Tuberculous Pleurisy with Simultaneous Bilateral Pleural Effusions: A Case Report

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Introduction

In recent years, pulmonary tuberculosis and tuberculous pleurisy have increased slightly among people in Japan. We describe our experience with tuberculous pleurisy in a 38-year-old Japanese man, who had simultaneous bilateral pleural effusions. Each effusion was bacteriologically cultured and cytologically tested. The cultures and the polymerase chain reaction (PCR) were positive for the right pleural effusion, but not the left one. The cell populations also differed between the right (94% polymorphonuclear [PMN] leukocytes PMN) and left (91% lymphocytes [LYMP]) pleural effusions. This patient was diagnosed as having tuberculous pleurisy with simultaneous bilateral pleural effusions. The results of cytologic analysis of the effusions were as follows: CD4 T cells and CD44 positive cells were increased with a high CD4/CD8 ratio in the left effusion, but not in the right one. These findings suggest that CD4 and CD44 double-positive T lymphocytes play an important role in the production of a pleural effusion. Tuberculosis infection can cause not only an inflammatory reaction but also an immune response at the same time.

Case

A 38-year-old Japanese man was seen at another clinic on March 19, 1995, with fever (38°C) and chest pain that had been continuing for one week. At that time, an antibiotic (cefotiam) and aspirin were prescribed by the physician. However, his symptoms persisted and he also developed fatigue. Therefore, he was admitted to our department on April 27. At that time, his chest X-ray films and CT scans showed bilateral pleural effusions, and he was initially diagnosed as having bacterial pleuritis (Fig. 1). On admission, his body temperature was 39.2°C. There were weak breath sounds in the bilateral lung fields and a friction rub in the right lower lung field. The white blood cell (WBC) count was 6400/ μ l with 64% neutrophils and 13.5% lymphocytes. CRP was 4.4 mg/dl, and the erythrocyte sedimentation rate was 73 mm in one hour. Thus, a moderate inflammatory process was noted. However, he sputum culture yielded only a normal flora, and the blood culture was negative. The PPD test was strongly positive ($0 \times 0/40 \times 24$ [11 $\times$ 8]mm). Serological examination showed no evidence of mycoplasma, RS virus, adenovirus or cytomegalovirus infection. The cold agglutinin test, RA test, and antinuclear antibody test were also negative.

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Fig. 1 Chest X ray film (left) and chest CT scan (right) taken on April 27, 1995, showing bilateral pleural effusions.

Fig. 2 Chest magnetic resonance image indicating medium intensity of the right pleural effusion compared with high intensity of the left one. (T1 weighted image, T2 weighted image: bottom)

The findings on chest magnetic resonance imaging indicated medium intensity of the right pleural effusion and high intensity of the left one, suggesting that the right effusion had a low protein content unlike the left one (Fig. 2). Thus, the two pleural effusions had different features. The total cell count of both effusions was increased ($1325/\mu\text{l}$ on the right and $1925/\mu\text{l}$ on the left). However, the cell populations of the pleural effusions were different, with 94% PMN leukocytes and 6% LYMP on the right versus 9% PMN leukocytes and 91% LYMP on the left. Culture for *Mycobacterium tuberculosis*

Table 1 Analysis of bilateral pleural effusions

	Right	Left
Color	Yellow & Exudate	Red & Exudate
Protein	3.2 g/dl	5.4 g/dl
Gulcose	13 mg/dl	23 mg/dl
ADA	114 IU/L	132 IU/L
LDH	1,839 IU/L	1,848 IU/L
Cell Counts	1,325 / μ l	1,925 / μ l
Cell Population	PMN 94% LYMP 6%	PMN 9% LYMP 91%
Cell surface markers		
CD4/CD8 Ratio	1.30	3.25
CD 4	48.0%	73.2%
CD 8	36.8%	22.5%
CD44	11.0%	93.1%
CD4 & CD44	9.0%	68.7%
$\gamma\delta$ -T cell receptor	11.0%	0.7%
<i>M. tuberculosis</i> Culture	(+)	(-)
Tuberculous PCR	(+)	(-)

and the tuberculosis PCR were positive on the right, but negative on the left (Table 1). This patient was eventually diagnosed as having tuberculous pleurisy with simultaneous bilateral pleural effusions. He was given isonicotinic acid hydrazide (400 mg/day), rifampicin (450 mg/day) and streptomycin sulfate (1 g/day). On day 20 of hospitalization, his leukocyte count had slightly decreased to 5200/ μ l and the CRP was 3.3 mg/dl. His pyrexia, dyspnea, and chest pain gradually improved with treatment.

We investigated the lymphocyte subpopulations in the right and left pleural effusion by two-color flowcytometry using fluorescein isothiocyanate-conjugated anti- $\gamma\delta$ T cell receptor, anti-CD8, and anti-CD44 as well as phycoerythrin-conjugated anti-CD4 (Becton Dickinson) monoclonal antibodies. Lymphocytes (10,000) were examined for cell surface markers with a flowcytometer (FCM: FACS Can [Becton Dickinson]), on April 25, 1995, when the clinical manifestations and pleural effusions were the most severe. The results obtained are shown in Table 1.

Discussion

Tuberculous pleural effusion is thought to result from a delayed hypersensitivity reaction which occurs in response to the presence of mycobacterial antigens in the pleural space¹⁾. In most patients, the differential WBC count of the effusion reveals more than 50–60% small lymphocytes^{2,3)}. The effusion is invariably an exudate^{4)–6)}. In patients with symptoms of less than 2 weeks' duration, the differential WBC count may reveal predominantly PMN leukocytes in the effusion⁷⁾, but if serial thoracentesis is performed the differential WBC count will change to predominantly small lymphocytes²⁾. The features of the left pleural effusion in our patient (Table 1) were consistent with those previously reported^{2,3)}. However, the right pleural effusion contained 94% PMN leukocytes, and was positive by culture and PCR. In a series of 62 patients with tuberculosis pleural effusion⁸⁾, 52 (83%) had predominately lymphocytes, 9 (15%) had mixed cellularity, and only 1 (2%) showed PMN leukocyte predominance in the pleural effusion. In addition only 2 (3%) had bilateral pleural effusions, but detailed analysis of the bilateral effusions was not performed. In our patient, the lymphocyte subpopulations in the right and left pleural effusions were different on FCM, 9% of the lymphocytes

on the right were CD44 & CD4 double-positive cells compared with 68.7% of the lymphocytes on the left. This finding suggested that 68.7% of the lymphocytes in the left pleural effusion were homing and recirculating helper T cells, and were involved in the immune response to tuberculous infection. There was a possibility that these T lymphocytes (CD4 & CD44 double-positive) also had a role as memory T cells⁹⁾.

Most tuberculous pleural effusions have a high level of adenosine deaminase (ADA) activity (> 45–70 IU/L) which is predominantly due to ADA isozyme type 2^{10)–12)}. In our patient, both pleural effusions had high levels of ADA activity (right: 114 IU/L, left: 132 IU/L). However, each pleural effusion had potentially different isozymes, because the right effusion contained predominantly PMN leukocytes and the left one contained predominantly lymphocytes.

These observations suggest that our patient with bilateral pleural effusions had two different types of reactions to tuberculous infection at the same time, a delayed hypersensitivity reaction involving lymphocytes on the left side and an acute inflammatory reaction involving predominantly PMN leukocytes on the right side.

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同時に左右異なる性状の胸水を認めた結核胸膜炎の1例

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要 旨

症例は38歳男性,発熱を主訴に入院.胸部X線,CT所見では,両側の iso-density の胸水が認められ,両側胸水を伴う結核性胸膜炎と診断した.しかしMRI所見は,左右異なる intensity が示され,胸水検索では左側はリンパ球優位,ADA 高値の結核性胸水の性状が観察されたが,右側は好中

球優位で結核菌培養,PCR は伴に陽性を示した.リンパ球検索では左側は,再循環型 Helper T 細胞が多かったが右側では僅かであった.本例は,左側:遅発性過敏性反応,右側:急性炎症性反応と結核菌感染に対して左右で異なる生体反応を同時に呈しており,結核性胸膜炎の発症を考える上で興味ある症例と思われた.