background, accompanied by fever and leukocytosis. Skin and blood cultures were negative. A diagnosis of Von Zumbusch type pustular psoriasis was made. We present two pediatric cases of generalized pustular psoriasis responding to acitretin rapidly and effectively.

Key Words: Psoriasis; child; acitretin

ÖZET


Anahtar Kelimeler: Psöriyazis; çocuk; asitretin

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Generalized pustular psoriasis (GPP) is a rare and severe type of psoriasis described by von Zumbusch in 1910.1 Although it is typically seen in adults, GPP may rarely affect children. Around 200 cases in children have been reported. GPP is the development of extensive sterile pustules with widespread erythema. The von Zumbusch type usually begins acutely and can be associated with painful skin, fever and chills. The course of the disease ranges from a benign, chronic process to an acute life-threatening episode. Treatment should be planned according to severity of disease and underlying risk factors. First-line therapies for childhood GPP are acitretin, acitretin in combination with oral prednisone, methotrexate,
and cyclosporine. We present two pediatric cases of pustular psoriasis who responded rapidly to acitretin.

CASE REPORT

CASE 1
A two-year-old girl presented to our clinic with an acute and widespread eruption. She had recovered from varicella recently. Her past medical history was otherwise unremarkable. Dermatological examination revealed erythematous scaly plaques on the scalp, neck, extremities, trunk and widespread erythema and pustules in the diaper area (Figure 1a). Pustules and lakes of pustules covering both palms and soles were observed (Figure 1b). Fever of 39°C, leukocytosis with neutrophilia, anemia, erythrocyte sedimentation rate 15 mm/h, hypoalbuminemia were present. Serum calcium, phosphate, C-reactive protein, hepatic and renal function tests were within normal limits and blood cultures were also negative. Hypochromic microcytic anemia was present on peripheral smear. Bacterial cultures taken from the pustules and did not grow any microorganisms. Scrapings of lesions did not demonstrate any hyphae or pseudohyphae. Histopathology of the skin lesion revealed a subcorneal spongiform pustule filled with neutrophils in parakeratotic epidermis. Perivascular neutrophilic and lymphocytic infiltration was present in the superficial dermis (Figure 2). Topical steroids were used without effect and pustulation spread all over the body. Acitretin at a dose of 10 mg/day (0.8 mg/kg/day) was initiated. Significant improvement was noted at the end of the first month. At the end of the second month, all lesions except those on the diaper area had cleared. The dose of acitretin was tapered to 0.5 mg/kg/day at the end of the third months due to complete recovery (Figure 3a, 3b). At present, the patient is being followed at a dose of 0.5 mg/kg/day.

CASE 2
A three-year-old boy, presented to our clinic with an acute episode which had precipitated after an upper respiratory infection requiring antibiotics. He had a history of a relapsing and remitting skin dis-
ease on the body for more than a year, for which he had used topical treatments. Upon admission, dermatological examination revealed widespread erythema and pustules on the neck, trunk and extremities. Body temperature was 38.5°C. Leukocytosis, neutrophilia, high erythrocyte sedimentation rate and C reactive protein were present. Serum albumin, calcium, phosphorus and hepatic and renal function tests were within normal limits. Repeated cultures from pustules were all negative. Blood and urine cultures were negative. Skin biopsy demonstrated parakeratosis and intraepidermal subcorneal pustules of varying sizes and a mild mixed inflammatory infiltrate in the dermis. Pustular psoriasis was diagnosed. Oral methylprednisolone (0.4 mg/kg/day), topical emollients and steroids were initiated. Although lesions responded somewhat, new crops of lesions continued to appear. Acitretin at a dose of 0.6 mg/kg/day was added and a significant response was observed within 15 days. Methylprednisolone was tapered and stopped and the patient was advised to continue treatment with acitretin at a dose of 0.5 mg/kg/gün. Three months after initiation of acitretin, all lesions except those on the neck had cleared (Figure 4). Topical steroids were added.

DISCUSSION

Although psoriasis vulgaris is a relatively common disease in children, pustular psoriasis is rare. In a study recruiting 277 pediatric patients with psoriasis, it has been reported that one patient (0.7%) had GPP. Unlike adult GPP, childhood GPP is generally not preceded by psoriasis vulgaris. Typically childhood GPP follows a benign course with rare serious, chronic morbidity.

Diagnostic criteria suggested by Umezawa et al. are as follows:

1-Systemic symptoms such as fever and malaise are present
2-Multiple, isolated aseptic pustules are present in the flushed skin all over the body or over a wide area
3-Kogoj’s spongiform pustules are histopathologically confirmed
Some of the following laboratory test results are obtained during the clinical course: Leukocytosis and shift to the left, precipitated ESR, positive C-reactive protein and high anti-streptolysin O antibody levels, increases in IgG or IgA, hypoprothrombinemia, hypocalcemia, etc.

Recurrence of the above-listed clinical and histological findings.

Childhood GPP is usually acute in onset and toxic symptoms are present. The original episode usually ends in a few days but repeated attacks of inflammation and formation of pustules may continue. Initiation of treatment rapidly is important to prevent life threatening complications such as infection and sepsis. Other complications include metabolic, hemodynamic and thermoregulatory disturbances occurring due to the disruption of the epidermal barrier.

Generalized pustular psoriasis is slightly more common in boys than girls, which is in contrast with nonpustular psoriasis in childhood and pustular psoriasis in adults. The von Zumbusch type of pustular psoriasis is more common in infants whereas annular forms begin later. It should be kept in mind that mixed patterns also occur. One of our patients was a girl and the other was a boy. Factors triggering GPP include infection, UV light, vaccination, emotional stress, withdrawal of corticosteroids, hypocalcemia and group A β-hemolytic streptococcal antigen. Case 1 had started after a viral infection and Case 2 had a previous bacterial infection.

Kwon et al. reviewed 358 patients with psoriasis under the age of 18 in a retrospective analysis. The patients were divided into two groups, one composed of children under age 13 and the other of adolescents aged 13-18. Psoriasis in childhood was associated with more severe clinical presentation and generalized pustular and guttate types were more frequently in this group. Systemic treatment was initiated in 32.4% of the patients and oral acitretin (11.2%) was the most frequently prescribed medication, followed by cyclosporine (4.2%). Our patients were both in the childhood age range and both had generalized pustular psoriasis.

Treatment is difficult since reported number of patients are few and the etiology of disease is not completely known. A standardized method for monitoring disease response to therapy is not available and there is lack of quality data on therapy. Treatment should be planned according to severity and underlying risk factors. Acitretin, cyclosporine, methotrexate, and etanercept are viewed as first-line therapies for GPP in childhood. Adalimumab, infliximab, and ultraviolet B phototherapy are second-line modalities.

Corticosteroid is an effective choice for acute or life-threatening GPP, but recurrence and long-term adverse effects are the main concerns surrounding it. Prednisone in oral form may be added to retinoids for acute disease. Case 1 was started on topical steroids for areas with pustules. In Case 2, systemic methylprednisolone was planned for 15 days in addition to acitretin. After three months, all lesions except some on the neck had regressed.

Acitretin is a nonimmunosuppressive treatment and is a first-line choice for generalized pustular, widespread guttate, and thin-plaque psoriasis. Clinical experience with acitretin in pediatric patients has shown that it is effective and well-tolerated. Retinoid therapy is the treatment of choice for severe inherited disorders of keratinization and has been used with success in pediatric patients with psoriasis. When treating severe or recalcitrant GPP, retinoids at doses less than 1 mg/kg/day are considered appropriately. We initiated acitretin at dosages of 0.6 and 0.8 mg/kg/day in our patients.

Ergin et al. reported successful treatment with retinoids of a 2.5-month-old infant who had pustular psoriasis. Acitretin was administered to the infant at a dose of 0.7 mg/kg/day along with prednisolone (0.3 mg/kg/day) which was tapered in a month. The acitretin dose was lowered to 0.5 mg/kg/day and lesions cleared in four months. The following remission period lasted 15 months. Of note, acitretin dosing intervals was arranged two days per week or every other day. This is practical since a pediatric formulation is not available.
Side effects of acitretin are in general minor and reversible. These include dryness of the skin and mucous membranes and elevation of serum lipids and liver enzymes. Serum lipids and liver enzymes remained normal in follow-up of our patients. Combination therapy allows physicians to maximize benefits and reduce adverse effects associated with various therapies. A major concern with acitretin therapy during childhood is the risk of skeletal toxicity. Premature closure of the epiphyses has been reported in two children receiving etretinate for congenital hyperkeratotic disorders. The duration of treatment was about five and seven years. Monitorization of serial skeletal surveys is recommended on a yearly basis in patients receiving treatment longer than six months. Nevertheless, Umezawa et al. reported a patient who had been on etretinate for 16 years at a dose of 0.22 mg/kg. Treatment was initiated when at the age of three and a total of 37 grams of etretinate was administered. No stunted growth, ligamentous calcification, hyperostosis, or hepatic toxicity was observed. In addition to etretinate, psoralen plus ultraviolet A and topical calcipotriol had been added for flares. Rosinska et al. followed 10 children with psoriasis for up to seven years without major side effects. Focal osteoporosis of one tibia was seen on radiography of one patient.

Girls in their reproductive age are also a source of concern and retinoids are relatively contraindicated in this group, depending on the patient's age and the severity of the disease. In conclusion, since GPP is rarely seen in children, information on its course and treatment is limited. We aimed to emphasize that acitretin is a rapidly effective and safe treatment option in pediatric patients with GPP.

REFERENCES