Pathologic Quiz Case

A 30-Year-Old Man With Lower Abdominal and Back Pain

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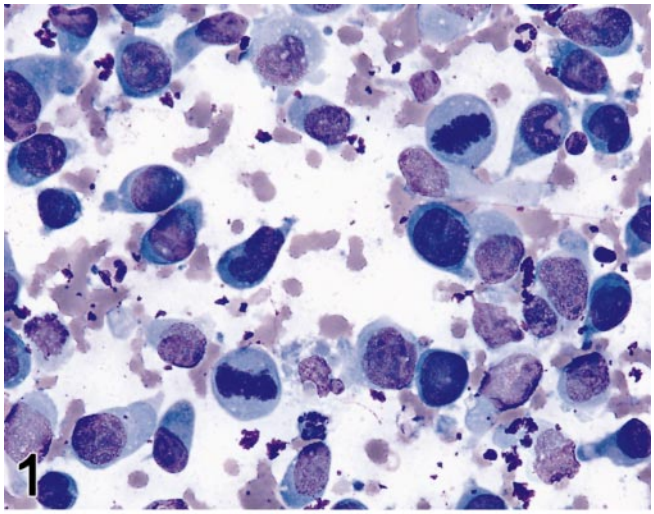
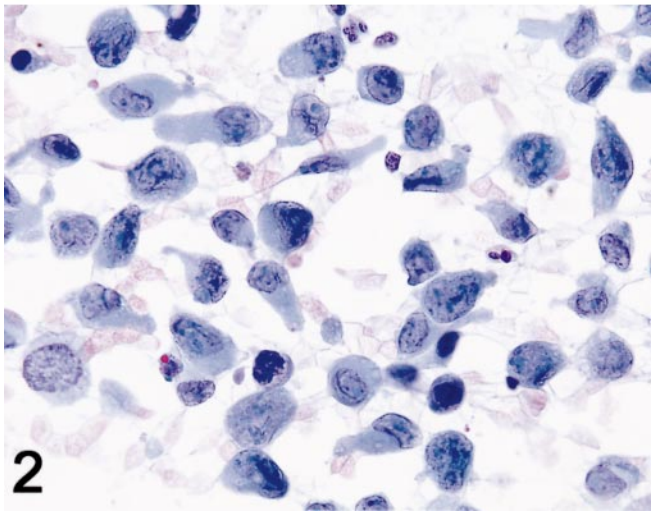
A 30-year-old man presented with lower abdominal and back pain, nausea, vomiting, and a significant weight loss (13.5 kg). He also complained of persistent fever and night sweats. On physical examination he was noted to be jaundiced. Imaging studies performed subsequently demonstrated ascites and a heterogeneous, hypovascular mass in the proximal pancreatic body and neck measuring 7.1 × 4.5 cm in size. Subsequent endoscopic retrograde cholangiopancreatography revealed ductal obstruction, and a stent was placed for decompression of his biliary system. His total serum bilirubin at that time was 7.9 mg/dL, which decreased progressively. His abdominal pain decreased but did not resolve. Other laboratory findings included a white blood cell count of 9510/μL, blood urea nitrogen value of 20 mg/dL, creatinine value of 0.5 mg/dL, albumin value or 3.4 g/dL, direct bilirubin value of 6.1 mg/dL, and aspartate aminotransferase value of 225 U/L, alanine aminotransferase value of 65 U/L, and lactate dehydrogenase value of 192 U/L.

An ultrasound-guided fine-needle aspiration of the pancreatic mass was performed. Smears were air-dried and stained with Diff-Quik for immediate on-site evaluation and wet-fixed in ethanol for subsequent Papanicolaou staining. Smears were hypercellular and comprised predominantly relatively large and pleomorphic, discohesive single cells (Figure 1). These cells had round to oval nuclei, often deeply indented, and contained a moderate amount of dense basophilic cytoplasm. Numerous mitoses were identified, as were scattered karyorrhectic nuclei, background foamy histiocytes, and neutrophils. Most of the cells showed an epithelioid morphology, with eccentrically placed nuclei, prominent nucleoli, and cuboidal to triangular cell shapes (Figure 2).

What is your diagnosis?





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Pathologic Diagnosis: Anaplastic Large Cell Lymphoma (Ki-1 Lymphoma) of the Pancreas

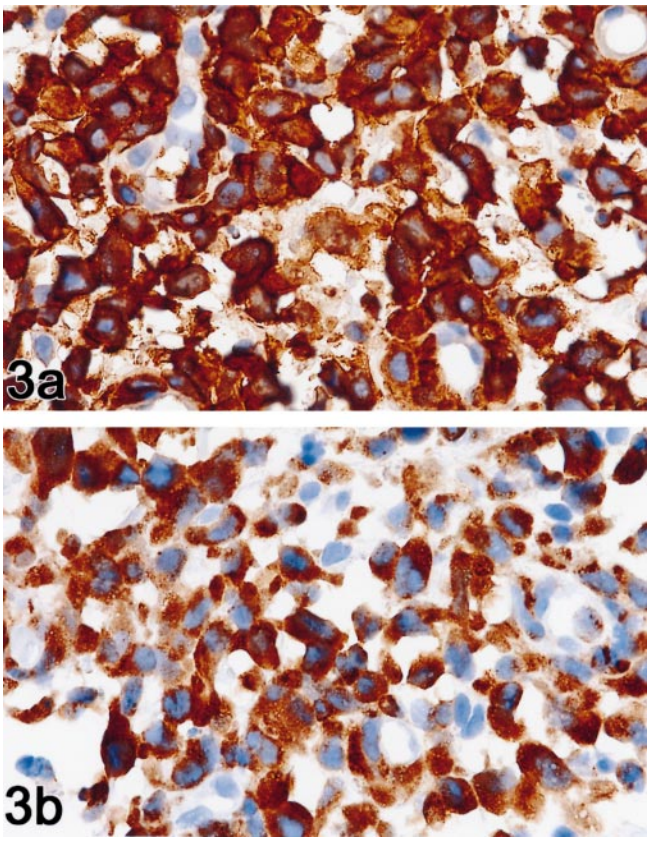
In this patient, the diagnosis of anaplastic large cell lymphoma (ALCL) was confirmed by ancillary testing. Immunostaining with CD30 (Ki-1) (Figure 3, a) and anaplastic lymphoma kinase (ALK) protein (Figure 3, b) showed diffuse positivity. No normal pancreatic tissue was identified.

Anaplastic large cell lymphoma, first described in 1985, is a rare clinicopathologic entity accounting for less than 5% of all non–Hodgkin lymphomas.[1] The distinct feature of ALCL is that it is restricted to a subset of CD30-positive diffuse large cell lymphomas of T cells or of a null cell lineage. Some of the cytologic features include large pleomorphic cells with an eccentric nucleus and an eosinophilic paranuclear region, resembling the neoplastic cells in Hodgkin lymphoma. The positive expression of CD30 (Ki-1), a lymphocyte activation antigen, is another shared feature of ALCL and Hodgkin lymphoma.[2–4]

Anaplastic large cell lymphoma may be primary, including the indolent cutaneous form and an aggressive systemic or secondary form. The systemic form of ALCL is associated with a characteristic t(2;5)(p23;q35) chromosomal translocation, which is present in about 80% of the ALK-positive ALCL. The remaining 15% to 20% ALK-positive ALCL express ALK variant fusion proteins.[4] Within the systemic ALCL, there may be ALK-positive ALCL and ALK-negative ALCL. ALK-positive systemic ALCL is most common during the first 3 decades of life and displays a male predominance. The latter may involve lymph nodes and extranodal sites.[5] The outcome of ALK-positive systemic ALCL is usually good. The ALK-negative systemic ALCL usually occurs in older patients and must be distinguished by cytomorphology and ancillary tests, because the outcome in this subset of patients is usually poor.[4,5]

There is a wide range of phenotypic and morphologic variability, including the common-type, small cell variant, lymphohistiocytic, and the giant cell variants. All variants share the existence of the characteristic large pleomorphic cells with eccentric nuclei and eosinophilic paranuclear regions. McCluggage et al[6] described the fine-needle aspiration cytology of 3 cases of CD30-positive ALCL. The cytomorphology showed single or poorly cohesive groups of large anaplastic cells with pleomorphic nuclei and large nucleoli. Each of the 3 cases presented as a diagnostic dilemma with a broad differential diagnosis, including anaplastic carcinoma, lymphoma, melanoma, and sarcoma.[6] Another series has shown the cytomorphology on fine-needle aspiration of the common variant of ALCL, with many loosely dispersed cells with eccentric kidney-shaped or embryo-like nuclei, often containing one to several prominent rod-shaped or angulated nucleoli and abundant amphophilic cytoplasm.[7] Also seen were cells with multilobated nuclei and multinucleated giant cells with a wreathlike arrangement of nuclei. In contrast, ''plasmacytoid'' cells and small to medium-sized tumor cells were predominantly noted in ALCL of the small cell variant.[7] Anaplastic large cell lymphoma cells may contain nuclei with huge nucleoli, simulating Reed-Sternberg cells. Intracytoplasmic inclusions have also been described in some cases in aspiration smears.

The present case posed a diagnostic challenge because the clinico-radiologic impression favored a primary pancreatic carcinoma and cytomorphology of the aspirate showed focal epithelioid features (Figure 2). However, flow cytometry carried out as a result of the on-site cytologic impression of a nonepithelial tumor revealed a 15% population of abnormal cells expressing CD44, CD4, CD6, and bright CD30. This was later supported by positive immunostaining with CD30 and ALK protein. The other diagnostic consideration at that time included a metastatic melanoma.



Primary ALCL of the pancreas is extremely rare[2,8] and should be considered in the differential diagnosis particularly when confronted with unusual morphologic appearance of the neoplastic cells. Selective use of appropriate ancillary methodology, including immunoperoxidase studies (with the characteristic surface membrane and cytoplasmic paranuclear dotlike staining for CD30) and flow cytometry, is extremely helpful.

References

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