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CASE REPORT

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Myelodysplasia presenting with pulmonary manifestations associated with neutrophilic dermatosis

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Abstract We present the case of a patient who suffered from severe pneumonia. Extensive diagnostic procedures revealed negative cultures and a severe neutrophilia in the bronchoalveolar lavage fluid suggestive of Sweet's syndrome. The persistent toxic leukocyte differentation (not induced by infection) suggested an underlying hematologic disorder. One week later, she developed cutaneous lesions indicative of neutrophilic dermatosis. Bone marrow investigation showed refractory anemia with excess of blasts (RAEB). Both the pulmonary and cutaneous infiltrates improved after treatment with chemotherapy.

Key words Sterile neutrophilic pulmonary infiltrates · Neutrophilic dermatosis · Myelodysplasia · Associated disorder

Introduction

Pulmonary infiltrations associated with neutrophilia and/or increased neutrophils in the bronchoalveolar lavage followed by neutrophilic dermatosis is rare. It has been reported in three case reports [1–3]. More frequently, neutrophilic dermatosis in combination with sterile pulmonary infiltrations has been seen (Table 1).

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Neutrophilic dermatosis such as Sweet's syndrome and pyoderma gangrenosum (PG) are different manifestations of the same entity. Sweet's syndrome was first described in 1964 [4]. The disorder is characterized by fever, multiple cutaneous lesions (tender nodules and plaques without ulceration) with dense infiltrations of neutrophils in the dermis [4]. PG is characterized by tender erythematous pustules or nodules, with ulceration, neutrophilic infiltrations, and sometimes bullae, although early lesions can mimic Sweet's syndrome [5].

In 20–54% of the cases of neutrophilic dermatosis a malignancy was found [6]. Reported associated disorders are myelodysplastic syndromes [6–10], myeloid malignancies [11], aplastic anemia [12], multiple myeloma [13], and lymphomas [5].

Some patients suffer from symptoms of PG together with symptoms indicative of Sweet's syndrome [14, 15]. It has been considered that Sweet's syndrome and PG may be different manifestations of the same entity. However, the etiology is not known.The following case history reports a woman with localized lung disease. Additionally, she showed features of Sweet's syndrome and PG. Bone marrow examination indicated a refractory anemia with excess of blasts (RAEB) [16]. We also review the relevant literature.

Case report

In February 1997, a 48-year-old, nonsmoking woman was admitted to our hospital because of a 4-day high-grade fever, right-sided pleuritic chest pain (without cough), and malaise. She had previously been in good health, using no medication. There was no history of allergy or recent infection.

Physical examination was unremarkable, except for fever with a temperature of 39.7 °C, dullness to percussion, and decreased breath sounds at the base of the right lung. The erythrocyte sedimentation rate was 126 mm in 1 h, the hemoglobin level was 6.1 mmol/l (7.5–10.0 mmol/l), mean erythrocyte volume 104 fl, reticulocytes 16 promille, white blood cell count 3.9×10^9/l with 1% blast cells, 1% myelocytes, 14% band forms, 73% polymorphonuclear leukocytes, 10% lymphocytes, 1% monocytes; her platelet count was 93×10^9/l. Renal and liver function tests were normal.

Table 1 Summary of case reports with neutrophilic dermatosis associated with pulmonary involvement

Patient (age, sex, reference)	Presenting with pulmonary involvement	Associated disorder	Treatment	Outcome
66-yr-female, 3	bilateral infiltrates	agnogenic myeloid metaplasia	local cutaneous injection of triamcinolon	improvement
53-yr-female, 1	right lower lobe infiltrates	ulcerative colitis	prednisolone 60 mg/day	improvement
60-yr-male, 2	right lower love infiltrates	refractory anemia with excess of blasts	prednisone 100 mg/day	improvement, recurrent pulmonary disease
67-yr-male, 19	no[1]	plantar pustulosis and vulval pustules	prednisone 60 mg/day	improvement, recurrent Sweet's syndrome
60-yr-male, 20	no[1]	monoclonal IgA gammopathy	1 mg/kg prednisolone	improvement
54-yr-male, 10	no[1]	myelodysplastic syndrome (refractory anemia)	240 mg, methylprednisol – one/day	improvement, recurrent cutaneous, pulmonary disease
35-yr-male, 6	no[1]	idiopathic thrombocytopenia	prednisone and dapson	improvement
46-yr-male, 6	no[1]	dermatomyositis	prednisone	improvement, recurrent cutaneous disease
74-yr-female, 6	no[1]	refractory anemia with excess of blasts	topically applied corticosteroids	improvement, later deterioration and death
61-yr-male, 6	no[1]	myeloproliferative disorder	prednisone	improvement, recurrent cutaneous and pulmonary disease

[1] = Development of pulmonary infiltrates later during the course of the disease

Serum vitamin B_{12} was 218 pmol/l (150–630 pmol/l), folate was 7.3 nmol/l (4.5–12.0 nmol/l). There were no signs of disseminated intravascular coagulation. A chest radiograph showed pulmonary infiltrates in the right lower and middle lobe with a pleural effusion (Fig. 1). Computed tomography was compatible, without evidence of cavity formation. Bronchoscopy revealed no endobronchial abnormalities.

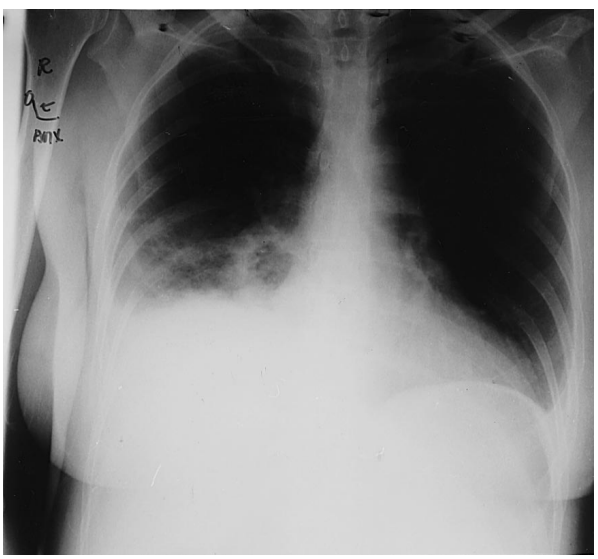

Fig. 1 Chest radiograph showing pulmonary infiltrates in the right and middle lobe

Cultures of sputum, bronchoalveolar lavage, blood, and urine remained sterile. Cellular analysis of bronchoalveolar lavage fluid disclosed an increased total cell count (22×10^4/ml), predominantly polymorphonuclear neutrophils (84%; normally <2%). Thoracocentesis revealed an exsudate with a protein content of 38.3 g/l, glucose content of 8.9 mmol/l, LDH content of 346 units/l, and the pleural effusion cell count was 2.6×10^9/l leukocytes. Culture of pleural effusion failed to demonstrate an infectious process. Cytological examination of the pleural effusion showed no malignant cells. Results of special stains and cultures for acid-fast bacilli, fungi, and viral organisms were all negative. Immune serology including ANCA, ANF, C4, C1q, and Rose Waaler Latex revealed no abnormalities. At this point the diagnosis of pneumonia of unknown origin with toxic leukocyte differentation was considered.

Despite empirical treatment with broad-spectrum antibiotics, the patient's clinical condition deteriorated and her fever persisted. One week after admittance she developed bullous cutaneous lesions on the dorsum of the left arm and several days later on her right arm and left foot (Fig. 2). Cultures of the cutaneous lesion were also sterile. Biopsy specimens were indicative of the diagnosis of Sweet's syndrome.

The cutaneous lesions progressed despite antibiotic treatment, and the patient developed cutaneous ulceration with necrosis. A second cutaneous biopsy showed no vasculitis but was indicative of PG.

A bone marrow aspirate and biopsy showed refractory anemia with an excess of blasts (RAEB, 14% blasts). Cytogenetics of bone marrow showed no abnormalities. The patient was treated with prednisone 1 mg/kg per day. Although initially there was slight clinical improvement after the onset of the corticosteroid,

Fig. 2 Bullous cutaneous lesion on the dorsum of the left arm

the cutaneous lesions progressed and the patient's pulmonary situation worsened. Therefore, the myelodysplasia was treated with chemotherapy (idarubicin 10 mg/m^2 on days 1, 3, and 5; cytarabine 100 mg/m^2 days 1–10; etoposide 100 mg/m^2 days 1–5). During this therapy the cutaneous and pulmonary infiltrates improved. However, during and after the chemotherapy the patient became platelet transfusion dependent and refractory to random platelets induced by high titers of circulating HLA antibodies. No compatible donor could be found, and the patient died of an intracerebral hemorrhage.

Discussion

This patient presented with pleuritic pain, malaise, fever, pulmonary infiltrates confirmed by chest roentgenogram, and a toxic leukocyte differentation in her blood. Initially, the diagnosis of infectious pneumonia was considered. However, cultures of bronchoalveolar lavage, sputum, pleural fluid, and blood were sterile.

During empirical treatment with antibiotics no clinical improvement was seen. The patient developed cutaneous lesions on her arms, consistent with Sweet's syndrome. Additionally, she developed cutaneous necrosis and ulcera. These lesions were indicative of PG (which diagnosis was supported by cutaneous biopsy). Bone marrow biopsy and aspiration showed refractory anemia with excess of blasts. Therefore, in this case the myelodysplastic syndrome presented with neutrophilic infiltration of the lung and a neutrophilic dermatosis. As suggested by Drent et al. [17] and demonstrated in our patient, the bronchoalveolar lavage with neutrophilia can give the clue to the diagnosis.

Ten previous case reports describing neutrophilic dermatosis associated with pulmonary involvement were found (Table 1). Seven of these ten patients suffered from an associated hematologic disorder. Thus, it is suggested that pulmonary manifestations associated with Sweet's syndrome and/or pyoderma gangrenosum are suggestive of hematologic disorders [10]. In the literature three cases of initial sterile neutrophilic pulmonary infiltrates have been described [1–3]. Only one of these cases was associated with RAEB [2].

When pulmonary neutrophilic infiltrates are seen (and/or neutrophilic dermatosis), after exclusion of infections an underlying systemic disorder may be considered. Disorders associated with neutrophilic dermatosis are hematologic disorders/malignancies and solid malignancies, inflammatory bowel disease, rheumatologic disorders such as rheumatoid arthritis, diabetes mellitus, Wegener's granulomatosis, chronic active hepatitis, granulocyte colony-stimulating factor therapy, human immunodeficiency virus, and erythema multiforme [5].

Caughman et al. suggested that Sweet's syndrome and PG are different expressions of the same disorder [18]. In patients with hematologic malignancies, PG often heralds a more aggressive stage of the underlying disease or relapse [19]. Thus, PG is probably the aggressive expression of neutrophilic dermatosis.

The treatment of choice for patients with PG/Sweet's syndrome is treatment of the underlying disorder. If no underlying disorder is identified, treatment with high doses of systemic corticosteroids can be initiated. Other options are thalidomide [19] or intralesional injections of triamcinolon for local control of the cutaneous lesions [3].

In conclusion, our case illustrates that sterile neutrophilic pulmonary lesions associated with neutrophilic dermatosis are suggestive of a hematologic malignancy. It is important to recognize neutrophilic dermatosis and/or neutrophilic pulmonary infiltrates because 50% of the patients will have a severe systemic disorder (most often a hematologic disease). Furthermore, this case demonstrates that lesions of Sweet's syndrome and PG may occur concomitantly.

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