

CASE REPORT

Obstructive Jaundice in a Patient with Mycosis Fungoides Metastatic to the Pancreas. EUS Findings

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ABSTRACT

Context Cutaneous T-cell lymphomas such as mycosis fungoides are uncommon neoplasms with a long and often relatively indolent course. Some eventually metastasize to lymph nodes or visceral organs but there are to our knowledge only two prior reports which describe clinically relevant pancreas involvement.

Case report We present the case of a 52-year-old man with mycosis fungoides who developed abdominal pain and jaundice. Endoscopic ultrasound guided-fine needle aspiration biopsies of a peculiar infiltrative appearing mass in the head of the pancreas revealed T-cell lymphoma cells.

Conclusion There is an increased incidence of second primaries in cutaneous T-cell lymphomas and a biopsy diagnosis of new intra-abdominal masses is essential.

INTRODUCTION

Cutaneous T-cell lymphomas are uncommon neoplasms with an incidence of 6.4 cases per million per year in the United States according to data of the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute. In the SEER study which extends over 30 years the majority (72%) of cases were classified as mycosis fungoides [1]. Mycosis fungoides is

in its early stages an indolent disease limited to the skin. The disease progresses in a variable and fairly unpredictable fashion to extracutaneous sites (lymph nodes and visceral organs) which is associated with a poor prognosis. Typically involved visceral sites are lungs and liver. Clinically relevant involvement of the pancreas by cutaneous T-cell lymphomas, however, appears to be extremely rare. We know of only two prior reports [2, 3]. This is the first report we are aware of in which EUS imaging and aspiration was used to diagnose cutaneous T-cell lymphoma metastatic to the pancreas.

CASE REPORT

A 52-year-old white male was diagnosed with a cutaneous T-cell lymphoma 5 years prior to the current presentation and had skin eruptions 3 years prior to the establishment of the diagnosis. He was initially treated with electron beam therapy which resulted in a complete response. Eighteen months prior he developed new skin lesions with multiple plaques on his cheek, neck, ear, armpit, forearm and back. Narrow band ultraviolet B therapy was recommended but treatment was only initiated with a delay of almost one year due to lack of transportation. The facial lesions continued to grow and he finally underwent electron beam therapy again with satisfactory results. A right axillary biopsy showed features again consistent with a cutaneous T-cell lymphoma. PCR performed

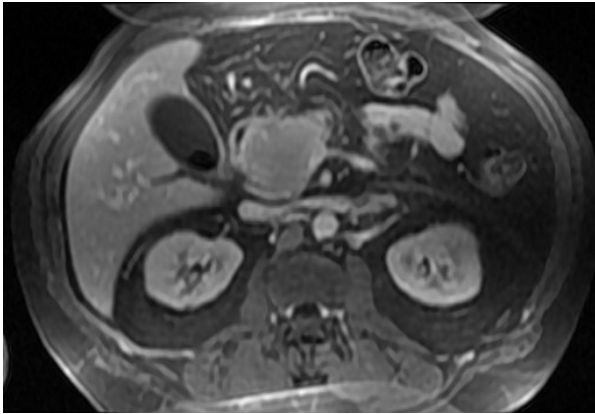


Figure 1. This T1-weighted gadolinium enhanced MRI image shows a 4.5 cm diameter mass in the pancreatic head.

on the tissue block showed a clonal T-cell proliferation identical to the one when the patient originally presented five years prior. One month prior to the current presentation he developed abdominal pain followed by jaundice. While a CT scan showed only an edematous appearing head of the pancreas, contrast-enhanced T1-weighted MR images revealed a high signal intensity mass (Figure 1).

An ERCP was performed which demonstrated a long stricture in the intrapancreatic portion of the bile duct (Figure 2). A 10-F plastic stent was placed which resulted in the resolution of the jaundice. Brush cytology was negative.

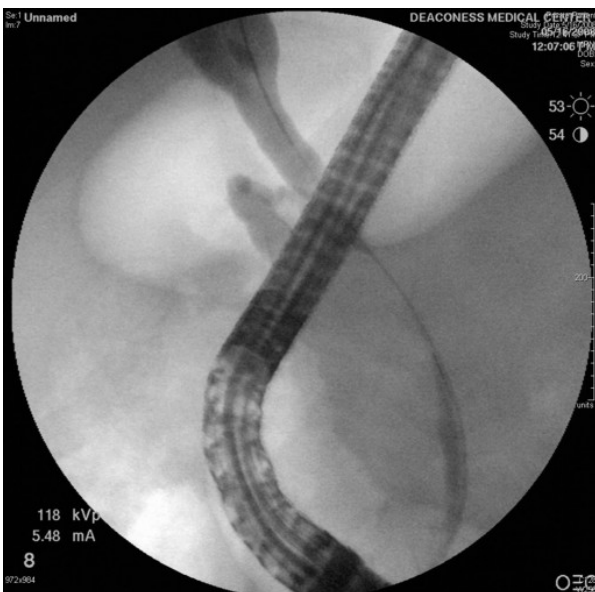


Figure 2. An ERCP reveals a long stricture in the intrapancreatic segment of the bile duct.



Figure 3. Endoscopic ultrasound showed a large hypoechoic somewhat lobulated appearing mass approximately 3.8 cm in size involving most of the head of the pancreas.

Endoscopic ultrasound showed a large hypoechoic somewhat lobulated appearing mass approximately 3.8 cm in size involving most of the head of the pancreas leaving only a small rim of unaffected appearing pancreas in the periphery. In contradistinction to a “space-occupying lesion” such as adenocarcinoma, the process was described as more “infiltrative appearing” in the original report and the examiner offered a differential diagnosis of autoimmune pancreatitis versus “other infiltrative process” prior to the results of the cytology being available. There was no encasement or invasion of major blood vessels and no apparent regional lymphadenopathy. The attached image shows sampling of the lesion with a 22-gauge FNA needle. The bile duct stent with air artifact and reverberation can be seen in the periphery of the lesion (Figure 3).

The cytology showed small neoplastic appearing cells with moderate quantities of somewhat eccentric appearing cytoplasm, variable nuclear size and shape with some angulated nuclei and scattered mitotic figures (Figures 4 and 5). Immunohistochemical staining for CD45 and CD3 was positive, CD5 mostly negative, CD20 negative, CD56 negative, pancytokeratin, synaptophysin and chromogranin negative (Figures 6, 7 and 8). These features were thought to be most

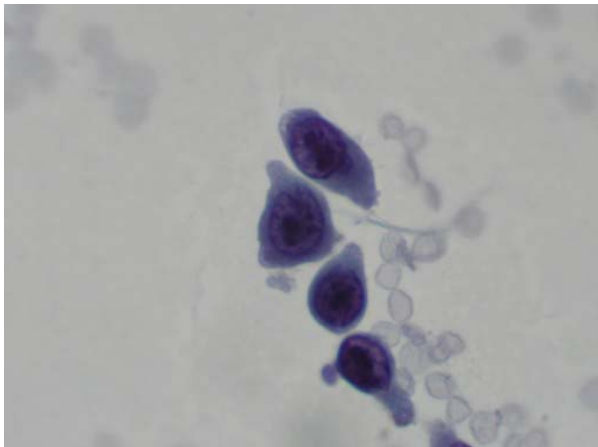


Figure 4. Concentrated smear of pancreatic aspirate reveals poorly cohesive, primitive cells, with large irregular nuclei and prominent nucleoli (x1,000).

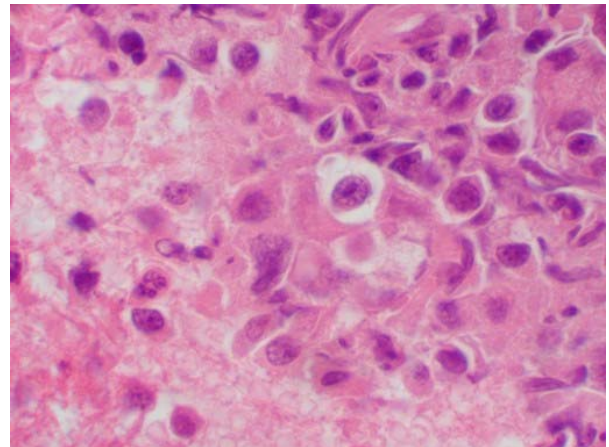


Figure 5. H&E stained cell block sections reveal dishesive tumor cells of variable size and shape (x1,000).

compatible with a non-Hodgkin's lymphoma of T-cell phenotype. For further staging the patient had a bone marrow aspirate done, which was negative, and a CT-PET scan, which showed mildly increased uptake in the pancreas head with a standardized uptake value of 2.8. Despite resolution of his jaundice following biliary stenting the patient continued to complain of left upper quadrant pain and he was therefore offered chemotherapy. He was treated with a dose adjusted EPOCH (etoposide, doxorubicin, vincristine, cyclophosphamide, prednisone) regimen. Eight weeks after his first ERCP and following EPOCH chemotherapy he presented for a routinely scheduled stent exchange. During this follow-up ERCP the bile duct stent was no longer present (having passed spontaneously) and the bile duct stricture had completely resolved. The follow-up PET-CT scan showed an unremarkable appearing pancreas without increased uptake but worsening skin lesions with progressive lymphoma (Figure 9).

DISCUSSION

Mycosis fungoides is the most common of the dermatotropic T-cell lymphoma and is currently incurable. It may evolve through patch, plaque and tumor stages to ultimately involve extracutaneous sites; either lymph nodes or viscera (stage IV disease). At this point the median life expectancy decreases to 1.5 years [4]. Many patients with stage Ia

(limited plaques) or may be even Ib stages (generalized plaques) may have no progression for decades and enjoy a normal life expectancy. The risk of disease progression within the first 10 years after diagnosis is about 5% to 10% for patients with stage Ia and between 17% and 39% for patients with stage Ib disease [5]. Once the skin lesions assume tumor shape (Ic) the risk of disease progression is higher and the time until this occurs shorter. The occurrence of visceral metastasis has been examined in a classic paper published in 1974 which also established that visceral involvement does not indicate transformation into a more aggressive or different type of lymphoma ("reticulum cell sarcoma") but represents dissemination of the original cancer [6]. In their autopsy series involvement of lung (75%), spleen (60%), liver (53%) and kidney (44%) and other organs was seen, frequently with grossly visible tumors. Of the 29 examined pancreata, 12 (41%) had evidence of microscopic involvement but no gross tumors were present consistent with a more infiltrative pattern.

Intrapancreatic metastases of extrapancreatic neoplasms are rare, often clinically silent, and are more frequently recognized in autopsy studies. The most common primaries are lung, kidney, melanoma and breast [7]. Enhancing lesions in the pancreas on MRI or CT are - in the right clinical context - most suggestive of a metastatic lesion. Still, the differentiation from a neuroendocrine tumor may be

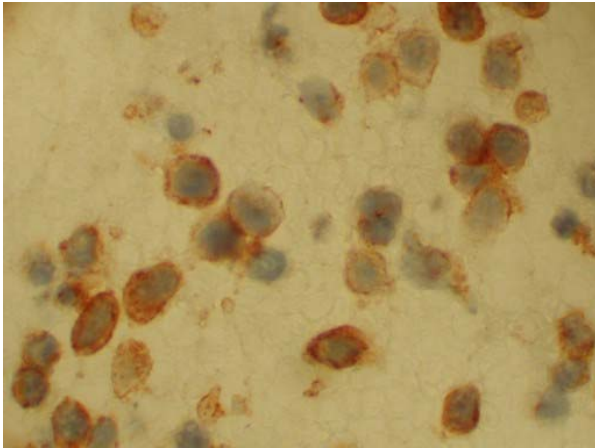


Figure 6. The neoplastic cells are strongly CD45 (leukocyte common antigen) positive, a marker for most hematolymphoid cells (x1,000).

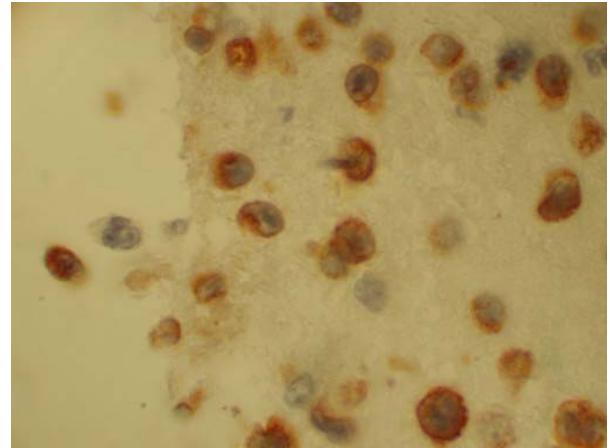


Figure 7. The neoplastic cells show intense decoration with CD3, a T-cell marker (x1,000).

impossible [8]. In a series of 24 patients with intrapancreatic metastases biopsied with EUS guidance pancreatic metastases were more likely to have well-defined margins (46% vs. 4%) compared with irregular margins (94% vs. 54%; $P < 0.0001$). No statistically significant difference between intrapancreatic metastases and a control group of primary pancreatic neoplasms was noted for tumor size, echogenicity, consistency, location, lesion number, or number of FNA passes performed [9]. No lymphomas were encountered in this series and all of the metastatic lesions were discrete rather than diffusely infiltrative. A diffusely infiltrative process in the pancreas is more suggestive of autoimmune pancreatitis [10] but may also be seen in secondary involvement by B-cell lymphomas [11].

We add our patient to the two previously described with clinically relevant pancreas involvement by cutaneous T-cell lymphoma. Shiozawa *et al.* report a rare and aggressive type of cutaneous T-cell lymphoma, disseminated pagetoid reticulosis, which within 18 months after initial presentation with erythematous lesions on the left temple led to the death of the patient with respiratory failure and jaundice. At autopsy the pancreas weighed 240 g and was swollen with massive infiltration of atypical lymphoid cells. Normal pancreatic tissue was almost entirely replaced by tumor cells [3]. The case of Kaplanski *et al.* is more like ours. A patient with a 4-year

history of mycosis fungoides presented with a clinically palpable pancreatic mass [2]. A third case with clinical jaundice and mycosis fungoides was caused by isolated involvement of the extrahepatic biliary tree by T-cell lymphoma but not involvement of the pancreas itself [12].

There is an increased risk of second malignancies, especially B-cell-lymphomas and melanomas, in patients with cutaneous T-cell lymphomas [13] and a new lesion found on CT scan or on PET-CT scan should not be equated with stage IV disease until biopsy confirmation has been obtained. Furthermore, so called large cell transformation, albeit rare, of mycosis fungoides is possible and worsens the prognosis [14].

EUS-FNA has evolved to be the method of choice for pancreatic biopsies in suspected

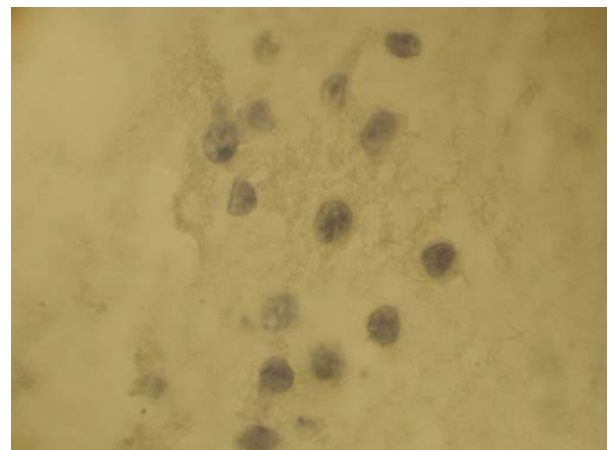


Figure 8. Tumor cells are negative for CD20, a B-cell marker (x1,000).

adenocarcinomas and the combination of immunocytochemistry on the cell block material with flow cytometry has been reported as being successful in diagnosing and adequately classifying pancreatic lymphomas in a few reports [15, 16]. A 19-gauge true-cut needle biopsy can sometimes provide a diagnosis when FNA fails [17].

Our patient responded well to combination chemotherapy with a complete resolution of his bile duct stricture but his skin lesions increased in size and number. Similar observations of improving visceral involvement with worsening dermatological manifestations have also been made by others (personal communication: Dr. Andrei Shustov, University of Washington, Seattle, USA) but we are not aware of published reports specifically addressing this phenomenon. Our patient will be offered further treatment with denileukin diftitox, a cytotoxic fusion protein approved for the treatment of patients with persistent or recurrent cutaneous T-cell lymphoma whose malignant cells express the CD25 component of the IL-2 receptor [18].



Figure 9. Skin lesions at the time of the patient's second ERCP.

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