Erythema Nodosum Associated with Pulmonary Aspergilloma

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Erythema nodosum is a cutaneous reaction pattern consisting of inflammatory, tender, nodular lesions located primarily over the extensor surface of the lower extremities. Many associated diseases have been mentioned. Herein, we report a rare case of pulmonary aspergilloma with the cutaneous manifestation of erythema nodosum in an immunocompetent 63-year-old male. He has suffered from painful nodules on lower legs with afternoon fever for 4 months. The skin biopsy on shin revealed erythema nodosum. After admission, chest x-ray examination showed right lung haziness and CT scanning revealed multiloculated cavity and ball-in-hole lesion. The skin nodules regressed soon after surgical resection of right lower lobe of the lung. Pathologically, limited fungal hyphae invasion in the periphery of the cavity was noted. Aspergillus fumigatus was cultured from the lesion. There was no relapse in 6-month follow-up. (Dermatol Sinica 19: 144-149, 2001)

Key words: Erythema nodosum, Immunocompetent, Pulmonary aspergilloma

結節性紅斑是一種好發於下肢伸側的疼痛性且皮下病灶，有多頭調查在性病因，我們報告一個罕見的與肺部肺麴菌瘤有關的病例。一位免疫功能正常的63歲男性，在下肢發生疼痛性結節有4個月之久並伴隨午後發燒，皮膚切片證實為結節性紅斑。住院檢查胸部X光發現右肺陰影，電腦斷層顯示右下肺有多淋巴性病變及空洞有球狀陰影，經內視鏡手術切除肺部病灶，病理顯示有黴菌球在病灶中央空洞外，周圍有少許菌絲進入肺實質內。病灶經培養得Aspergillus fumigatus。病人皮膚結節及發燒於術後2週內緩解，經半年追蹤皮膚病灶未復發。 (中華皮誌19: 144-149, 2001)
Erythema nodosum (EN) occurs primarily on the lower extremities and is an eruption of tender nodules as a result of inflammation of the underlying fat. It usually manifests as red, warm, painful plaques and nodules, 1 to several centimeters in diameter, varying in number from 1 to over 10. The shins, ankles, and knees are affected most often, typically in a symmetric distribution. In more extensive cases the trunk, upper extremities and rarely the face can be involved. EN may be associated with a wide variety of diseases and thus its appearance should prompt a search for an underlying etiology.

CASE REPORT

A 63-year-old rather healthy gentleman presented with a 4-month history of recurrent, painful subcutaneous lesions on the legs associated with intermittent afternoon fever. There were also oral ulcers and body weight loss of 8 kg in the previous 4 months. He was diagnosed as panniculitis and had been treated with courses of prednisolone in the past 4 months. He lived as a schoolteacher and never had the habit of smoking. There was no constitutional cough or sputum production.

On admission, the physical examination showed that the body temperature was 37.8°C, heart rate 66 beats/min, respiratory rate 20/min. On dorsa of bilateral feet, there were confluent patches of erythema with local heat. Multiple subcutaneous nodules with erythematous to brownish overlying skin were noted on the shins and calves (Fig. 1). A biopsy specimen was taken from a nodule on the inner aspect of the right shin. Microscopically, it revealed septal panniculitis with mononuclear cells infiltration (Fig. 2). The large septal vessels were spared, and neither leukocytoclastic vasculitis nor fat necrosis was observed. A perivascular inflammatory infiltrate was also noted in the dermis.

**Fig. 1**
There were more than 20 subcutaneous tender nodules with the erythematous and brownish overlying skin (arrow) on the lower legs. The size varied from 0.5 to 2 cm in diameter.

**Fig. 2**
The septa are edematous and infiltrated with mononuclear cells, extension into the periphery of the fat lobules. (H & E stain x20)
The complete blood cell count showed Hb 11.4 g/dl, Plt 315k/mm³, WBC 12510/mm³, Seg 50%, Eos 2%, Mono 5%, Lymph 43%. Other laboratory tests including rheumatoid factor, anti-HCV, anti-HIV, HbsAg, ASLO, ANA, STS and tuberculin skin test were either negative or within normal limits. But his chest x-ray taken on admission revealed a hazy density in the right middle lung field (Fig. 3). Chest CT scan showed multi-loculated bullous formation with a ball-in-hole picture in the right middle lung (Fig. 4). Blood culture, sputum culture and bronchoscopic bronchial lavage culture all failed to identify the possible infectious organism. The pulmonary function test did not show any obstructive or restrictive pulmonary disease. The patient still suffered from afternoon fever and painful skin lesions. Thus he received a thoracoscopic lobectomy of the right lower lung 2 weeks later. The surgical specimen showed a cavity filled with brownish, muddy substance. (Fig. 5) A culture of the pulmonary fungal ball yielded Aspergillus fumigatus. Pathological study of the lung tissue revealed a bronchial cyst partly lined by squamous metaplastic epithelium and the mucosa is eroded. The cystic cavity is filled with hyphal mass (Fig. 6). Focal lung parenchyma with granulomatous inflammation and few hyphae invasion were noted. There is no evidence of lung malignancy or caseous granuloma in the bronchial section. After operation, fever and the skin lesions of the legs subsided spontaneously in 2 weeks. We followed this case for 6 months and there has been no sign of recurrence.

DISCUSSION

EN is defined as a hypodermal septal inflammation associated without the involvement of the septal blood vessels, which provokes red, tender nodules of the lower limbs. EN occurs most commonly in young women, with a peak incidence of age 20 to 40 years. In addition to the cutaneous findings, patients may have fever, malaise, arthralgia, or arthritis. Typically the eruption is self-limited, lasting an average of 3 to 6 weeks. Up to 1/3 of patients have recurrences.2 As to our patient, he was a 63-year-old man and had suffered from recurrent painful nodules on the legs for 4 months. Several diseases should be considered in the differential diagnosis. These include lupus erythematosus, sarcoidosis, infection, insect bite reaction, traumatic ecchymoses, EN, lipodermatosclerosis, eosinophilic faciitis, nodular faciitis, polyarteritis nodosa, leukemia and lymphoma.3,4 Skin biopsy may help in their differentiation.

Various conditions can be associated with EN, most of them being infectious diseases, medications, and malignant diseases.5 The relative frequencies of the causative diseases of EN are variable among different studies.2,6 Associated infections include bacterial, deep fungal, and viral infections, with the most common being streptococcal infections, which usually precede the development of skin lesions.
by 2 to 3 weeks. In up to 50% of patients, the diagnosis is idiopathic, however, and work-up for underlying disease in otherwise healthy patients is usually unrewarding and probably not indicated. The diagnosis of EN is typically clinical. On the initial patient evaluation, a thorough history and physical examination should be performed. A chest x-ray should also be considered to exclude tuberculosis, fungal infection, or sarcoidosis. It was the admission chest x-ray of our patient that revealed a hazy patch on the right lung field, and prompted us for further diagnostic procedures. The subsequent chest CT scanning disclosed a ball-in-hole picture which suggested a fungal infection of the lung. Finally the culture yielded *Aspergillus fumigatus* that led us to suspect the possible association of pulmonary aspergilloma and EN. Pathologically, although hyphae did invade focally (Fig. 6) in this patient, the invasion was even mild and limited, which is different from that of invasive aspergillosis.

Aspergillums can colonize the damaged bronchial tree, pulmonary cysts, or cavities of patients with underlying lung disease such as tuberculosis, sarcoidosis, bronchiectasis, histoplasmosis, pulmonary sequestration, necrotizing pneumonia, bullous emphysema or primary lung cancer. Few of the cases (3%) could be noted in primary aspergillus invasion.

All the common species of Aspergillus which cause disease in humans are ubiquitous in the environment, growing on dead leaves, stored grain, compost piles, hay, and other decaying vegetation. Inhalation of Aspergillus spores is extremely common, but disease is rare. Invasion of lung tissue is almost entirely confined to immunocompromised patients. Although the prevalence of pulmonary tuberculosis is high in Taiwan yet we failed to demonstrate previous tuberculous infection of this patient including negative tuberculin skin test, sputum culture, pulmonary tissue culture for mycobacteria and absence of TB granuloma reaction in resected lung tissue. Survey of other possible causes of lung cavitation were not rewarding which included a negative medical history and roentgenographic study, no restrictive or obstructive impairment in pulmonary function test, no evidence of hemolytic anemia, lymphopenia, hypercalcemia, paraproteinemia, and negative finding in bronchoalveolar lavage. Thus, why our patient, an immunocompetent host, sustained pulmonary aspergilloma without any predisposing condition is unclear. A thorough review of the English literature did not reveal any report showing the association of EN with pulmonary aspergilloma in an
Systemic steroids can be used with caution, especially if an underlying infection has not been ruled out. Our patient was not treated with any anti-inflammatory agents or steroids after admission. The lesions of EN cleared up dramatically after surgical excision of the lung aspergilloma. We have followed this case for 6 months and there has been no recurrence of EN. Our case report suggests that eradication of the underlying disease, if present, is the most appropriate treatment for EN.

REFERENCES