Pulmonary puzzle

Muscle weakness in extremities and diffuse centrilobular nodules in lungs

CLINICAL PRESENTATION

A 72-year-old female was admitted to our hospital because of abnormal lung shadows. Two years before admission, she had complained of paraesthesia in her hands. A gait disturbance appeared a year later and gradually worsened resulting in her losing the ability to walk altogether. She had also become constipated and developed a urinary disorder.

She had undergone total gastrectomy for gastric cancer 15 years ago and had received a blood transfusion at that time. On physical examination, she presented with muscle weakness in all four extremities, thermal hypoesthesia, an inability to sense vibration and dysautonomia.

Table 1 Laboratory data on admission

Haematology	
WBC	9900/μl
Neu	74%
Eo	3%
Ba	1%
Mo	6%
Ly	16%
RBC	328×10^4/μl
Hb	9.8 g/dl
Hct	29.4%
MCV	89.6 fl
MCH	29.9 pg
MCHC	33.3%
Plt	35.0×10^4/μl
Biochemistry	
TP	7.1 g/dl
Alb	3.4 g/dl
BUN	25 mg/dl
Cr	1.07 mg/dl
Na	134 mEq/l
K	3.4 mEq/l
Cl	101 mEq/l
Ca	8.9 mg/dl
LDH	204 U/l
AST	15 U/l
ALT	11 U/l
ALP	264 U/l
T-Bil	0.3 mg/dl
CK	73 IU/l
Serology	
CRP	0.97 mg/dl
IgG	1724 mg/dl
IgA	641 mg/dl
IgM	99 mg/dl
ACE	13.2 IU/l
Lysozyme	13.2 μg/ml
KL-6	710 U/ml
RF	81 IU/ml
MPO-ANCA	<10 EU
PR3-ANCA	<10 EU
ESR	69 mm/h
Tumour markers	
CEA	2.9 ng/ml
CA19-9	15.6 IU/ml
sIL-2R	1930 U/ml
PPD skin test (−)	
Viral infection	
HIV-Ab (−)	
HTLV-1-Ab (+)	×262144 (serum)×32 (CSF)
HTLV-1 provirus (CSF)	4.5×10^4 copy/ml (free) 1.4×10^3 copy/ml (intracellular)
BALF	
Total cell count 35.7×10^4/ml	
Mo	94.5%
Neu	1.0%
Ly	4.5%
Eo	0.0%
CD4:CD8 ratio 1.4	

ACE, angiotensin-converting enzyme; Alb, albumin; ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate aminotransferase; Ba, basophils; BALF, bronchoalveolar lavage fluid; BUN, blood urea nitrogen; CEA, carcinoembryonic antigen; CK, creatine kinase; Cr, creatinine; CRP, C reactive protein; CSF, cerebrospinal fluid; Eo, eosinophils; ESR, erythrocyte sedimentation rate; Hb, haemoglobin; Hct, haematocrit; HTLV-1-Ab, human T-lymphotropic virus type 1 antibody; LDH, lactate dehydrogenase; Ly, lymphocytes; MCH, mean corpuscular haemoglobin; MCHC, mean corpuscular haemoglobin concentration; MCV, mean corpuscular volume; Mo, monocytes; MPO-ANCA, myeloperoxidase antineutrophil cytoplasmic antibodies; Neu, neutrophils; Plt, platelet count; PPD, purified protein derivative; RBC, red blood cell; RF, rheumatoid factor; T-Bil, total bilirubin; TP, total protein; WBC, white blood cell.

She had no fever. Laboratory findings indicated high lysozyme. Purified protein derivative (PPD) skin test was negative (table 1). MRI revealed T2 high-intensity areas in the cervical and thoracic spinal cord (figure 1A). Chest radiography revealed diffuse reticulonodular shadows in both lungs (figure 1B). High-resolution CT demonstrated diffuse centrilobular nodules, ground-glass opacity and bronchiectasis in both lungs (figure 1C). No acid-fast bacillus or bacterium was cultured in bronchoalveolar lavage fluid (BALF). Lacking any specific findings to diagnose in the BALF analysis and the transbronchial lung biopsy specimen, we performed a thoracoscopic lung biopsy. Microscopic findings showed lymphocyte infiltration along the bronchioles, small blood vessels and alveolar walls. Loose ill-defined epithelioid non-necrotising granulomas and giant cells were also seen along the bronchioles and small blood vessels (figure 1D,E). The granulomas varied in size, but were relatively small overall. On immunohistochemical staining, the infiltrating cells were predominantly T cells without monoclonality.

QUESTION

What is the diagnosis?

See page 552 for the answer

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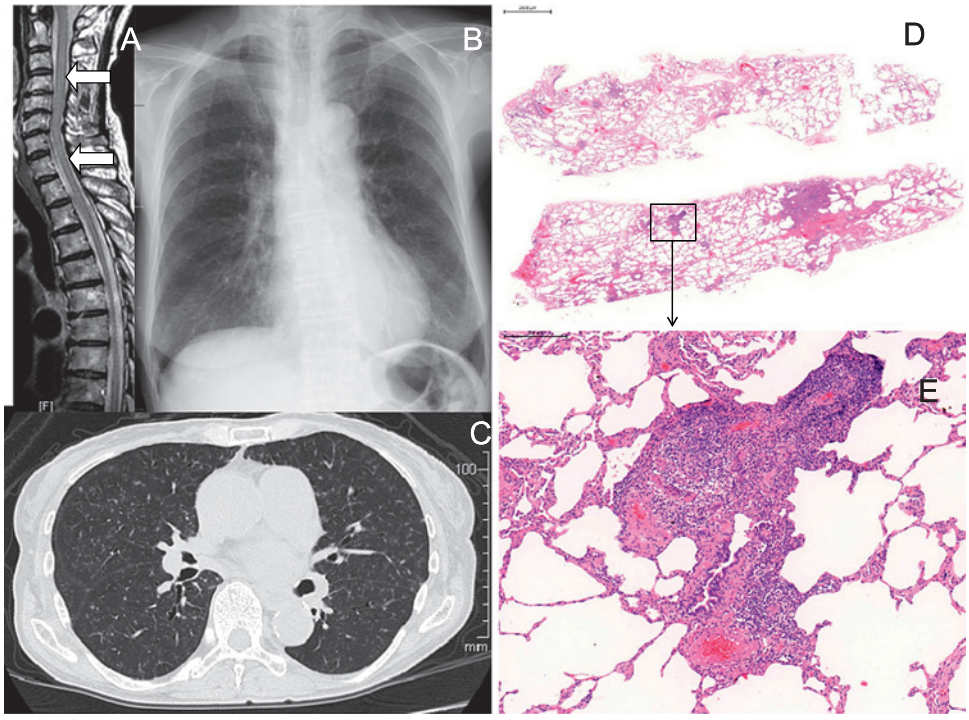

Figure 1 (A) MRI showing T2 high-intensity areas in the cervical and thoracic spinal cord. (B) Chest radiography shows diffuse reticulonodular shadows in both lungs. (C) Thin-section chest CT reveals diffuse centrilobular nodules, ground-glass opacity and bronchiectasis in both lungs. (D) Panoramic view showing multiple 1 mm-sized nodules distributed along the bronchovascular bundle and perilobular area (H&E staining). (E) Peribronchiolar and perivascular infiltration of lymphocytes with multinucleated giant cells and ill-defined granuloma (H&E staining).

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ANSWER

From the question on the page 546

The neurological findings and MRI findings in this case were compatible with both sarcoidosis and human T-lymphotropic virus type 1 (HTLV-1)-associated myelopathy/tropical spastic paraparesis. The diffuse small nodules on the chest CT were consistent with those seen in both sarcoidosis and HTLV-1-associated bronchiolo-alveolar disorder (HABA). Negative PPD skin test, high serum lysozyme and granulomas are all suggestive of sarcoidosis.

Granulomas in sarcoidosis are relatively large and discrete, mainly consist of epithelioid cells and are distributed along the lymphatics.[1] The inflammation is typically localised around the granulomas.[1] In this case, the granulomas were very loose and small. The predominant cells composing the granulomas were mutinucleated giant cells. The granulomas in this case were different from granulomas observed in sarcoidosis. Moreover, a large number of lymphocytes infiltrated into the bronchioles and small blood vessels breaking the elastic fibre layer in the vessel walls, which was too prominent for sarcoidosis.

HABA with granuloma has rarely been reported. In fact, HABA has been documented to be free of granuloma.[2] However, we diagnosed HABA in our patient based on the pathological findings, high-titre HTLV-1 antibodies in both serum and cerebrospinal fluid and the HTLV-1 provirus detected. The centrilobular nodules on CT disappeared immediately after prednisolone administration and the patient's neurological symptoms promptly improved.

On several occasions, strong similarities between the clinical findings of HABA and sarcoidosis have led to the misdiagnosis of sarcoidosis before the subsequent identification of HTLV-1-associated disease.[2–5] Identification of HTLV-1 infection should be included in the differential diagnosis of sarcoidosis.

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