A 48-year-old man was transferred to our hospital because of persistent, massive bilateral pleural effusions and dyspnea. He had been in his usual state of good health until 2 weeks prior to admission, when he developed fever, chills, myalgias, and a sore throat. On admission to the other hospital, bilateral pleural effusions were noted. Despite multiple drainage procedures, the effusions reaccumulated and persisted.

**Physical Examination**


**Laboratory Findings**

WBC, 8,200, with 75 percent neutrophils, 7 percent bands, 12 percent lymphocytes, and 6 percent monocytes; erythrocyte sedimentation rate (Westergren), 97 mm/h. Antinuclear antibody test, negative. Rheumatoid factor (RF): 1:2,560. Chest radiograph: (Fig 1). Pleural fluid analysis of specimen obtained from right thoracentesis: appearance, yellow, hazy; nucleated cells: 850/mm³; differential, 96 percent segmented neutrophils, 2 percent lymphocytes, 2 percent mono-

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Diagnostic test: Review of pleural fluid cytology

Diagnosis: Rheumatoid pleurisy

The differential diagnosis of a pleural effusion with low pH, low glucose, and high LDH values includes bacterial empyema, paragonimiasis, tuberculosis, malignancy, and rheumatoid pleuritis. Cytologic analysis of pleural fluid can be helpful and, in this case, was diagnostic for rheumatoid pleuritis when granular amorphous material and elongated macrophages were demonstrated (Fig 2). These findings represented two of the three unique and pathognomonic cytologic features described in rheumatoid pleural effusions. The complete cytologic triad consists of elongated macrophages, giant multinucleated macrophages, and a background of granular necrotic debris; these cellular features are similar to the histologic findings in rheumatoid synovitis, granulomatous rheumatoid pleuritis, and subcutaneous nodules.

Nosanchuk and Naylor initially described the diagnostic triad, which they ascribed to exfoliation of pleural components from regions of granulomatous rheumatoid pleuritis. Thoracoscopy has shown that the pleural surface in rheumatoid pleuritis appears "gritty" and thickened with numerous small granules, about 0.5 mm in diameter. The appearance of the parietal pleura on microscopic examination resembles an "opened-out" rheumatoid nodule with its three component layers parallel to the pleural surface. These layers include fibrinous necrosis on the surface, palisading elongated cells, and granulation tissue with cellular infiltration including giant cells. This inflammatory covering is easily detached from the pleural surface, which may explain the high frequency of nondiagnostic blind pleural biopsies in patients with rheumatoid pleurisy.

In their series, Nosanchuk and Naylor found that 24 patients who had some or all of these cytologic features in their pleural fluid had rheumatoid arthritis; only half of the patients exhibited all 3 elements, and 5 had only granular material. Faurschou et al reported on the cytologic analysis of pleural fluid taken during 1,200 thoracoscopy procedures; 9 specimens demonstrated the triad, and all 9 were from patients who had rheumatoid arthritis. Interestingly, 1 of the 9 patients in the latter series had normal serum and pleural fluid glucose. Therefore, it appears that the specificity of the cytologic findings is high, but no assessment of sensitivity can be made based on the data from existing series.

Other cytologic changes have been observed in rheumatoid pleural effusions but are nondiagnostic. Mesothelial cells were noticeably absent from 23 of 24 pleural fluid specimens in the largest series to date. Elevated pleural rheumatoid factor and "RA cells" (ragocytes, which are leukocytes with small, spherical cytoplasmic inclusions) have been found in other diseases. Cholesterol crystals may be observed and likely reflect the chronic nature of the fluid.

In the present patient, because of the high serum rheumatoid factor level, the extremely low pleural fluid glucose concentration, and the absence of an identifiable infectious or malignant cause of the effusions, a presumptive diagnosis of rheumatoid pleurisy was made. The features of his presentation that were less typical for, but not inconsistent with, rheumatoid pleurisy were the onset of pleural effusions prior to arthritis (7 percent of cases), bilateral effusions (25 percent of cases), and massive effusions (rare). Subsequent review of his pleural fluid cytology confirmed the diagnosis of rheumatoid pleurisy by demonstrating granular amorphous material and elongated macrophages.

The patient was treated with prednisone, 60 mg/d, because of the severity of his pleuritis. His pleural effusions resolved, his forced vital capacity improved to near normal, and he resumed unrestricted work as a carpenter within 9 months. His fever, which abated by hospital day 14, was presumably due to severe rheumatoid pleurisy. Earlier recognition of his condition would have been facilitated by alerting the cytopathologist of the possibility of rheumatoid pleurisy. Appropriate therapy would have been instituted earlier, and the patient would have been spared multiple drainage procedures and diagnostic tests.

Clinical Pearls

1. The characteristic pleural fluid cytologic triad of rheumatoid pleurisy consists of elongated macrophages, giant multinucleated macrophages, and granular cell debris.

2. In the proper clinical setting with suggestive pleural fluid chemistries (glucose <30 mg/dl, pH <7.00, LDH >1000 U/L), only one or two elements of the pleural fluid cytologic triad can be diagnostic.

3. The cytopathologist should be alerted to search specifically for components of the diagnostic triad.
when rheumatoid pleurisy is suspected.

SUGGESTED READING
Faurschou P, Francis D, Faarup P. Thoracoscopic, histological and clinical findings in nine cases of rheumatoid pleural effusion.

Thorax 1985; 40:371-75