Crystalline Inclusions in Granulocytic Sarcoma
Report of 2 Cases and Ultrastructural Studies

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Two cases of granulocytic sarcoma were found to contain numerous crystalline inclusions identified on hematoxylin-eosin–stained sections as clusters of pointed needlelike crystals present in foci of necrosis or within macrophages. The crystals were negative for chloroacetate esterase and myeloperoxidase. Electron microscopy demonstrated homogeneously dense, bipyramidal structures, indistinguishable from Charcot-Leyden crystals. Granulocytic sarcomas may contain crystalline inclusions similar to Charcot-Leyden crystals; these structures should be distinguished from crystalline immunoglobulin inclusions occurring in cases of plasma cell myeloma and lymphoplasmacytic lymphoma, which may have a similar appearance. (Arch Pathol Lab Med. 2002;126:85–86)

The cells of acute granulocytic leukemia have been reported to contain a variety of inclusions, including Auer rods, “hexagonal” or “light green” crystals, pseudo-Chediak-Higashi granules, Charcot-Leyden crystals, and other unclassified inclusions. These inclusions have not, to our knowledge, been reported as a histologic feature of granulocytic sarcoma (GS). In this article, we report 2 cases of GS with numerous crystalline inclusions. These cases demonstrated the ultrastructural features of Charcot-Leyden crystals. Recognition of these crystals is important to avoid diagnostic confusion with plasma cell myeloma or lymphoplasmacytic lymphoma, which may contain morphologically similar immunoglobulin inclusions.

REPORT OF CASES

Case 1
A 58-year-old woman presented to the oral surgery service with a lytic lesion of the left os pubis. Complete blood count on admission revealed the following values: hemoglobin, 97 g/L; hematocrit, 0.294; platelets, 646 × 10^9/L; and white blood cells, 10.6 × 10^9/L with a normal differential. A core needle biopsy was performed and interpreted as round cell tumor suspicious for lymphoma. Immunohistochemical and ultrastructural studies established a diagnosis of GS, and the patient was referred for radiation and chemotherapy elsewhere.

MATERIALS AND METHODS

Tissue for histology was fixed in 10% neutral buffered formalin and processed for paraffin embedding. Immunohistochemistry was performed on deparaffinized sections by standard techniques. Tissue for ultrastructural studies was fixed in 3% glutaraldehyde, postfixed in osmium, and stained with uranyl acetate and lead citrate.

RESULTS

Pathology and Immunohistochemistry

Case 1.—The specimen consisted of bone and overlying mucosa infiltrated by a monotonous population of medium-sized blasts with round to ovoid nuclei and moderately abundant amorphophilic cytoplasm. Scattered macrophages were present, containing abundant intracytoplasmic, eosinophilic, needlelike crystals (Figure 1). Immunohistochemical studies showed the blasts were positive for CD43 and myeloperoxidase, and negative for CD20 and CD79a. The intracytoplasmic crystals were negative for myeloperoxidase.

Case 2.—The specimen consisted of a core biopsy infiltrated by a monotonous population of medium-sized blasts with round to ovoid nuclei and moderately abundant amorphophilic cytoplasm. Scattered clusters of extracellular, eosinophilic, needlelike crystals were present, particularly in areas of necrosis (Figure 2). Immunohistochemical studies showed the blasts were positive for myeloperoxidase and leukocyte common antigen, and negative for CD20, CD79a, and terminal deoxynucleotidyl transferase. Cytochemical staining (Leder stain) showed the blasts were positive for chloroacetate esterase, whereas the crystals were negative for myeloperoxidase and chloroacetate esterase.

Ultrastructural Studies

Electron microscopy was performed on tissue from case 2. Semithin sections were examined to select areas containing crystals. Electron microscopy demonstrated characteristic electron-dense, bipyramidal structures (Figure 3).

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COMMENT

Acute granulocytic leukemia may contain a variety of intracellular inclusions, including Auer rods, hexagonal or light green crystals, pseudo-Chediak-Higashi granules, Charcot-Leyden crystals, and other unclassified inclusions.1–6 These inclusions have not, to our knowledge, been reported as a histologic feature of GS. In the present study, we describe 2 cases of GS with numerous needlelike crystals, which had the ultrastructural features of Charcot-Leyden crystals.7 These crystals were present as intracytoplasmic inclusions in macrophages (crystal-storing histiocytes) in case 1 and as clusters associated with foci of necrosis in case 2. Eosinophils were not a prominent feature in either case.

Charcot-Leyden crystals are bipyramidal needlelike crystals that are usually found in association with eosinophils, most characteristically in the sputum of patients with allergic asthma, but also in tissue in other allergic and hematologic disorders.6 Charcot-Leyden crystals are composed of the enzyme lysophospholipase (also referred to as Charcot-Leyden crystal protein), which is present in the granules of eosinophils and basophils.9 Charcot-Leyden crystals have been reported rarely in cases of acute granulocytic leukemia,6 but have not, to our knowledge, been previously reported as a histologic feature of GS. The presence of Charcot-Leyden crystals in these cases may reflect the potential of the leukemic blasts to differentiate into eosinophils and basophils; Charcot-Leyden crystal protein is inducible in the human acute promyelocytic leukemia cell line, HL-60.10

The presence of Charcot-Leyden crystals in GS is a potential cause of diagnostic confusion, since morphologically similar crystalline inclusions may be found in cases of myeloma and lymphoplasmacytic lymphoma.8 The latter are typically positive for periodic acid–Schiff reaction and contain immunoglobulin. The presence of crystals contributed to the misdiagnosis of malignant lymphoma in case 1, because the crystal-containing macrophages mimicked the findings in crystal-storing histiocytosis associated with lymphoplasmacytic lymphoma.7 The correct diagnosis was only established retrospectively, when the patient developed overt acute granulocytic leukemia, prompting review of the previous biopsy.

In summary, pathologists should be aware of the possible presence of Charcot-Leyden-like crystals in cases of GS; these structures should be distinguished from morphologically similar crystals in plasma cell myeloma and lymphoplasmacytic lymphoma.

References