# Pathologic Quiz Case

## A 50-Year-Old Man With a Lung Mass, Respiratory Distress, and Pericardial Effusion

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A 50-year-old man presented with a lung mass, a large pericardial effusion, and gradually worsening respiratory distress. Three years earlier, he had presented to the emergency department with swelling of his left third toe accompanied by a yellowish purulent discharge. At that time, he was admitted to the hospital for 4 days of intravenous antibiotic therapy with no improvement. A subsequent orthopedic consultation and work-up including imaging studies revealed a 4.5 × 5.0-cm enhancing mass in the right mid thigh in between the gracilis and adductor muscles. After a tissue biopsy diagnosis, he underwent a resection of the toe and the thigh mass. Subsequently, he was treated with chemotherapy for 3 years.

Accepted for publication November 6, 2003.

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The authors have no relevant financial interest in the products or companies described in this article.

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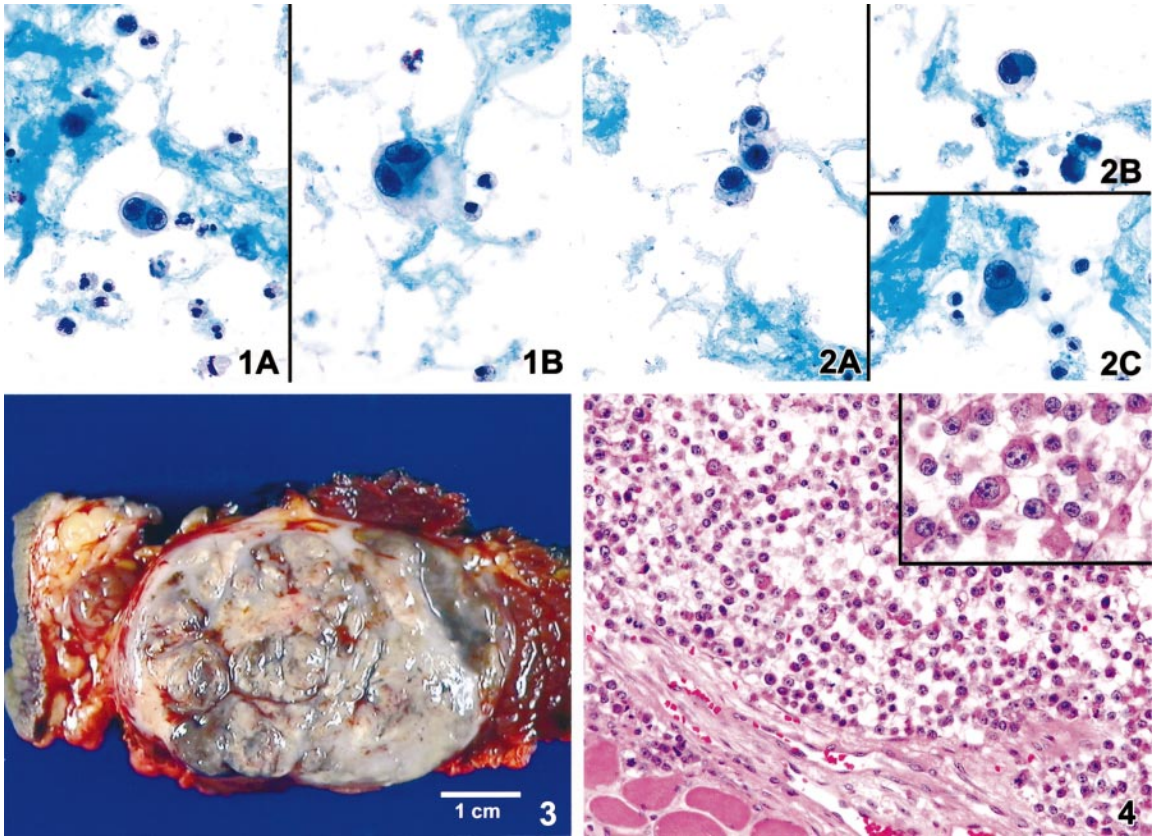
At this admission, the pericardial effusion was drained and submitted for cytopathologic examination. Papanicolaou-stained cytospin preparations were made, and the cytologic examination showed scattered large atypical cells in a background of abundant fibrin, blood, and few mesothelial cells. The cells appeared singly without any intact tissue fragments. They had round-to-oval shapes and were often binucleated with an open chromatin pattern and single prominent nucleoli (Figure 1, A and B). An eccentric placement of the nucleus often gave these cells a ''plasmacytoid'' appearance (Figure 2, A). Another prominent characteristic was the presence of a distinctive cytoplasmic inclusion seen as a dense globoid body adherent to the nucleus (Figure 2, B and C). The patient's previous neoplasm resected from the thigh was also reviewed, which had a well-circumscribed, nodular, gray-white, partially necrotic gross appearance (Figure 3). Histopathology showed cells quite similar to those seen in the pericardial fluid with round and monotonous nuclei, having an ''epithelioid'' appearance, and prominent nucleoli and dense eosinophilic cytoplasm (Figure 4).

**What is your diagnosis?**



## Pathologic Diagnosis: Metastatic Clear Cell Sarcoma (Malignant Melanoma of Soft Parts)

Clear cell sarcoma (CCS), also referred to as malignant melanoma of soft parts, was initially described by Enzinger[1] in 1968 as ''clear cell sarcoma of tendons and aponeuroses.'' CCS is a rare subtype of soft-tissue sarcoma with phenotypic (but not histogenetic) features of both melanoma and soft-tissue sarcomas. Most of the patients are young with a median age of 30 years. The most common anatomic location is the lower extremity (in approximately 75% of the cases). The origin of CCS is not entirely clear. Using immunohistochemistry, CCS is positive for melanocytic markers such as S100 protein and HMB-45 and negative for epithelial markers such as cytokeratins.

CCS is characterized by the chromosomal translocation t(12;22)(q13;q12) fusing the 5′ end of the *EWS* gene on chromosome 22 to the *ATF1* gene on chromosome 12. The latter translocation has been described in a majority of the CCS cases. The EWS/ATF1 chimeric product interferes with p53-mediated transactivation.[2] The characteristic CCS translocation is not seen in cutaneous and uveal melanomas.

CCS is an aggressive lesion, and patients who have it often have metastatic disease to the lymph nodes and lung. However, its clinical course is usually more indolent than that of metastatic malignant melanoma. The present case describes the cytopathologic features of CCS in a pericardial effusion, an extremely rare occurrence. Without knowing the previous history in this case, the metastatic malignant cells presented a broad differential diagnosis on the basis of the cytomorphologic features. First and foremost was a metastatic adenocarcinoma because of the ''epithelioid'' appearance of the cells. However, no acinar or gland formation was noted nor were cells with mucin vacuoles. A mucin stain or immunostaining for epithelial markers would be of help in this scenario. Metastatic malignant melanoma is also a close mimicker of this diagnosis because of the ''plasmacytoid'' appearance of the CCS cells as well as the frequent binucleation with the so-called ''bugs eye'' nuclei. Both CCS and melanoma may contain pigment and stain with HMB-45. Epithelioid mesothelioma and other epithelioid sarcomas should also be considered. However, in this case, the diagnosis was relatively straightforward, as the histopathologic material from the previous resection was readily available for morphologic comparison.

A few reports describing the cytomorphologic features of CCS on fine-needle aspiration have been published.[3–6] The cytologic features include cellular smears with cohesive cellular fragments as well as dispersed single cells. The cells are polygonal with abundant cytoplasm, eccentric nuclei, and often prominent nucleoli.[6,7] In rare cases, melanin may be seen in the smears.[5] Nuclei with intranuclear pseudoinclusions may be seen.[7] Creager et al[4] reported the cytomorphologic features of CCS from fine-needle aspiration and exfoliated specimens. According to this article, a significant diagnostic pitfall in CCS relates to the formation of microacinar structures, mimicking adenocarcinoma. The authors also described a rare case of the granular cell variant of CCS.

In the management of CCS, early diagnosis and initial radical surgery are important for a good outcome. Once regional lymph node metastasis or hematogenous spread has occurred, the prognosis is usually adverse. Typically, only 40% to 50% of CCS patients are long-term survivors. In one series, follow-up information on 29 patients was obtained. The 5-year survival rate of these patients was 54%. Patients with a tumor 2 cm or smaller had better survival rates than patients with a larger but still-localized tumor ($P = .009$).[8] Prognostic factors include tumor size, necrosis, and local recurrence.

In summary, we have described the cytomorphologic features of CCS in an effusion sample. The unusual clinical presentation and cytomorphology, along with the prior history of CCS, made this a challenging case. Although an uncommon occurrence, an awareness of this entity will help the physician render an accurate diagnosis by ruling out other morphologically similar entities, which will, in turn, lead to appropriate and timely patient management.

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