Mod Rheumatol (2008) 18:100–104
DOI 10.1007/s10165-007-0016-x

CASE REPORT

A case of pulmonary asbestosis presenting with temporal arteritis involving multiple medium-sized vessels

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Received: 22 February 2007 / Accepted: 1 October 2007 / Published online: 26 December 2007

Abstract A 76-year-old woman with pulmonary asbestosis was admitted with fever and polymyalgia. She subsequently developed a visual disorder, hemoptysis, and hemoperitoneum. A biopsy of the temporal artery revealed the presence of giant-cell arteritis. CT and angiography showed hemorrhaging from the bronchial and abdominal arteries. These observations suggested temporal arteritis in which medium-sized vessels were involved. This case implies the association between vasculitis and asbestosis, and suggests a problem in the classification of vasculitides.

Keywords Temporal arteritis · Medium-sized vessel vasculitis · Hemoptysis · Abdominal hemorrhage · Pulmonary asbestosis

Introduction

Systemic vasculitis is a systemic autoimmune disorder whose etiology is still largely unknown. Although many efforts have been made to clarify the pathogenesis, environmental factors such as inhalational or industrial materials has not been well focused on before recent investigations showing the existence of a relationship between vasculitis and silicosis [1–6]. Asbestos is also a critical material that can induce pneumoconiosis, pleural plaques, lung cancer, and malignant mesothelioma. Although the association of asbestos with immunity has been investigated, quite a few studies provided insight into the relationship between asbestos and vasculitis [7–9].

The current classification of vasculitis syndrome, defined at the Chapel Hill Conference, is based upon the size of the suffering vessels and/or upon the detection of anti-neutrophil cytoplasmic-antibody (ANCA) [10], which has provided a definitive description especially in small-sized vessel vasculitis [11]. In contrast, since the diagnosis is still largely dependent on characteristic epidemiologic manifestations [12] in large- and medium-sized vessel vasculitides, diagnostic confusion often occurs in atypical cases.

Here, we describe a case of pulmonary asbestosis presenting with temporal arteritis with atypical manifestations, hemoptysis and hemoperitoneum.

Case report

A 76-year-old female with a 10-year history of asbestos exposure developed a low-grade fever, mild dyspnea on effort, dry cough, and polymyalgia. She visited several clinics and eventually chest computed tomography (CT) indicated pulmonary fibrosis. Oral glucocorticoids were administered (initially 20 mg of daily prednisolone) for half a year before her initial visit to our hospital. Though the dyspnea, cough, and pulmonary symptoms had not improved, fever and polymyalgia were dramatically reduced. However, because she again developed slight fever and mild polymyalgia while tapering glucocorticoids, she was referred to our hospital. Chest X-ray and chest CT showed reticular and/or reticulo-nodular shadows in both lungs, indicating pulmonary fibrosis (Fig. 1a, b). We

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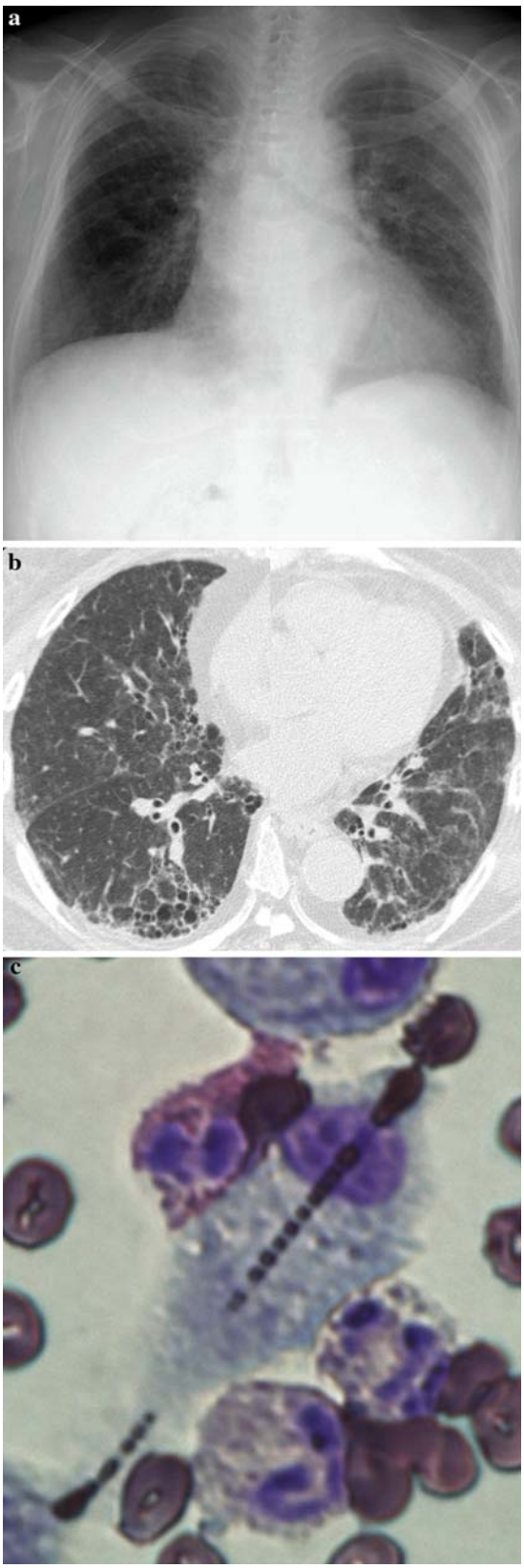

Fig. 1 Chest X-ray (**a**) and CT (**b**) upon the first visit to our hospital. Reticular and/or reticulo-nodular shadows in both lungs were observed. Asbestos body (**c**) was detected in the BALF

performed bronchoscopy on her, and several asbestos bodies were detected in her bronchoalveolar lavage fluid (BALF) (Fig. 1c). Transbronchial lung biopsy (TBLB) specimens showed non-specific parenchymal fibrosis. Our final diagnosis was pneumoconiosis due to asbestos exposure, thus the dose of glucocorticoids was reduced and finally discontinued. Two weeks after the termination of glucocorticoids, she developed a spiking fever and a severe polymyalgia located in the proximal portion of both upper and lower limbs and was then admitted to our hospital. Laboratory test results are shown in Table 1. Tests showed her C-reactive protein (CRP) value to be greater than 20 mg/dl and she had elevated erythrocyte sedimentation rate (ESR) with leukocytosis, as well as a positive-test for rheumatoid factor (RF) and low tittered positive-test for MPO-ANCA. Anti-nuclear antibody (ANA) was negative. She displayed slight fine crackles on both sides of the lower back chest and mild pitting edema on both upper and lower limbs. Severe myalgia and a strong inflammatory response made us consider the presence of polymyalgia rheumatica (PMR), however, no other causative factors, such as infection, an adverse reaction to drugs, and the presence of neoplasms, were detectable. On the following day, she suddenly complained of right-sided visual abnormality resulting from central retinal artery occlusion that was detected ophthalmoscopically in her right eye. A biopsy of right temporal artery was performed and the specimen showed infiltration of inflammatory cells with giant cells (Fig. 2) and thus we made a diagnosis of temporal arteritis (TA). Immediately, she was administered glucocorticoids pulse therapy (intravenous 500 mg of methylprednisolone for 3 days) followed by 40 mg daily of oral prednisolone. The spiking fever and polymyalgia disappeared and CRP was depressed after starting treatment. However, she developed hemoptysis on the seventh hospital day. Chest CT showed a shadow, assumed to be a hematoma and the origin of bleeding, in the right middle lobar bronchus. Because widespread ground-glass opacity was not accompanied, the hemoptysis was suspected to be due to a rupture of the bronchial artery rather than an alveolar hemorrhage (Fig. 3). With the application of hemostatics, hemoptysis was attenuated, however, hemorrhagic shock with hemoperitoneum (Fig. 4) suddenly appeared on the following day. Abdominal arterial angiography showed a ruptured aneurysm in the left gastric artery, which was treated with coil-embolization. Since her pathophysiological status indicated classical polyarteritis nodosa (cPN)-like multiple systemic vasculitis, daily oral cyclophosphamide (100 mg daily) was administered along with the prednisolone, as soon as her blood pressure and other vital signs were determined to have stabilized. No further complications were observed and she was discharged from our hospital. Her condition is presently monitored on an outpatient basis.

Table 1 Laboratory results upon hospital admission

ESR	95 (mm)
Occult blood (stool)	Negative
Urinalysis	
Protein	–
Occult blood	–
Sediments	Normal
CBC	
WBC	22,200 (μl)
Ne	88.5 (%)
Ly	5.7 (%)
Mo	4.1 (%)
Eo	1.6 (%)
Ba	0.1 (%)
RBC	327 × 104 (μl)
Hb	8.6 (g/dl)
Hct	27 (%)
Plt	40.7 × 104 (μl)
Coagulation system	
PT	17.9 (s)
APTT	41.5 (s)
Fibrinogen	593 (mg/dl)
FDP	10.5 (μg/dl)
D-dimer	3.8 (μg/dl)
Lupus anticoagulant	1.2
Biochemistry	
TP	5.6 (g/dl)
Alb	2.3 (g/dl)
BUN	20 (mg/dl)
Cr	1.04 (mg/dl)
UA	3.6 (mg/dl)
LDH	118 (IU/l)
AST	26 (IU/l)
ALT	13 (IU/l)
ALP	386 (IU/l)
γ-GTP	69 (IU/l)
T-Bil	0.5 (mg/dl)
Na	137 (mEq/l)
K	4.7 (mEq/l)
Cl	102 (mEq/l)
Ca	4 (mEq/l)
CK	29 (IU/l)
Glu	121 (mg/dl)
Fe	9 (μg/dl)
UIBC	123 (μg/dl)
Ferritin	377.2 (ng/ml)
CRP	20.4 (mg/dl)
KL-6	214 (U/ml)
Serology	
RF	270 (U/ml)
MMP-3	157 (ng/ml)
ANA	<×80
CH50	52.1 (U/ml)
C3	96 (mg/dl)
C4	12 (mg/dl)
MPO-ANCA	14.5 (U/ml)
PR3-ANCA	<1.3 (U/ml)
Anti CL-IgG	9.4 (U/ml)
Anti CL-β2GPI	<1.3 (U/ml)
β-D-glucan	<3.95 (pg/ml)
HBs-Ag	–
HBs-Ab	–
HCV-Ab	–
TPHA	–
Blood culture	Negative
Nerve conduction study	Normal

Discussion

This report presents a case of pulmonary asbestosis showing temporal arteritis with bronchial and abdominal hemorrhage, indicating the involvement of visceral arteries.

Recent investigations have shown a possible association between environmental materials and systemic vasculitis [4, 5]. Silica especially is focused upon as a causative factor for developing ANCA-associated angiitis [2, 6]. On the other hand, though asbestos is also a major material triggering pneumoconiosis as silica, the association between asbestos and vasculitis is controversial. Since the 1960s, the relationship between asbestosis and autoimmunity has been discussed [8]. RF and ANA were reported to be associated with asbestos exposure [13]. Pelclova and coworkers reported that MPO-ANCA positivity was higher in those who had exposed to asbestos. Philteos and Inoue reported cases of microscopic polyangiitis possibly associated with asbestosis [2, 14]. However, although Rihova described a clear association between silica and ANCA-associated vasculitis, the association between asbestos and vasculitis was not confirmed. It is true that the picture of pneumoconiosis of silica and that of asbestos are different. Silicosis is characterized with calcification whereas asbestosis is characterized with carcinogenesis. Such a difference may be due to the immunological dissimilarity. Wu reported the difference between silica and asbestos in the view of CD69, a cell-surface antigen, expression [15]. In the present case, positive tests for RF and ANCA were observed, and these markers decreased to the normal range in line with the resolution of fever and the diminishment in serum CRP level following immunosuppressant therapy. Although the association of RF and ANCA with neither

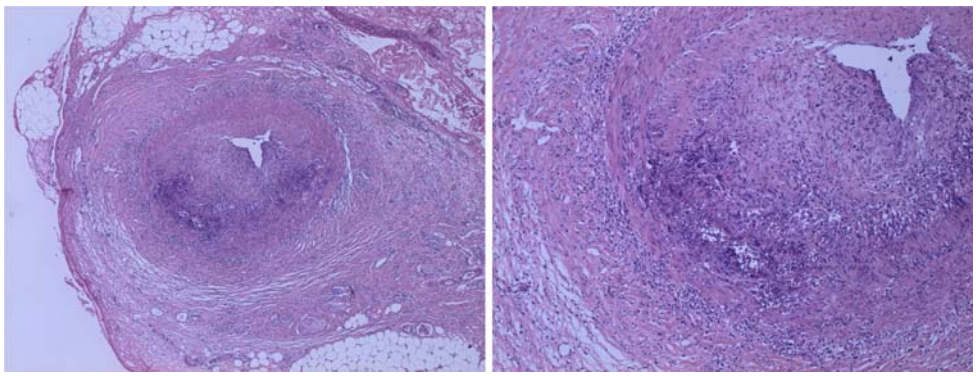

Fig. 2 Hematoxylin-Eosin staining of right temporal artery biopsy specimen. *Left picture*, with 40-fold magnification, shows many inflammatory cells infiltrating into the vessel wall of temporal artery and ruptured internal erastic membrane. *Right picture*, with 100-fold magnification, shows giant cell formation

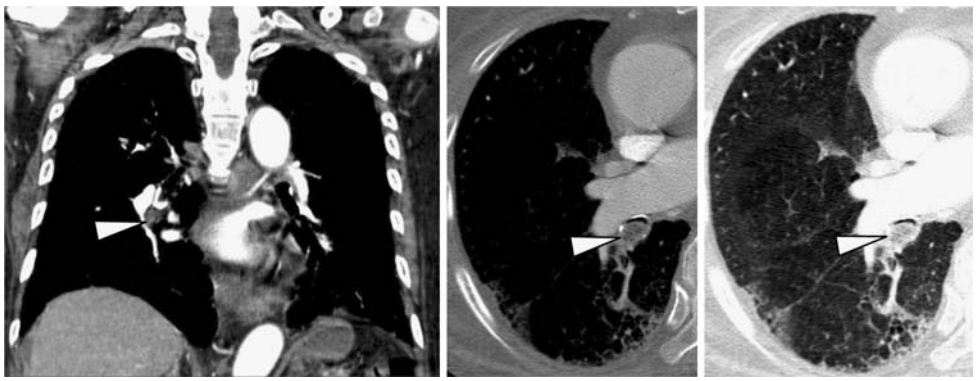

Fig. 3 Chest CT after hemoptysis. A low-density intrabronchial shadow (*arrow head*) in right middle lobar bronchus, which was supposed the origin of bleeding, without widespread ground-glass opacity, thus indicating that hemoptysis was due to a rupture of the bronchial artery rather than due to alveolar hemorrhaging

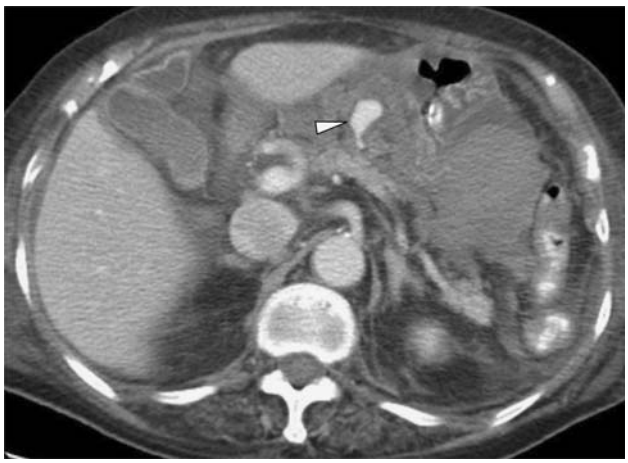

Fig. 4 Abdominal CT after hemoperitoneum and hypovolemic shock. Abdominal arterial angiography showed a rupture of the aneurysm in the left gastric artery (*arrow head*), which was treated with coil-embolization

temporal arteritis nor cPN has been confirmed, these markers seemed to be linked with the disease activity in this patient. It was obvious that this patient had underlying immunological abnormalities as evidenced by the presence of autoantibodies, and there was also a possibility that exposure to asbestos might have induced these abnormalities. However, to the best of our knowledge, no case of large-vessel vasculitis accompanying pulmonary asbestosis has ever been previously reported.

In the present classification [10], accurate discrimination between large-vessel vasculitis and medium-sized vessel vasculitis is complicated because the border between large and medium-sized vessels is ambiguous. Furthermore, large-vessel vasculitis often involves not only large but also medium-sized vessel, and vice versa. Temporal arteritis is pathologically characterized by GCA. Thus, "temporal arteritis" and "GCA" are often used to indicate the same disease [16]. On the other hand, PN is characterized by necrotizing vasculitis in multiple medium-sized vessels [12]. However, previous reports showed that necrotizing vasculitis could occur in the temporal artery, and inflammation of the temporal arteritis could occur in systemic necrotizing vasculitis patient [17–19]. Therefore, it is impossible to distinguish GCA from necrotizing vasculitis without biopsy of the temporal artery [19].

First, the condition of the present case was recognized as typical temporal arteritis when GCA was observed in biopsy specimen of the temporal artery. Accompanying visual dysfunction, which is also a typical symptom in temporal arteritis, supported this recognition. However, bronchial and abdominal involvements, which are rarely reported in cases of temporal arteritis [20], appeared after initiating glucocorticoids. Because the lesions were assumed to be multiple medium-sized visceral vessels,

which are rather typical in cPN, a diagnosis of "multiple systemic vasculitis" was made, thus leading to the administration of cyclophosphamide. Unfortunately, because the bronchial and abdominal lesions were not histopathologically verified, the presence of either granulomatous GCA or necrotizing vasculitis in bronchial artery and left gastric artery could not be determined. Although histological proof was not obtained, we believe that both temporal and visceral lesions have a similar etiology because the series of vascular events occurred within several days after the beginning of her symptoms related to severe inflammation. The presence of congenital vascular deformity as a cause of vascular rupture cannot be excluded, however, it is an extremely rare disease and merely accompanies inflammation. We therefore concluded that this patient had visceral arterial vasculitis as well as temporal arteritis and added cyclophosphamide. This case might suggest that temporal arteritis should be divided into two groups; those with or without extracephalic lesions. In the former cases, it should be considered to add immunosuppressants on glucocorticoids.

This case showed hemorrhage (which is rather atypical in cPN and in temporal arteritis) as well as occlusive symptoms. Interestingly, the hemorrhage appeared after initiating glucocorticoids and the addition of cyclophosphamide appeared to effectively manage it. Temporal arteritis is generally controllable with steroid therapy, thus, the inflammation in her vessels seemed to contain a condition requiring an immunosuppressant.

Since terminological or conceptual confusions still exist in systemic vasculitis, a better pathological or ethiological understanding of vasculitis is required for optimal clinical application. This case reflected a possible association of asbestos and the deficiencies in the current classification of systemic vasculitis, also provide information to consider more precise pathogenesis and classifications to avoid confusion in large- and medium-sized vasculitis.

Acknowledgments We thank Dr. Takahito Okazaki and Professor Kaoru Kurisu, Department of Neurosurgery, Hiroshima University Hospital, for their technical support in performing the temporal artery biopsy, Dr. Kohji Arihiro and Professor Yasuteru Inai, Department of Pathology, Hiroshima University Hospital, for assistance of histopathological evaluation, and Dr. Jun Horiguchi, Dr. Naoyuki Toyota, and Professor Katsuhide Ito, Department of Radiology, for radiological diagnostic and therapeutic support.

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