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Steroid refractory interstitial pneumonitis in a patient with juvenile dermatomyositis

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Interstitial pneumonitis is a severe complication of juvenile dermatomyositis. We report a 4-year-old girl with juvenile dermatomyositis. Coughing, shortness of breath, and general malaise developed during steroid treatment. The histology of her lung biopsy is compatible with interstitial pneumonitis. Aggressive treatment including intravenous methylprednisolone pulse therapy, intravenous immunoglobulin, and oral cyclosporin all failed. Creatinine phosphokinase level was within the normal range during the disease course. The clinical features are discussed and the importance of a differential diagnosis of interstitial pneumonitis in patients with juvenile dermatomyositis is emphasized.

Key words: Cyclosporin, interstitial pneumonitis, juvenile dermatomyositis

Juvenile dermatomyositis (JDM) is an uncommon disease with favorable outcomes in long-term follow-ups [1,2]. However, its association with interstitial pneumonitis (IP) often adversely affects the prognosis. Yasushi *et al* [2] found that the disease course and its response to steroids of IP correlated well with creatinine phosphokinase (CPK) at the onset of IP. Poorer prognosis was observed in patients without CPK elevation at the onset of IP. In addition to a poorer prognosis, IP without CPK elevation is often misdiagnosed as a common airway infection.

Case Report

A 4-year-old girl with a 1-month history of JDM was admitted for evaluation of progressive cough and general malaise of 10 days. Diagnosis was based on bilateral symmetrical weakness of the proximal muscle, typical heliotroph rash and Gottron's papules. She received imuran (2.5 mg/kg/d) and prednisolone (2 mg/kg/d) after diagnosis. Prednisolone was tapered to 1 mg/kg per day 1 month later for significant clinical improvement. After reducing the dose of prednisolone, respiratory symptoms appeared 2 weeks later and gradually progressed to a shortness of breath.

On initial examination, sinus tachycardia (135/min) was noted under normal body temperature (36.3°C) and respiratory rate (28/min). There was no new skin rash or periungual capillary change. Her muscle strength test was normal. Auscultation revealed bilateral fine rales. Laboratory tests showed an erythrocyte sedimentation rate of 32 mm/h, white blood cell count of 4800 /mm^3, serum C-reactive protein level of less than 0.7 mg/dL, serum CPK level of less than 20 U/L. The serum aspartate aminotransferase (AST) was 269 mg/dL (normal range, <40 mg/dL) and returned gradually to normal range within a week as did other elevated liver enzymes. A room-air blood gas showed a $Paco_2$ pressure of 30.2 mm Hg and PaO_2 pressure of 45.7 mm Hg. Chest radiography revealed diffuse interstitial infiltration.

Video-assisted transthoracoscopic lung biopsy was performed on Day 3 of admission. The histologic finding was compatible with IP. Special staining was negative for acid-fast bacilli, fungi, and *Pneumocystis carinii*. No virus was identified by tissue culture and serology.

While awaiting the final results of lung biopsy, her respiratory condition deteriorated and she was intubated on Day 7 of admission. Treatment was implemented, including 1 mg/kg intravenous solumedrol daily, 2 gm/kg intravenous γ-globulin, and 30 mg/kg per day intravenous pulse methylprednisolone for 3 days. Upon completion of methylprednisolone pulse therapy, pneumomediastinum developed and progressed to pneumothorax and extensive subcutaneous emphysema. *Aspergillus flavus* was isolated from the lung biopsy specimen 10 days after her lung biopsy and amphotericin B (1 gm/kg/d) was administrated intravenously. Fungal culture of the sputum before

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administration of amphotericin B and subsequent cultures were all negative. The von Willebrand's factor (vWF) was high before (392 mg/dL) and after (274 mg/dL) the first methylprednisolone pulse therapy. Cyclosporin was initiated at 5 mg/kg per day since Week 3 after admission, but she remained on a high ventilation setting (FIO_2 = 1) for the next 2 weeks, and another course of intravenous methylprednisolone pulse therapy was given. Her condition kept deteriorating and she died of respiratory failure and sepsis 6 weeks after the onset of the respiratory symptoms.

Discussion

Juvenile dermatomyositis is a multisystem disease with vasculopathy presenting predominantly on the skin and muscle. Unlike the high frequency of lung involvement in adult polymyositis or dermatomyositis (DM), interstitial lung disease is rarely reported in JDM. Trapani *et al* [4] disclosed asymptomatic lung involvement in JDM at disease onset or during follow-up in a small-series (n = 12) study. This finding suggests that early investigation of the lung condition in every JDM patient is of value because any subsequent deterioration may result in a poor prognosis. Early diagnosis and aggressive intervention may modulate its negative impact.

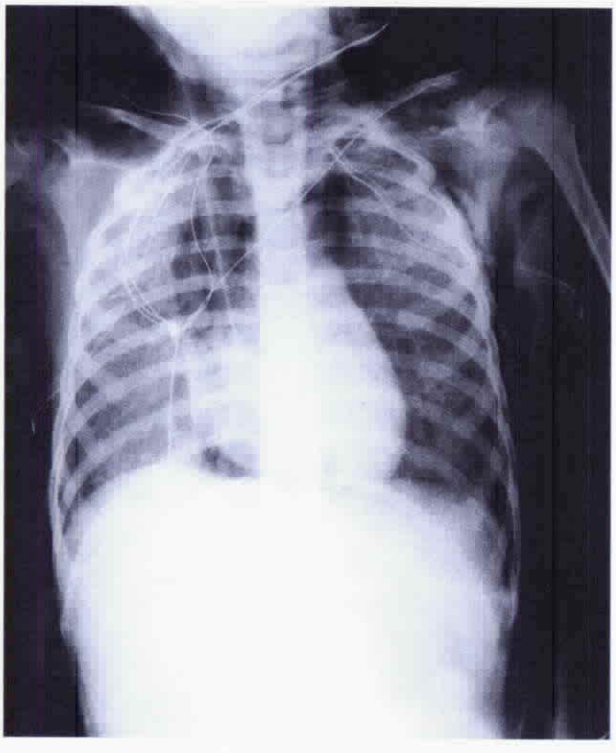

Fig. 1. Chest film taken at Day 15 of hospitalization demonstrating pneumomediastinum and extensive subcutaneous emphysema.

Because the occurrence of IP is not parallel to clinical improvement, the involvement of a new trigger factor such as a viral infection, or other atypical infection, was strongly suspected. However, tissue culture and serology were all negative. We considered *A. flavus* as a colonization or contamination, because it was isolated 10 days later and myceleal invasion was not observed in the biopsy specimen. A similar clinical course was reported in both adult and pediatric patients sharing the same characteristics–normal or slightly elevated CPK levels at the onset of IP [3,5]. Both had IP following progressive courses upon good responses to oral steroid treatment. In addition, pneumomediastinum is considered a characteristic complication of DM, because it is very rare in IP associated with other connective tissue disease. Some studies have established a correlation between vasculopathy and air leakage [6]. It is speculated that the clinical manifestation as a whole reflects the disease activity on the lung in the absence of cutaneous vasculopathy or myositis. The elevation of vWF in this patient further supports this opinion, although it does have a high false-positive rate [7].

With regard to corticosteroid-resistant IP in DM, there is no standard, efficient therapy. Various second-line immunosuppressant drugs have been tested and most efforts were in vain, except intravenous cyclophosphamide and oral cyclosporin therapy [5,6,8,9]. The response to cyclosporin is normally dramatic and significant progress can be observed within 1 week. However, success is limited to those with normal CPK and progressive IP. However, in this case we did not observe any benefit from cyclosporin as well as other rescue therapies, including intravenous methylprednisolone pulse therapy and intravenous immunoglobulin.

Juvenile dermatomyositis is thought to be heterogenous based on its different clinical presentations, response to drugs, laboratory parameters, and prognosis. Physicians should be extremely careful when managing JDM patients with normal CPK. This is particularly essential for serial evaluation of the lung condition. Once interstitial lung disease is detected, more aggressive treatment should be considered. Although cyclosporin treatment failed in this patient, early diagnosis and treatment should have modified the clinical course.

References

1. Huber AM, Lang B, LeBlanc CM, Birdi N, Bolaria RK, Malleson P, MacNeil I, Momy JA, Avery G, Feldman BM. Medium- and long-term functional outcomes in a multicenter

cohort of children with juvenile dermatomyositis. Arthritis Rheum 2000;43:541-9.
2. See Y, Giam YC, Chng HH. A retrospective study of 13 oriental children with juvenile dermatomyositis. Ann Acad Med (Singapore) 1997;26:210-4.
3. Yasushi N, Kazuhiro K, Katuhiko T, Satoshi M, Norihiko W, Masaki H, Yasuhiko K, Mitsuru K, Yasushi S, Itsuo I. Corticosteroid resistant interstitial pneumonitis in dermatomyositis/polymyositis: prediction and treatment with cyclosporin. J Rheumatol 1999;26:1527-33.
4. Trapani S, Camiciottoli G, Vierucci A, Pistolesi M, Falcini F. Pulmonary involvement in juvenile dermatomyositis: a two-year longitudinal study. Rheumatol 2001;40:216-20.
5. Yamanishi Y, Maeda H, Konishi F, Hiyama K, Yamana S, Ishioka S, Yamakido M. Dermatomyositis associated with rapidly progressive fatal interstitial pneumonitis and pneumomediastinum. Scand J Rheumatol 1999;28:58-61.
6. Hajime K, Shigeko I, Hisanori N, Mie S. Pneumomediastinum in dermatomyositis: association with cutaneous vasculopathy. Ann Rheum Dis 2000;59:372-6.
7. Bloom BJ, Tucker LB, Miller LC, Schaller JG. von Willebrand factor in juvenile dermatomyositis. J Rheumatol 1995;22:320-5.
8. Maeda K, Kimura R, Komu K, Igarashi T. Cyclosporin treatment for polymyositis/dermatomyositis: is it possible to rescue the deteriorating cases with interstitial pneumonitis? Scand J Rheumatol 1997;26:24-9.
9. Mimura T, Kanda H, Kubo K. Treatment of steroid-resistant polymyositis and dermatomyositis. Nippon Rhinsho 2001;59:2062-70.