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【 CASE REPORT 】

Relapsing Polychondritis with a Cobble-stone Appearance of the Tracheal Mucosa, Preceded by Posterior Reversible Encephalopathy Syndrome

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Abstract:
A 25-year-old woman had convulsions and disturbance of consciousness. Head magnetic resonance imaging (MRI) showed punctate areas in the occipital lobes with increased signals on T2-weighted imaging. The MRI abnormalities responded well to steroid pulse therapy, so we made a diagnosis of posterior reversible encephalopathy syndrome (PRES). Three months later, she developed a fever and dyspnea. Chest computed tomography revealed marked thickness of the tracheal and bronchial wall, and bronchoscopy showed a cobble-stone appearance of the tracheal mucosa, indicative of relapsing polychondritis (RPC). We consider that PRES had developed due to autoimmune vasculitis in the brain with RPC.

Key words: relapsing polychondritis, posterior reversible encephalopathy syndrome, tracheal stenosis

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Introduction

Hinchey et al. first proposed the clinical radiographic syndrome posterior reversible encephalopathy syndrome (PRES) in 1996 (1). PRES has clinical symptoms of convulsions, disturbance of consciousness and visual changes, which are associated with the characteristic neuroimaging finding of edema of the posterior cerebral white matter. This syndrome is characterized by image findings and clinical manifestations and can be reversed with treatment. Casey et al. reported that their lesions were not only in the white matter but also in the gray matter (2). Lesions can also develop in the cortex, basal ganglia and brainstem. Therefore, the disease has been called PRES and this term has become used increasingly more often.

Relapsing polychondritis (RPC) is a rare autoimmune disease associated with inflammation in the systemic cartilage, particularly in the pinna, nose, larynx and bronchus. In 1923, this disease was reported as polychondropathia by Jackson-Wartenhorst followed by someone labeling it as RPC in 1960 (3). A large percentage of patients with RPC are positive for antibodies against cartilaginous ingredients. (4). The initial symptom of RPC is often pinna chondritis. In addition, inflammation can develop in the systemic articular cartilage, eyes, skin, airway cartilage, and cardiovascular system. It is necessary to pay attention to lesions of the larynx, trachea and bronchi in particular, as they can cause airway obstruction.

We herein report a rare case of RPC with a cobble-stone appearance of the tracheal mucosa, preceded by PRES.

Case Report

A 25-year-old woman was admitted to the Department of Neurology complaining of convulsions and disturbance of consciousness in July 2014. She was not taking any medications. Her consciousness was E3V3M5 on the Glasgow coma scale. Her blood pressure was 143/94 mmHg. She presented with an elevated body temperature (37.5℃), but her physical findings of the chest and abdomen were normal. No abnormal neurological findings were noted.

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Table 1. Laboratory Findings on the First Admission.

Hematology		Biochemistry		Immunological test		Cerebrospinal fluid	
WBC	15,190 /μL	AST	33 IU/L	CRP	4.4 mg/dL	Protein	41 mg/dL
RBC	501 ×10⁴/μL	ALT	18 IU/L	IgG	1348 mg/dL	Glucose	80 mg/dL
Hb	13.7 g/dL	LDH	316 IU/L	IgA	341 mg/dL	Leukocyte	2 /μL
Ht	39.2 %	ALP	192 IU/L	IgM	217 mg/dL	Lymphocyte	2 /μL
MCV	78.2 fL	g-GTP	18 IU/L	ANA	80 times	HSV IgM	-
MCHC	34.9 %	T-Bil	0.6 mg/dL		Homo	VZV IgM	-
Plt	29.5 ×10⁴/μL	CK	1,442 IU/L		Spec		
		Cre	0.6 mg/dL	dsDNA	<10 U/mL		
		Na	134 mEq/L	Sm	<7 U/mL		
		K	3.5 mEq/L	RNP	<7 U/mL		
		Cl	101 mEq/L	MPO-ANCA	<10 U/mL		
		Ferritin	82.3 ng/mL	PR3-ANCA	<10 U/mL		
				HSV IgM	0.29		
				VZV IgM	0.29		

WBC: white blood cell, RBC: red blood cell count, Hb: hemoglobin, Ht: hematocrit, MCV: mean corpuscular volume, MCHC: mean corpuscular hemoglobin concentration, Plt: platelet count, AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDH: lactate dehydrogenase, ALP: alkaline phosphatase, g-GTP: gamma-glutamyl transpeptidase, T-Bil: total bilirubin, CK: creatinine kinase, Cre: creatinine, CRP: C-reative protein, ANA: antinuclear antibody, Homo: homogenious, Spec: speckled, MPO-ANCA: myeloperoxidase-anti-neutrophil cytoplasmic antibodies, PR3-ANCA: proteinase-3-anti-neutrophil cytoplasmic antibodies, HSV IgM: anti-herpes simplex virus IgM antibody, VZV IgM: anti-varicella zoster virus IgM antibody

Only a mild elevation in the values of white blood cell count (WBC; 15,190/μL), C-reactive protein (CRP; 4.4 mg/dL) and creatinine kinase (CK; 1,442 IU/L) were found (Table 1). The cerebrospinal fluid analysis results were normal.

Head magnetic resonance imaging (MRI) with T2-weighted imaging, fluid-attenuated inversion recovery (FLAIR) and apparent diffusion coefficient (ADC) maps indicated punctate areas with an increased signal intensity at the parietal and posterior lobes (Fig. 1a-c). Because of the possibility of viral encephalitis, she was treated with acyclovir 1,500 mg/day for 5 days and 1,000 mg of intravenous methylprednisolone for 3 days. We did not continue the oral administration of prednisolone after intravenous methylprednisolone. Her blood pressure was normal. The convulsions improved the day after 325 mg/day of fosphenytoin, and it was changed to 500 mg/day of oral phenytoin. She completely recovered, and the abnormal MRI findings disappeared (Fig. 1d-f). She was diagnosed with PRES and discharged in August 2014. At discharge, her serum CRP levels had returned to the normal range. She did not continue taking an anticonvulsant.

She subsequently developed a fever, arthritis, cough and dyspnea in October 2014. She was readmitted in November because of an elevated serum CRP level (18.1 mg/dL). She had a fever (38.4℃), but her other vital signs were normal. Stridor was audible upon auscultation of the chest, and abdominal examinations were normal. Her auricles and nose appeared normal, but bilateral transmission deafness was observed. She did not have joint swelling or vascular murmur.

Laboratory examinations showed a WBC count of 10,660/μL (75% neutrophils, 13.7% lymphocytes, 10% monocytes, 0.9% eosinophils and 0.4% basophils), CRP 18.1 mg/dL and anti-type 2 collagen antibody 119 EU/mL (Table 2). Chest computed tomography (CT) revealed marked thickening of the tracheal and bronchial wall, resulting in bronchial stenosis (Fig. 2a, b). Bronchoscopy demonstrated a cobble-stone appearance of the tracheal mucosa and luminal stenosis (Fig. 3a, b). A biopsy was not performed in this case since it was deemed to be too risky due to the presence of severe stenosis of the airway and because the mucosa tended to bleed easily. A biopsy of the rib cartilage was performed after the initiation of therapy but failed to demonstrate chondritis pathologically. She was diagnosed with RPC according to the criteria of Damiani (5).

Treatment with 1,000 mg of intravenous methylprednisolone for 3 days followed by the oral administration of prednisolone (45 mg/day) improved her symptoms of fever, arthritis and hypacusis. Subsequent CT and bronchoscopy performed a month later revealed improvement of the wall thickness and luminal stenosis of the trachea and bronchi (Fig. 2c, d and Fig. 3c, d). She was discharged with 30 mg/day of prednisolone.

Discussion

Many cases with PRES have been reported recently, but its incidence is unknown. The reported cases have come from all age groups, from children to the elderly (6, 7). Although the pathogenesis of PRES remains unclear, it is related to cerebral autoregulatory failure and endothelial dysfunction (1).

There are many medical conditions associated with PRES. The causes of PRES are classified into medicines, underlying diseases and others (8). PRES can develop in patients who have been prescribed immunosuppressive agents for treatment of autoimmune diseases, among which cy-

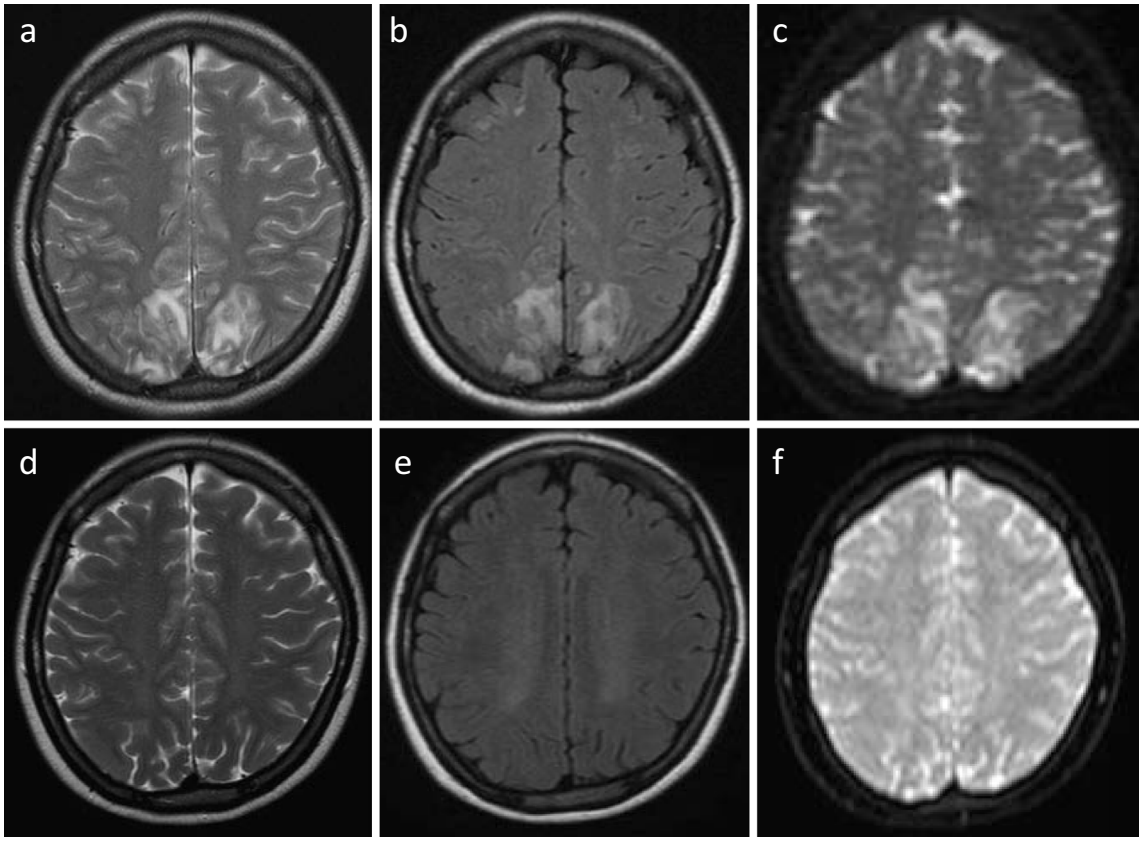

Figure 1. **Head MRI scans on admission (a-c) and after treatment (d-f). T2-weighted imaging (a, d), fluid-attenuated inversion recovery (FLAIR) (b, e), and apparent diffusion coefficient (ADC) maps (c, f).**

Table 2. **Laboratory Findings on the Second Admission.**

Hematology		Biochemistry		Immunological test			
WBC	10,660 /μL	AST	20 IU/L	CRP	18.1 mg/dL	C3	132 U/mL
RBC	484 ×10⁴/μL	ALT	16 IU/L	IgG	1,270 mg/dL	C4	42 U/mL
Hb	14.8 g/dL	LDH	157 IU/L	IgA	319 mg/dL	CH50	>60 U/mL
Ht	39.6 %	ALP	255 IU/L	IgM	185 mg/dL	Type 2 collagen	119 EU/mL
MCV	78.0 fL	g-GTP	15 IU/L	ANA	80 times		
MCHC	35.0 %	T-Bil	0.5 mg/dL		Homo		
Plt	30.1 ×10⁴/μL	CK	90 IU/L		Spec		
		Cre	0.47 mg/dL	dsDNA	<10 U/mL		
		Na	136 mEq/L	Sm	<7 U/mL		
		K	4.1 mEq/L	RNP	<7 U/mL		
		Cl	101 mEq/L	MPO-ANCA	<10 U/mL		
				PR3-ANCA	<10 U/mL		
				SS-A	<7 U/mL		
				SS-B	<7 U/mL		

WBC: white blood cell, RBC: red blood cell count, Hb: hemoglobin, Ht: hematocrit, MCV: mean corpuscular volume, MCHC: mean corpuscular hemoglobin concentration, Plt: platelet count, AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDH: lactate dehydrogenase, ALP: alkaline phosphatase, g-GTP: gamma-glutamyl transpeptidase, T-Bil: total bilirubin, CK: creatinine kinase, Cre: creatinine, CRP: C-reative protein, ANA: antinuclear antibody, Homo: homogenious, Spec: speckled, MPO-ANCA: myeloperoxidase-anti-neutrophil cytoplasmic antibodies, PR3-ANCA: proteinase-3-anti-neutrophil cytoplasmic antibodies, Type 2 collagen: anti-type2 collagen antibody

closporine is most often reported. Other agents associated with PRES are tacrolimus, interferon and monoclonal antibody against vascular endothelial growth factor (9). The underlying diseases are hypertension, pregnancy-induced hypertension syndrome, infections and autoimmune diseases, including systemic lupus erythematosus, polyarteritis no-

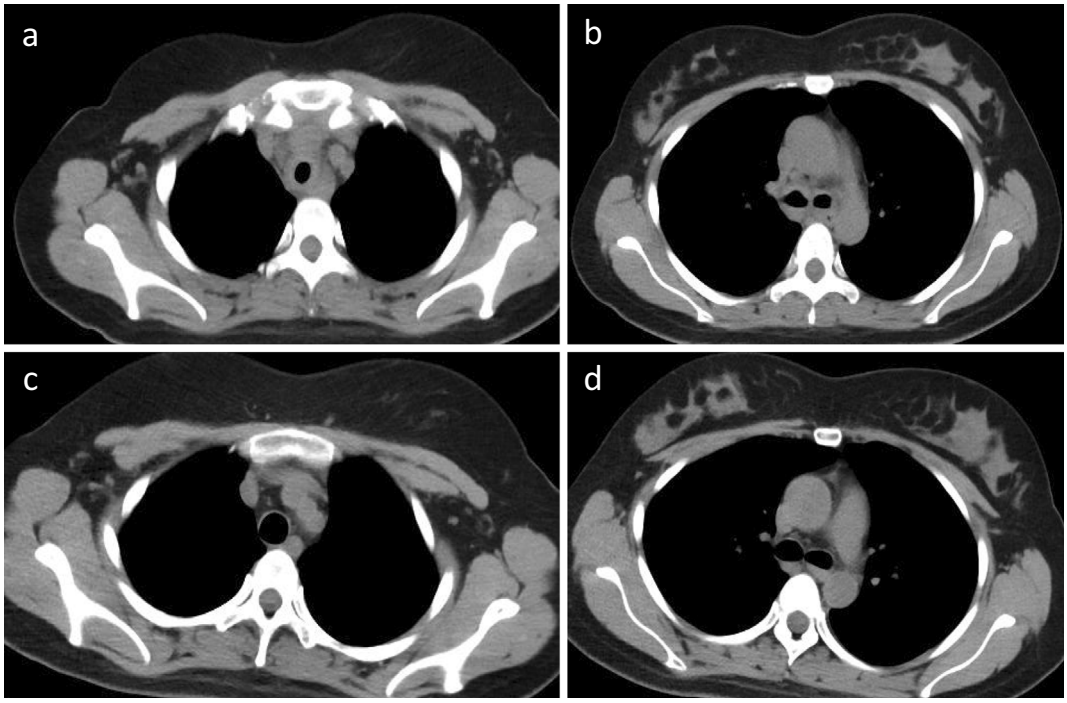

Figure 2. **CT scans on admission (a, b) and after treatment (c, d).**

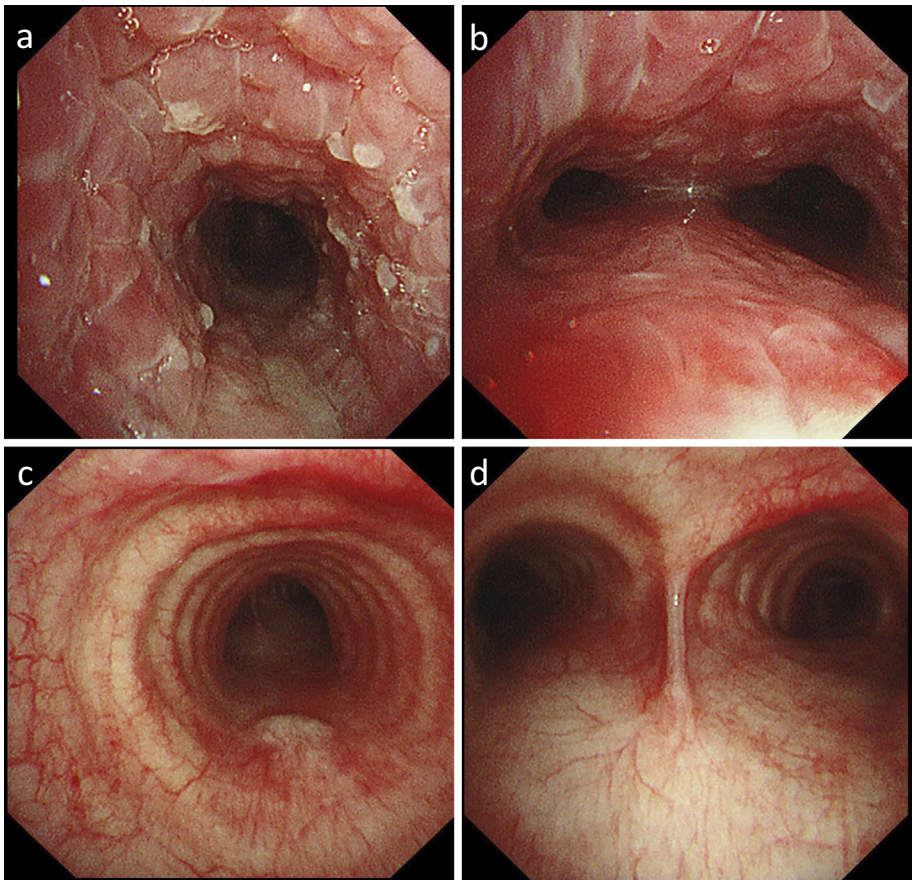

Figure 3. **Bronchoscopy findings on admission (a, b) and after treatment (c, d).**

dosa, granulomatosis with polyangitis and Takayasu arthritis (10-12). To our knowledge, there have been no reports of PRES caused by RPC. Our patients' case may have been caused by high blood pressure.

Typical MRI findings of the brain in PRES are symmetrical and posterior punctate areas of increased signal on T2-

weighted imaging and FLAIR (13), hypo- or isointense signals on diffusion-weighted imaging and an increased signal on apparent diffusion coefficient (ADC) maps (14). There are no specific diagnostic criteria for PRES. Diagnoses of PRES have been made based on the MRI findings, resolution of neurological symptoms and MRI abnormalities within days to weeks after the initiation of treatments. The present patient had typical PRES findings on MRI.

RPC is a rare autoimmune disease associated with cartilaginous inflammation, particularly in the pinna, nose, larynx and bronchi (15). Laryngeal and bronchial lesions occur in more than half of the patients and induce laryngeal pain, hoarseness, cough, wheezing and dyspnea. Stenosis of the trachea and bronchi exists in about one-quarter of cases (16) and must be treated quickly with immunosuppressive agents, as these symptoms can become life-threatening. Her tracheal stenosis and dyspnea promptly improved with 1,000 mg of intravenous methylprednisolone for 3 days and subsequently administered prednisolone, as others have reported (17, 18).

The bronchoscope findings are classified as follows: 1) inflammation of the trachea and trachea trochlea and enlargement and bulging due to edematous changes, 2) stenosis, applanation and obstruction of the bronchial lumen caused by destruction of the bronchial cartilage and 3) an esophagus-like appearance with loss of the trochlea. These findings are mixed in reality (19). A cobble-stone appearance is quite rare, and our investigation of over 60 case reports of RPC in the literature found only 1 definite case revealed by bronchoscopy in the tracheal mucosa (19, 20). In Crohn's disease, focal ulcerations around normal mucosa with polypoid mucosal changes can lead to a cobble-stone appearance (21). This appearance consists of deep linear ulcers and inflamed or normal tissue. A gap was observed between the stones in the deep ulcer and the stones in inflamed or normal tissue. We hypothesized that the cobble-stone appearance of the tracheal mucosa in the present patient was shaped by the spread of severe inflammation from the trachea trochlea to the mucosa, which was supported by the marked tracheal thickening demonstrated on CT (Fig. 2a, b).

We herein report for the first time a rare case of RPC with a cobble-stone appearance of the tracheal mucosa, preceded by PRES. Unfortunately, the association between PRES and RPC has not been proven because there were no pathological findings of PRES in our patients.

The authors state that they have no Conflict of Interest (COI).

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