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Letter

A case of microscopic polyangiitis with skin manifestations in a seven-year-old girl

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Abstract

A case of a 7-year-old girl with microscopic polyangiitis (MPA) with a skin eruption characterized by maculopapular, erythematous and purpuric lesions on the face, elbows, and knees is presented. Anti-neutrophil cytoplasmic autoantibodies (ANCA) with myeloperoxidase specificity (MPO-ANCA) were identified. Chest X-ray and computed tomography scan revealed diffuse infiltrates in both lung fields, suggesting alveolar hemorrhage. Microscopic hematuria was detected but a renal biopsy showed no abnormalities. Histological examination of a skin biopsy from a purpuric papule showed leukocytoclastic vasculitis of the small vessels in the entire dermis. The patient was treated with prednisolone and mizoribine, resulting in an improvement in the skin lesions except for those on the knee.

Keywords: leukocytoclastic vasculitis, microscopic polyangiitis, mizoribine, MPO-ANCA, pediatric patients, skin manifestations

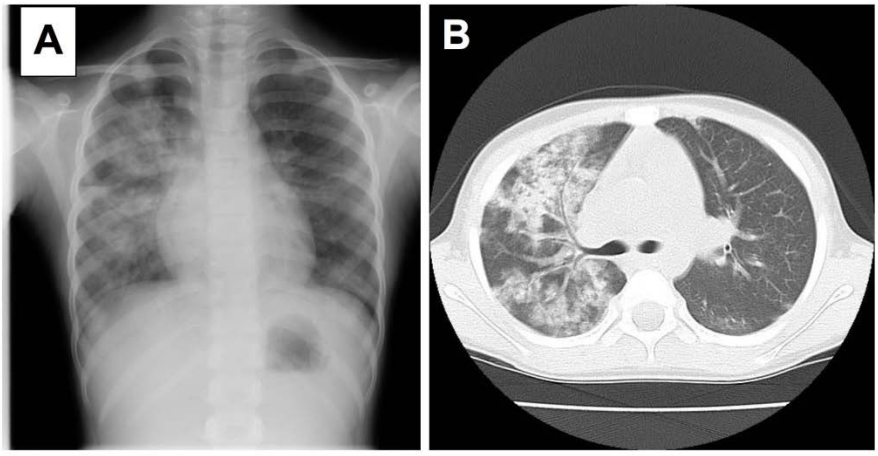
Introduction

Microscopic polyangiitis (MPA) is a primary systemic vasculitis of microvessels including capillaries, microarteries, and veins without immune complex deposition [1, 2]. It is characterized by the presence of circulating anti-neutrophil cytoplasmic autoantibodies (ANCA), especially anti-myeloperoxidase antibodies (MPO-ANCA) [1, 2]. The average age of onset is between 50–60 years [2] and childhood MPA is very rare [3-5]. Skin lesions are found in 30–60% of patients with MPA [2]. However, skin lesions of MPA in pediatric patients have not been examined in detail. Herein, we describe a case of childhood MPA with skin manifestations.

Case report

A 7-year-old girl was admitted to the department of Pediatrics of Kakogawa West City Hospital because of marked anemia (hemoglobin 3.4 g/dl), fever, and cough on February 17, 2008. Chest X-ray (Figure 1A) and computed tomography scan (Figure 1B) revealed diffuse infiltrates in both lung fields with greater prominence in the right lung, suggesting alveolar hemorrhage. On physical examination, maculopapular, erythematous, and purpuric lesions were observed on the cheeks (Figure 2), elbows, and knees. Although a definitive diagnosis was

not reached at this time, the patient was treated with a blood transfusion, antibiotics, and topical corticosteroids, resulting in an improvement in symptoms and laboratory parameters within a week. On March 7, 2008, a similar skin eruption reappeared and was accompanied by knee joint pain, myalgia in the lower extremities, fever, cough, nasal discharge and hemoptysis. Alveolar hemorrhage was suspected and the patient was readmitted. Physical examination revealed skin lesions on the cheeks, elbows and knees similar to those seen in the first admission. In addition, palpable purpura was observed on the legs (Figure. 3) and dorsum o feet. Laboratory findings were as follows: leukocyte count 6270/mm^3 (normal 3500–8500), neutrophils 69% (normal 30–65), eosinophils 5% (normal 0–6), monocytes 7% (normal 4–12), lymphocytes 17% (normal 20–55), atypical lymphocytes 2% (normal < 0), red blood cell count 381 × 10^4/mm^3 (normal 350–450 × 10^4), hemoglobin 8.9 g/dl (normal 11–16), platelet 31.6 × 10^4/mm^3 (normal 12–40 × 10^4), C-reactive protein 10.23 mg/dl (normal 0–0.3), erythrocyte sedimentation rate 53 mm/first hour (normal , 20), aspartate amino transferase 16 IU/l (normal 8–40), alanine aminotransferase 7 IU/l (normal 5–35), γ-glutamic transferase 11 IU/l (normal 9–79), alkaline phosphatase 269 IU/l (normal 110–370), lactate dehydrogenase 244 IU/l (normal 105–210), blood urea nitrogen 4 mg/dl (normal 10–22), creatinine 0.22 mg/dl (normal 0.4–1.1), total protein 6.6 g/dl (normal 6.5–8.3), albumin 3.2 g/dl (normal 3.8–5.1), KL6 352 U/ml (normal 0–499.99), IgG 1279 mg/dl (normal 932–1976), IgA 264 mg/dl (normal 102–408 mg/dl), IgM 192 mg/dl (normal 68–355), antinuclear antibody < 40 (normal < 40), anti-DNA antibody < 2.0 IU/ml (normal < 6.0), MPO-ANCA 34 EU (normal < 20), and proteinase 3 (PR3)-ANCA <10 EU (normal <10), anti-glomerular basement membrane (GBM) antibody <10 EU (normal < 10), and cryoglobulin negative (normal negative). Proteinuria and microscopic hematuria were not found. Microscopic hematuria was detected but a renal biopsy specimen disclosed no abnormalities. Histopathological examination of a skin biopsy taken from a purpuric papule showed a normal epidermis and leukocytoclastic vasculitis of the small- and medium-sized blood vessels with neutrophilic infiltrate with leukocytoclasia and extravasation of erythrocytes, affecting the entire dermis (Figure 4). Direct immunofluorescence studies were negative. Based on the clinical (palpable purpura and alveolar hemorrhage), histological (leukocytoclastic vasculitis of the small- and medium-sized blood vessels) and laboratory (positive for MPA-ANCA) findings, the patient was diagnosed with MPA associated with skin manifestations and was treated with methylprednisolone pulse therapy (30 mg/kg daily over 3 days) followed by oral prednisolone at 45 mg/day (2 mg/kg/day). Her symptoms including the skin lesions regressed within 2 weeks and MPO-ANCA became undetectable. Histopathological examination of a renal biopsy showed no abnormalities. Prednisolone was tapered and the patient was discharged on April 22 with prednisolone at 15mg/day. During the subsequent 8 months of follow-up, the skin eruption did not recur and MPO-ANCA remained negative after the prednisolone dose was tapered to a maintenance dose of 7.5 mg on alternate days. However, in January 2009, a skin eruption similar to that seen in the first and second episodes reappeared on the cheeks, elbows and knees (Fig. 5) with a concomitant rise in MPO-ANCA. Histopathological examination of a skin biopsy from an erythematous papule on the right knee revealed a subcorneal pustule containing neutrophils and focal spongiosis with several vesicles in the epidermis (Figure 6A). Prominent leukocytoclastic vasculitis affecting small- and medium-sized blood vessels was present in the entire dermis. In addition, massive interstitial infiltration of neutrophils and histiocytes accompanied by nuclear dust was evident in the collagen bundles (Figure 6B). Direct immunofluorescence was negative. The dose of prednisolone was increased to 15 mg/day and mizoribine at 250 mg/day was added; this combined therapy resulted in an improvement of the skin lesions except for those on the knees and MPO-ANCA became undetectable. The patient continued on the regimen of prednisolone 15 mg/day and mizoribine 100–250 mg/day successfully without clinical relapse. However, the skin lesions on the knees did not completely regress and intermittently worsened with slight elevation of MPO-ANCA.



Figures 1. Images of the chest X-ray (A) and computed tomography scan (B) showing diffuse infiltrates in both lung fields, especially in the right lung.

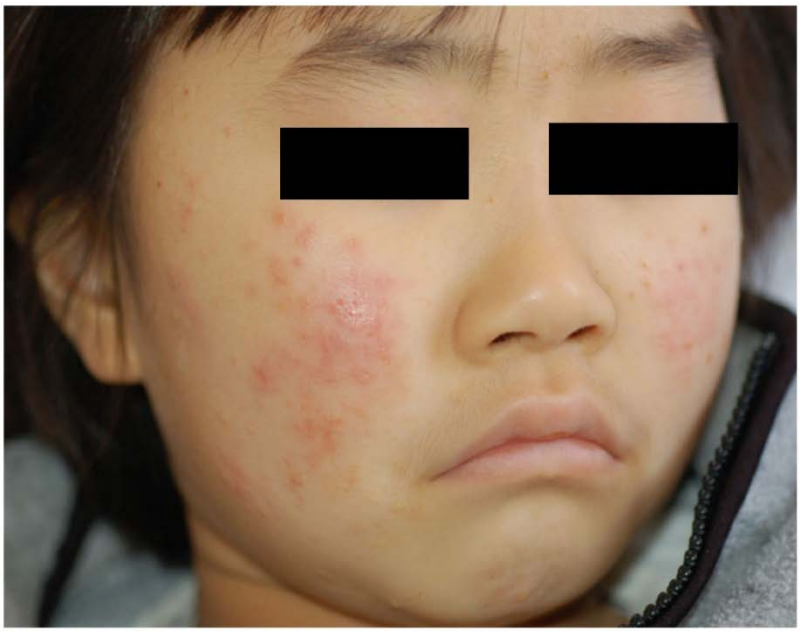


Figure 2. Maculopapular, erythematous and purpuric lesions on both cheeks in the first episode.

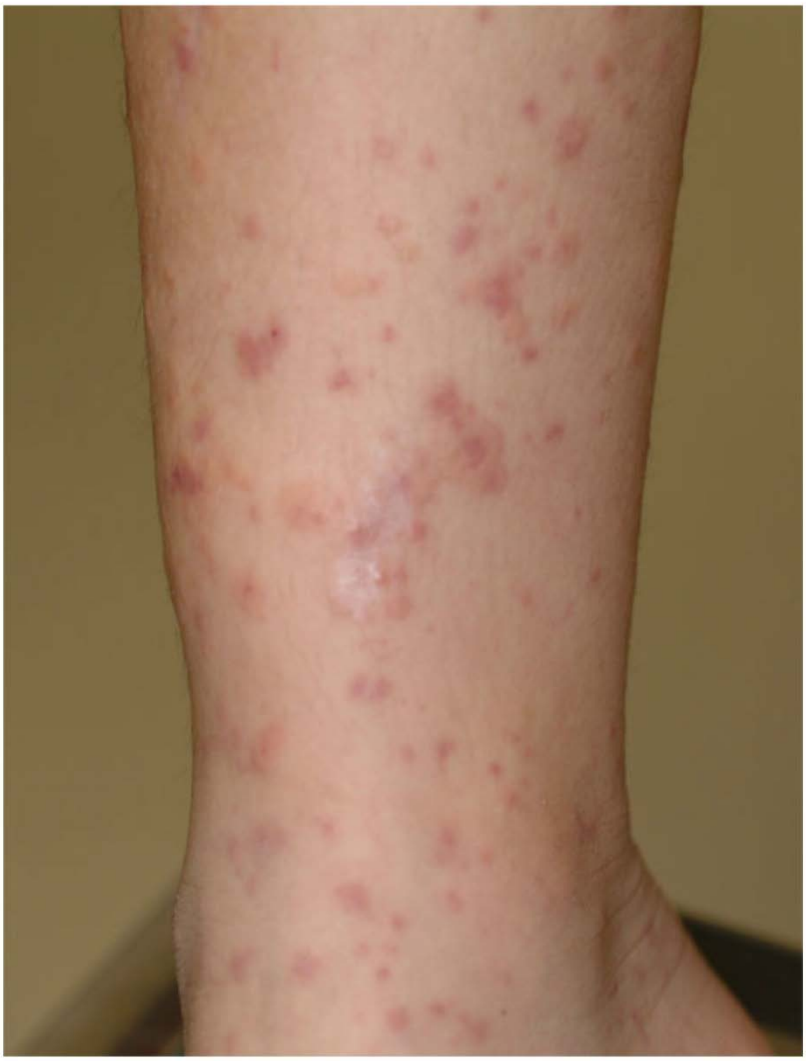


Figure 3 Palpable purpura on the right leg in the second episode.

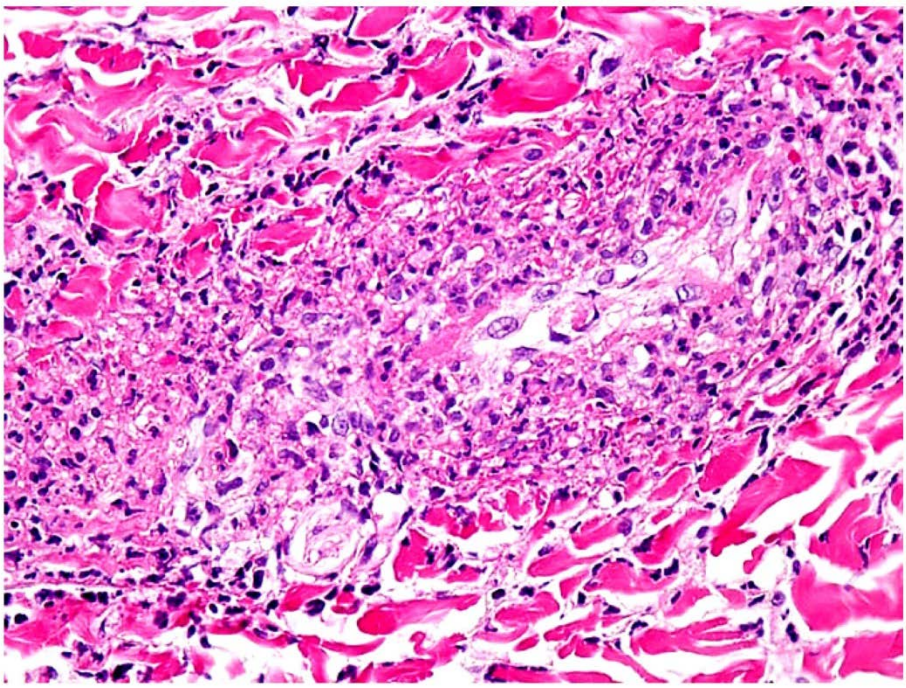


Figure 4. Histopathological examination of a biopsy taken from a purpuric papule showing small-vessel leukocytoclastic vasculitis with neutrophilic infiltrate with leukocytoclasia and extravasation of erythrocytes (hematoxylin and eosin, original magnification × 200).

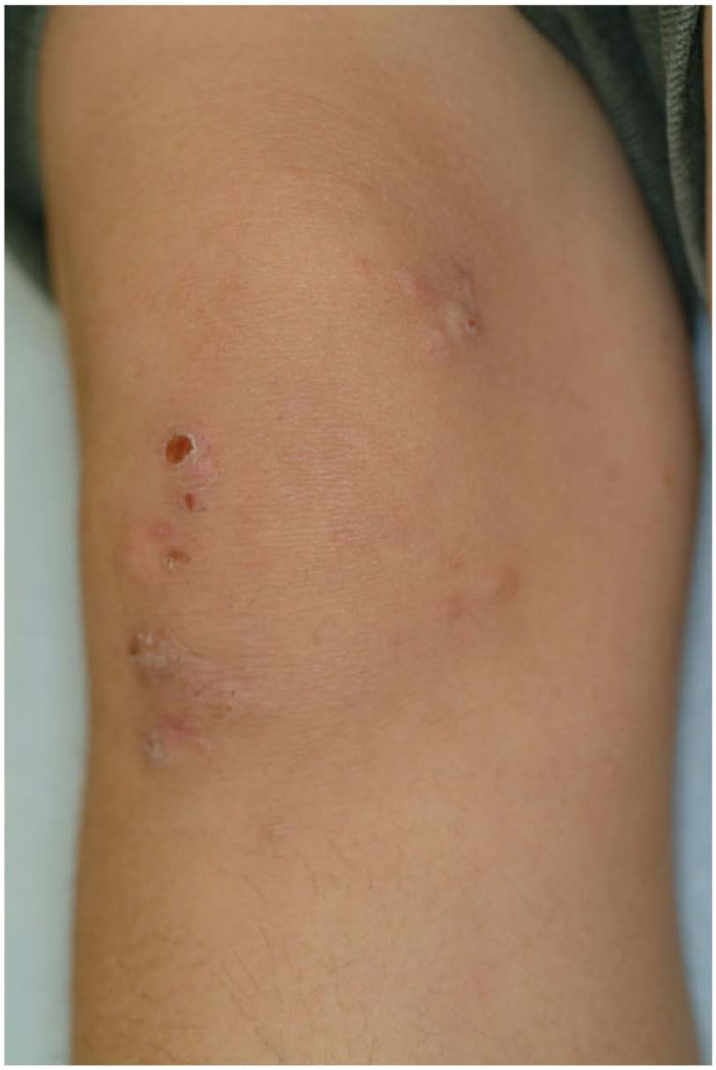
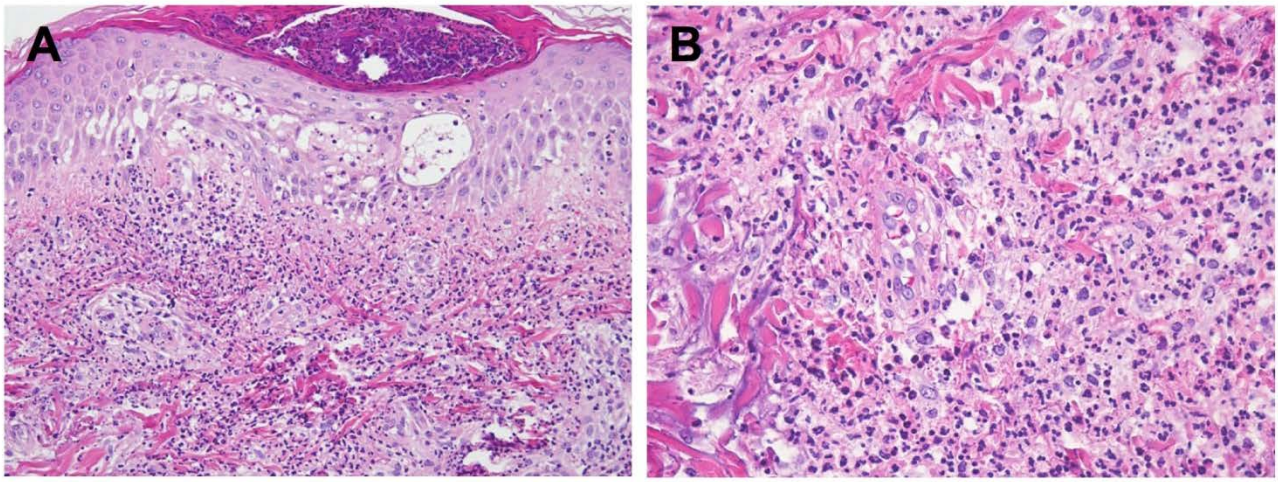


Figure 5. Palpable purpura, maculopapular, erythematous, and purpuric lesions on the right knee in the third episode.



Figures 6. Histopathological findings of an erythematous papule on the right knee in the third episode. A subcorneal pustule containing neutrophils, focal spongiosis ,and several vesicles in the epidermis were observed (hematoxylin and eosin, original magnification x 40) (A). Massive interstitial infiltration of neutrophils and histiocytes accompanied by nuclear dust was present in the collagen bundles (hematoxylin and eosin, original magnification × 200) (B).

Discussion

The following signs and symptoms are included in variable combinations in the Chapel Hill consensus criteria for MPA: 1) presence of rapidly progressive necrotizing glomerulonephritis (RPGN) and/or alveolar hemorrhage, which could be associated with other systemic manifestations of vasculitis, 2) histological demonstration of small vessel vasculitis or segmental pauci-immune necrotizing glomerulonephritis, or 3) symptoms suggesting small-vessel involvement, e.g., purpura without glomerulonephritis and/or alveolar hemorrage [1, 6]. Although RPGN is very common (79-90%) in MPA [1, 6], it was not present in the present case.

Three groups retrospectively analyzed the clinical features of pediatric cases of MPA without a complete explanation of the dermatologic manifestations in their reviews [4, 7, 8]. Peñas et al [9] described clinically and histopathologically the skin lesions of a 14-year-old girl with MPA. In their case, skin manifestations included purpuric macules and papules, vesicles, nodules, and splinter hemorrhages, which resolved with prednisone and cyclophosphamide. We used the immunosuppressive agent, mizoribine, combined with prednisolone after the third episode of the skin eruption, resulting in clinical improvement. Mizoribine is a nucleoside of the imidazole class and is approved by the Japanese Ministry of Health, Labor, and Welfare for the prevention of rejection in renal transplantation [10]. Recently, it has been used in combination with other immunosuppressants such as cyclosporine, tacrolimus, and corticosteroids, not only for transplantation, but also for ANCA-related vasculitis [10]. A case of steroid-resistant, ANCA-related vasculitis was successfully treated using mizoribine [11]. The present case suggests that mizoribine is effective for MPA.

In the present case, the severity of skin lesions correlated well with the levels of MPO-ANCA, suggesting that MPO-ANCA may play a role in the pathogenesis of the skin lesions. Further studies are necessary to clarify the precise role of MPO-ANCA in the etiology of the skin manifestations in MPA.

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