A Patient with Wegener's Granulomatosis with Initial Clinical Presentations of Henoch-Schönlein Purpura

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Abstract

The initial presentation of a patient with Wegener's granulomatosis was indistinguishable from that of Henoch-Schönlein purpura. The patient presented with skin purpura and pulmonary hemorrhage followed by purpura in the colon. The diagnosis of this patient at that time was Henoch-Schönlein purpura. With time, massive lesions in the sinus and those with cavities in the lung became apparent, and a specimen obtained from the sinus massive lesion was disclosed to be granulomatous inflammation. Retrospectively, the proteinase 3 antineutrophil cytoplasmic antibody turned out to be strongly positive in her stored serum from the time of the initial presentation. (Internal Medicine 40: 1050–1054, 2001)

Key words: leukocytoclastic vasculitis, pulmonary hemorrhage, antineutrophil cytoplasmic antibody (ANCA), cytoplasmic-pattern antineutrophil cytoplasmic antibody (cANCA), proteinase 3 antineutrophil cytoplasmic antibody (PR3-ANCA), polyangiitis overlap syndrome

Introduction

There are about a dozen primary or idiopathic forms of vasculitis recognized to date. The nature and their relationship with each other remains unclear. Both Henoch-Schönlein purpura and Wegener's granulomatosis comprise vasculitic syndrome involving the same blood vessel distribution, but these two are distinct disease entities.

Henoch-Schönlein purpura is frequently seen in childhood between the ages of 2 and 11 years, while adults with this disease are occasionally encountered. Henoch-Schönlein purpura is characterized by nonthrombocytopenic purpura, the histol-

ogy of which is leukocytoclastic vasculitis, caused by IgA-dominant immune complex deposits, arthritis, gastrointestinal hemorrhage, and glomerulonephritis.

On the other hand, Wegener's granulomatosis is a rare disease of unknown prevalence which occurs in any age group, but most commonly in the 40s and 50s age bracket. Wegener's granulomatosis is recognized as a distinct clinical entity because of the granulomatous vasculitis of the upper and lower respiratory tract along with glomerulonephritis with little or no immune complex deposits. There are three pathogenic features of Wegener's granulomatosis: leukocytoclastic vasculitis, necrotizing granulomatous vasculitis in small to medium-size vessels, and ischemia due to vasculitic circulatory disturbance. The accurate diagnosis, however, can be obscured or delayed because of atypical presentation and gradual involvement of both the respiratory tract and kidneys. Recently, cytoplasmic-pattern antineutrophil autoantibodies (cANCA) with an antigen specificity for proteinase 3 (PR3-ANCA) are recognized as very sensitive serologic markers for the diagnosis of Wegener's granulomatosis (1).

Here, we present a case of a patient who had typical clinical presentations of Henoch-Schönlein purpura when she was young, and, with time, developed typical clinical presentations of Wegener's granulomatosis.

Case Report

The complex clinical course of this patient is summarized in Fig. 1. A 19-year-old woman with fever and polyarthralgia suddenly suffered from purpura on the leg followed by cough with hemoptysis in 1987. She was hospitalized at the Department of Internal Medicine II, Fukushima Medical University Hospital because of worsening dyspnea. The most relevant laboratory data on admission were follows: WBC: 5,900/mm³ (normal: 2,800–8,800); eosinophilic leukocyte: 4% (normal: 0.5–5); γ -globulin: 13.3% (normal: 11.0–23.0); IgA: 175 mg/dl (normal: 126–517); CH50: 40 U (normal: 30–45). Roent-

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Received for publication January 16, 2001; Accepted for publication June 8, 2001

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Figure 1. Clinical course, treatment and serum titers for PR3-ANCA of the patient. The patient with polyarthralgia and purpura suddenly suffered from hemoptysis in 1987. The patient presented melena with purpura on the skin and in the colon in 1990. Simultaneously, she started to suffer from tonsillitis and sinusitis. With time, the massive lesions in the sinus and the lung became apparent. The titer for PR3-ANCA in her stored serum at the initial presentation was 18.3 U/ml (normal: <0.35). Arrows in the course of prednisolone therapy indicate methylprednisolone pulse therapy. Vertical line and dotted horizontal line indicate titers for PR3-ANCA and normal range for PR3-ANCA titer, respectively. PR3-ANCA: proteinase 3 antineutrophil cytoplasmic antibody.

genographic examination of the lung (Fig. 2A) in combination with bronchofiberscopic examination revealed that she had pulmonary hemorrhage. CT scan revealed diffuse parenchymal-infiltrating shadows of both lung fields without tumorous lesions (Fig. 2B). Histopathological examination of the purpuric lesions disclosed leukocytoclastic vasculitis in the middle layer of the dermis (data not shown). Administration of 60 mg/day prednisolone relieved these symptoms in two months.

When she was 23 years old, polyarthralgia appeared followed by skin purpura and melena. Colonofiberscopic examination revealed purpuric lesions (Fig. 3), strongly suggesting that her diagnosis was Henoch-Schönlein purpura. Simultaneously, she started to suffer from tonsillitis and sinusitis.

With time, massive lesions in the sinus and those in the lung with cavities (Fig. 4A, B) became apparent. When she was 28 years old, a specimen was taken from the massive lesions in the sinus, and was disclosed to be a granulomatous inflammation (Fig. 5). Considering the histology of massive lesions in the sinus and the presence of massive lesions with cavities in the lung, a diagnosis of Wegener's granulomatosis is most likely. Histopathological examination of her kidney was not performed

because the findings of urinalyses were almost within the normal limit in her clinical course.

Retrospectively, the presence of PR3-ANCA and myeloperoxidase (MPO)-ANCA were determined in her stored serum since the previously unavailable analyses for PR3-ANCA and MPO-ANCA became available in these days. Her serum at the initial presentation turned out to be strongly positive for PR3-ANCA (18.3 U/ml, normal: <0.35), as shown in Fig. 1, and negative for MPO-ANCA (8.0 U/ml, normal: <9.0).

Discussion

ANCA-associated vasculitis, microscopic polyangiitis and Churg-Strauss syndrome should be considered in the differential diagnosis in this case. MPO-ANCA which is frequently detected in these diseases was negative and granulomatous inflammation seen in this patient was not suggestive of the diagnosis of microscopic polyangiitis. Bronchial asthma and mononeuritis multiplex usually seen in patients with Churg-Strauss syndrome were not observed in this patient.

Our patient initially presented clinical features of Henoch-

A

B

Figure 2. Chest roentgenogram showing pulmonary hemorrhage. She was hospitalized with pulmonary hemorrhage when she was 19 years old. Chest roentgenogram shows diffuse infiltrating shadows of both lung fields without massive lesions (A). CT scan reveals diffuse parenchymal-infiltrating shadows of both lung fields without tumorous lesions (B).

Figure 3. Colonofiberscopic findings showing purpuric lesions. Colonofiberscopic examination revealed purpuric lesions as indicated by arrows.

Schönlein purpura and, with time, those of Wegener's granulomatosis. We proposed three possible diagnoses.

First, she had two distinct diseases; Henoch-Schönlein purpura and Wegener's granulomatosis, and they were overlapped. Polyangiitis overlap syndrome could be the diagnosis for this patient. Polyangiitis overlap syndrome is a relatively new syndrome proposed by Leavitt and Fauci in 1986 (2). The overlap of polyarteritis nodosa and Churg-Strauss syndrome is the most common in this disease entity. However, it seems that clinical features of Henoch-Schönlein purpura mainly appeared in the earlier phase of her clinical course, followed by those of Wegener's granulomatosis in the later phase of her clinical course. Therefore, the term of "overlap" is not precisely appropriate.

Second, she had two distinct diseases; Henoch-Schönlein purpura followed by Wegener's granulomatosis, and they are distinct from each other. The clinical presentations of Henoch-Schönlein purpura mainly appeared from 1986 to 1993. Massive lesions in the sinus and the lungs became apparent in 1993, however the clinical presentations suggestive of Wegener's granulomatosis, such as tonsillitis and sinusitis, appeared in 1990. The clinical presentations of the two diseases seem to have gradually become altered with time, resulting in overlapping at least in part, of the clinical features of Henoch-Schönlein purpura and those of Wegener's granulomatosis in 1990, suggesting that both diseases are closely related and not distinct from each other.

Third, she had only one disease; Wegener's granulomatosis whose clinical presentations were not typical, but rather typi-

A

B

Figure 4. Chest roentgenogram showing massive lesions with cavities. Chest roentgenogram, taken when she was 28 years old, shows two massive lesions with cavities as indicated by arrows in the right lung field (A). CT scan reveals massive lesions with cavities in the lung (B).

Figure 5. Histological findings of the massive lesions in the sinus. The specimen from the massive lesions in the sinus was disclosed to be a granulomatous inflammation (HE stain, ×100).

cal as Henoch-Schönlein purpura followed by Wegener's granulomatosis with typical clinical presentations.

Diffuse pulmonary hemorrhage has been increasingly recognized as a complication of the above-mentioned diseases (3). Pulmonary hemorrhage may occur in patients with Henoch-Schönlein purpura (4, 5), but is quite uncommon in patients with Wegener's granulomatosis who do not have granulomatous lesions in the lung. Therefore, her clinical presentations such as melena, colonic purpura and skin purpura with histology of leukocytoclastic vasculitis in combination with pulmo-

nary hemorrhage should be interpreted as Henoch-Schönlein purpura.

However, McHugh et al reported five pediatric patients with Wegener's granulomatosis, and three out of the five patients had pulmonary hemorrhage without granulomatous lesions in the lung (6). Therefore, it seems that pulmonary hemorrhage may be a more common form of pediatric Wegener's granulomatosis, though it is quite unusual during the initial presentation in adults (7). Regarding pediatric Wegener's granulomatosis, atypical clinical presentations other than those in adulthood have been frequently reported. Hall et al reported four pediatric patients with Wegener's granulomatosis in whom the initial clinical findings were suggestive of Henoch-Schönlein purpura (8). Additionally, von Scheven et al also reported a similar case (9).

A 95% specificity of PR3-ANCA for Wegener's granulomatosis has been reported (10), but not for Henoch-Schönlein purpura (11). When the present patient presented with pulmonary hemorrhage, the PR3-ANCA titer was strongly positive as shown in the Fig. 1. Taken together, we concluded that she had been suffering from Wegener's granulomatosis whose initial clinical presentations are indistinguishable from those of Henoch-Schönlein purpura. There has been no appropriate explanation for the occurrence of clinical features which are indistinguishable from those of Henoch-Schönlein purpura in pediatric patients with Wegener's granulomatosis. The findings of the present case suggest that pediatric or young patients diagnosed as having Henoch-Schönlein purpura should be tested for the presence of ANCA and followed up for the possibility of Wegener's granulomatosis with atypical presentations.

Acknowledgments: The authors are grateful to Ms. C. Abe and Ms. K. Omata for preparing this manuscript.

This work was supported in part by a grant from the Foundation for the Research Committee for the Treatment of Early Rheumatoid Arthritis, supported by the Japanese Ministry of Health and Welfare.

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