□ CASE REPORT □

Acute Idiopathic Thrombocytopenic Purpura Complicated with Diffuse Alveolar Hemorrhage in an Elderly Patient

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Abstract

Idiopathic thrombocytopenic purpura (ITP) is a hemorrhagic disease that often occurs in the elderly. It generally presents as a chronic disease with insidious onset, and is frequently resistant to various therapies. Compared to patients less than 40 years old, those older than 60 years tend to show a higher rate of ITP-related mortality. The present report describes a 73-year-old patient with acute ITP who experienced diffuse alveolar hemorrhage that responded well to high-dose intravenous immunoglobulin therapy combined with corticosteroid pulse therapy.

Key words: idiopathic thrombocytopenic purpura, diffuse alveolar hemorrhage

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Introduction

Idiopathic thrombocytopenic purpura (ITP) is characterized by immune-mediated platelet destruction by the reticuloendothelial system and classified based on duration (acute or chronic) and age (childhood or adult). Childhood ITP is generally a benign, self-limiting disease that equally affects girls and boys. Severe hemorrhagic complications are rare and only 20% of childhood ITP patients progress to chronic disease. In contrast, adult ITP is associated with woman predominance, an 80% chronicity rate and an increased frequency of complications (1-3).

The prognosis of ITP is determined primarily by the risk of spontaneous hemorrhage associated with a low platelet count. The estimated risk of fatal hemorrhagic events is approximately 5% throughout the lifetime of patients with ITP. However, the incidence of major hemorrhagic complications and of ITP-related mortality is particularly high among elderly patients with ITP. Most fatal hemorrhages involve intracranial hemorrhage (3-6). We describe an elderly patient with acute ITP accompanied by diffuse alveolar hemorrhage (DAH).

Case Report

A 73-year-old man was admitted to our hospital in January, 2006 after 3 days of hemoptysis and dyspnea. Two weeks before admission, he had developed a febrile illness with general malaise and fatigability, but had taken no medication to relieve his symptoms. Three days before admission, generalized purpura appeared on his extremities and trunk, along with mucosal hemorrhage and hemoptysis. His medical history was unremarkable, and he was not taking any medication. On admission, he was febrile, with a body temperature of 37.9°C, a regular heart rate of 96 beats/min and blood pressure of 104/54 mmHg. A physical examination revealed diffuse scattered ecchymoses, hematoma on the palate, anemic conjunctivae, and coarse crackles in both lungs. His lymph nodes and spleen were apparently normal.

Laboratory examination revealed an extremely low platelet count ($<0.1 \times 10^4/\mu\text{L}$), elevated white blood cell (WBC) count (17,000/ μL) and serum C-reactive protein (CRP) levels (10.6 mg/dL). Disseminated intravascular coagulation was excluded based on levels of fibrinogen, fibrin degradation products and the cross-linked fragment, D-dimer. He

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Figure 1. Chest radiography and computed tomography images of the patient. A: Postero-anterior chest radiography of the thorax shows diffuse air-space consolidation. B: Computed tomography on admission reveals widely distributed ground-glass opacification of alveolar spaces with patchy consolidation. C: Chest radiography on the day after admission shows more abnormal shadowing and new patchy infiltrates throughout both lung fields. D and E: Obvious improvement is seen after treatment, although small bilateral pleural effusions persist.

was negative for human immunodeficiency virus and serological testing did not uncover infection with any other viral source. Arterial blood gas values in room air were as follows: PaO_2 72.3 Torr; PaCO_2 35.4 Torr; pH 7.559, and an abnormal alveolar-arterial (A-a) oxygen gradient (33.4 Torr). Bone marrow aspirates appeared morphologically normal, with a normal megakaryocyte count. Cytogenetic analysis of marrow cells also yielded normal results. Chest radiography on admission showed diffuse air-space consolidation with reticulonodular infiltration (Fig. 1A). Computed tomography (CT) of the chest showed widely distributed ground-glass alveolar opacification with patchy consolidation throughout both lung fields (Fig. 1B).

Platelet and red cell transfusions as well as broad-spectrum antibiotics (cefazopran) were started. His respiratory status continued to deteriorate on the day after admission, the platelet count remained at $<0.1 \times 10^4/\mu\text{L}$ and chest radiography revealed more abnormal shadows and new patchy infiltrates despite improved CRP levels (9.7 mg/dL) (Fig. 1C). Additional laboratory tests provided no evidence of secondary thrombocytopenia, suggesting a diagnosis of ITP. Tracheal intubation with ventilatory support and catecholamine administration (dopamine and dobutamine) were initiated due to rapid clinical deterioration with the development of hypotension and respiratory failure. However, the WBC count and CRP levels gradually improved. Bronchoscopy was performed through the endobronchial tube. Bleeding from the tracheo-bronchial tree was not evident, but foamy blood was aspirated from peripheral locations, suggesting blood in alveolar spaces. The culture of the aspirates was negative for any bacteria. These characteristics

suggested alveolar hemorrhage, although neither bronchoalveolar lavage nor a lung biopsy could be performed due to the condition of the patient. Foamy blood was continuously suctioned from the intubation tube thereafter. Pulsed doses of methylprednisolone (1,000 mg/day) were started together with platelet transfusions. On day 3, the patient received 0.5 g/kg/day of IVIg for 5 days to accelerate the clinical recovery (1). Follow-up chest radiography revealed a gradual improvement that preceded normalization of the platelet count. Methylprednisolone (2 mg/kg/day) was started again after the administration of IVIg. The catecholamine dosage was gradually reduced and tracheal extubation was performed on day 15, though the patient had developed left pneumothorax while on mechanical ventilation. The platelet count increased to $4.2 \times 10^4/\mu\text{L}$ on day 16. Methylprednisolone was gradually tapered as necessary to control the clinical course, and was eventually stopped 6 weeks after admission. Chest radiography and CT on day 21 showed obvious improvement in the DAH (Fig. 1D and E). The platelet count had returned to normal at $>30.0 \times 10^4/\mu\text{L}$ without any medication at 8-months of follow-up.

Discussion

DAH is rare in patients with ITP, and no reports in the literature have described DAH as a complication of ITP. Damage to the alveolar microcirculation in DAH seems to be secondary to various immune-mediated mechanisms. Heterogeneous disorders including systemic lupus erythematosus, antiphospholipid syndrome, Bechet's disease, Goodpasture's syndrome, microscopic polyarteritis, Henoch-

Table 1. Laboratory Findings on Admission I

Hematology		Blood chemistry		Serology/Others	
WBC	17000 / μ L	TP	5.3 g/dL	anti-nuclear Ab	(-)
Neu	49.0%	Alb	2.6 g/dL	anti-ds DNA Ab	(-)
Eos	3.0%	LDH	245 U/L	direct Coomb's	(-)
Baso	1.0%	GOT	21 U/L	indirect Coomb's	(-)
Mono	8.0%	GPT	24 U/L	anti-H.pylori Ab	15 U/mL
Lym	39.0%	ALP	214 U/L	HBs-Ag	(-)
RBC	233×10^4 / μ L	γ -GTP	14 U/L	HBs-Ab	(-)
Hb	7.0 g/dL	T.Bil	0.9 mg/dL	HCV-Ab	(-)
Ht	20.8%	BUN	33.0 mg/dL	HIV-Ab	(-)
PLT	$< 0.1 \times 10^4$ / μ L	Cr	0.7 mg/dL	CMV IgM	(-)
Reti	52‰	CK	150 U/L	CMV IgG	(+)
Coagulation		Na	141 mEq/L	EBV VCAIgM	(-)
		K	4.8 mEq/L	EBV VCAIgG	(-)
		Cl	104 mEq/L	B-D glucan	(-)
		CRP	10.6 mg/dL	Bone marrow aspiration	
		IgG	1075 mg/dL	NCC	4.98×10^4 / μ L
PT-INR	1.53	IgA	203 mg/dL	MgK	55 / μ L
APTT	36.6sec	IgM	112 mg/dL	Karyotype	
Fib	449mg/dL				
FDP	11 μ g/mL				
D-dimer	6.0 μ g/mL				
AT-III	84%			46,XY	(20/20)

Schonlein purpura, and Wegener's granulomatosis can generally cause DAH. Nephritis and hematuria were absent and auto-antibodies were negative in the present patient, indicating acute ITP, which could have been coincidental rather than etiological. In light of the worsening clinical status of the patient, particularly on admission, pneumonia might have exacerbated the development of DAH, since the CRP level is not always associated with the severity of infection among the elderly. Moreover, the radiographic features of the non-segmental, butterfly-like, pleural thickening or effusion in our patient suggested other causes such as left heart failure or pneumonia rather than DAH. However, bleeding from the tracheo-bronchial tree was not evident, whereas foamy blood was continuously aspirated from peripheral locations, and the culture of the aspirates was negative for any bacteria. These findings indicated a diagnosis of alveolar hemorrhage. The immediate response to high-dose IVIg therapy combined with pulsed corticosteroid therapy also suggested that DAH was associated with ITP.

Most patients with DAH display little or no hemoptysis, despite large amounts of intra-alveolar hemorrhage. Radiological signs are sometimes florid, but are more often non-specific. DAH usually presents as amorphous ground-glass attenuation on high-resolution CT of the thorax, although this clinical picture has a wide differential diagnosis (7).

Due to the clinical severity of this condition, DAH should be considered when elderly patients with ITP present with dyspnea, hemoptysis, an increased A-a gradient, anemia and diffuse alveolar filling on chest radiographs (2).

Treatment of complications associated with ITP generally includes critical care measures, high-dose parenteral glucocorticoid therapy and IVIg, either alone or in combination with platelet transfusions, though the benefit of such treatment regimens remains questionable (1). High-dose IVIg therapy appears to improve symptoms sooner than high-dose parenteral glucocorticoid therapy (8) and thus represents an appropriate first-line therapy in emergency situations. High-dose IVIg therapy combined with pulse-dose corticosteroid therapy was beneficial for our patient.

In conclusion, we present a unique case of DAH in the setting of acute ITP. Clinicians should be aware of a possible association between ITP and DAH, particularly among the elderly. In addition, the medical history, as well as the physical and targeted laboratory findings should be carefully evaluated, particularly when patients have concurrent infectious diseases.

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