Pathologic Quiz Case

Retroperitoneal Soft Tissue Mass Presenting With Acute Renal Failure

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A 79-year-old, previously healthy man presented with left lower quadrant abdominal pain, decreased appetite, and fatigue that had been present for 2 weeks. He had no history of prior surgeries, took no medications, and denied fever or weight loss. He was treated empirically with a 7-day course of oral antibiotics for presumed diverticulitis. His symptoms failed to improve, and routine laboratory tests were ordered; laboratory values indicated acute renal failure with a serum creatinine level of 857 μmol/L (9.7 mg/dL) and mild normocytic/normochromic anemia. A renal ultrasound was performed, showing bilateral hydronephrosis. Ureteral stents were placed, followed by an abdominal computed tomographic scan to investigate the cause of his urinary obstruction. The computed tomographic scan (Figure 1) showed a large retroperitoneal soft tissue mass encasing both ureters and lymphadenopathy. The needle positioned in the mass obtained the diagnostic biopsy material. Figure 2 shows a low-power field of the core biopsy, featuring sheets of large cells with abundant granular cytoplasm accompanied by aggregates of small bland lymphocytes. At ×100 magnification (Figure 3), the cytoplasm of the large cells is filled with abundant refractile eosinophilic granules. The nuclei of these cells are small and without atypia. Lymphocytes with plasmacytic differentiation are scattered among the larger cells. No necrosis or mitoses are seen.

What is your diagnosis?
Pathologic Diagnosis: Crystal-Storing Histiocytosis

The large granular cells stained strongly positive for CD68 and \( \kappa \) light chain. Stains for keratin, HMB-45, leukocyte common antigen, L26, CD3, periodic acid–Schiff with diastase, smooth muscle and muscle-specific actin, S100, Congo red, and \( \lambda \) light chain were all negative. The granular intracellular material did not polarize, but bright fluorescence was observed when viewing a hematoxylin–eosin–stained slide under ultraviolet light microscopy (Figure 4). Flow cytometry performed on the core biopsy showed a monoclonal population of CD45-, CD19-, and CD20-positive and CD5- and CD10-negative B cells with bright surface \( \kappa \) light chain expression and a \( \kappa : \lambda \) ratio of 14:1. Serum protein electrophoresis was normal. Trace \( \kappa \) light chain proteinuria was found, prompting a bone marrow biopsy to rule out multiple myeloma. The bone marrow biopsy was hypercellular and had aggregates of small lymphocytes. Collections of small lymphocytes with plasmacytoid nuclear chromatin were seen throughout the aspirate. Flow cytometry performed on the aspirate showed the same monoclonal population of B cells as seen in the retroperitoneal core biopsy, with a \( \kappa : \lambda \) ratio of 56:1. Given the results of this workup, the diagnosis was established as crystal-storing histiocytosis (CSH) with an underlying lymphoplasmacytic lymphoma.

The differential diagnosis of this retroperitoneal soft tissue mass composed of large cells with abundant eosinophilic granular cytoplasm includes several neoplastic diseases. A granular cell tumor was considered, but such tumors are positive for S100. The patient’s age is compatible with a rhabdomyoma, but these lesions present in the head and neck, and have actin-positive cells. “Mulberry cells” of hibernomas may appear similar to the cells seen in our tissue biopsy, but hibernomas have S100-positive cytoplasmic rimming, clear lipid droplets, and present less commonly in the retroperitoneum. Negative stains for HMB-45 and actin ruled out angiomyolipoma. Retroperitoneal paragangliomas have a “zellenballen” architecture with S100-positive sustentacular cells. Alveolar soft part sarcomas present in the extremities of younger patients, are positive for periodic acid–Schiff with diastase, and have necrosis or atypia to suggest a malignant sarcomatous process. Nests or aggregates of cells divided by thin-walled vascular structures are other important features of these tumors. Finally, an oncocytoma involving the retroperitoneum would be positive for keratin.

Reactive and storage diseases must also be considered. A history of surgery, which was absent in our case, would suggest a granular cell reaction. Michaelis-Gutmann bodies would be diagnostic of malakoplakia. Special stains (periodic acid–Schiff with diastase, Congo red, and colloidal iron) and presence of polarizable material can help rule out foreign material, such as silicone and polyvinylpyrrolidone (PVP). Gaucher disease has long been confused with CSH, although Gaucher cells have paler, so-called wrinkled-paper cytoplasm. Clinical features of sphenomegaly and an abnormal glucocerebrosidase level are diagnostic. Lastly, systemic mastocytosis is accompanied by eosinophils and paler granular cells than those seen in CSH, with positive Leder stain and appropriate clinical scenario. In addition to morphologic and immunohistochemical staining differences, none of the differential diagnoses mentioned would stain positively for \( \kappa \) or \( \lambda \) light chain, nor would flow cytometry show a monoclonal B-cell process.

Crystal-storing histiocytosis was first described in 1917 by Glaus, with an autopsy featuring a diagnosis of so-called granular myeloma. His descriptions and drawings of large granular cells replacing the bone marrow depict what is now termed crystal-storing histiocytosis. Additional autopsy cases led to further understanding of the disease, with electron microscopy—and later immunohistochemistry—helping to characterize the nature and origin of the crystals. Crystal-storing histiocytosis has since been reported throughout the body, including lymphoreticular sites (spleen, bone marrow, lymph nodes, and thymus), soft tissues (retroperitoneum, breast, and subcutaneous), visceral organs (heart, lungs, pleura, kidneys, adrenal glands, urinary bladder, pancreas, liver, and gastrointestinal tract), and head and neck (meninges, corneas, nasopharynx, larynx, tongue, thyroid, and parotid gland). So-called pseudo-Gaucher cells are seen in chronic myelogenous leukemia. So-called pseudo-pseudo-Gaucher cells of CSH differ from those of Gaucher disease and chronic myelogenous leukemia by their refractile eosinophilic crystals with hematoxylin–eosin. Due to the hydrophobic nature of these crystals, routine staining with eosin yields bright fluorescence under ultraviolet light, another distinguishing feature. Electron microscopy in Gaucher disease reveals tubular structures, compared to the rhomboid to needlelike membrane-bound inclusions of CSH.

Disorders associated with CSH include multiple myeloma/monoclonal gammopathies of undetermined significance, lymphoplasmacytic lymphoma (with or without Waldenström macroglobulinemia), and more rarely mucosa-associated lymphoid tissue lymphoma and amyloidosis. It has been suggested that the reported associations between Gaucher disease and multiple myeloma represent cases of misdiagnosed CSH. The pathogenesis of CSH begins with paraprotein, abnormal in amount and structure and produced by neoplastic cells, followed by phagocytosis by tissue macrophages. Impaired lysosomal proteolysis leads to membrane-bound inclusions that undergo crystallization. Nearly all cases reported in the literature have been associated with \( \kappa \) light chain rather than \( \lambda \). Light chain is believed to be less soluble under intralysosomal conditions than \( \lambda \). There has been no consistent association with a particular heavy chain, although immunoglobulin M is reported more often (57% of cases in one series). Immunohistochemical stains may fail to reveal deposition of light or heavy chains. In such cases, ancillary

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studies such as flow cytometry, as was performed in our case, can be critical in showing an underlying lymphoproliferative disorder.

Crystal-storing histiocytosis requires no specific treatment and usually responds to treatment of the patient’s underlying neoplastic disease. The patient described in this quiz case was treated with corticosteroids and chlorambucil for his lymphoma. His creatinine levels stabilized to 124 to 141 µmol/L (1.4–1.6 mg/dL), and the ureteral stents were removed. A follow-up computed tomographic scan 9 months after initial presentation showed decreased size of the retroperitoneal soft tissue mass and lymphadenopathy.

References