Secondary Pancreatic Diffuse Large B-Cell Lymphoma: A EUS Diagnosis of a Rare Cause of Pancreatic Mass

Germana de Nucci1, Nicola Imperatore1,2, Enzo Domenico Mandelli1, Marta Nicola3, Franca Di Nuovo3, Gianpiero Manes1

1Gastroenterology and Digestive Endoscopy Unit, ASST Rhodense Garbagnate Milanese, Milan, Italy
2Gastroenterology, Department of Clinical Medicine and Surgery, School of Medicine Federico II of Naples, Italy
3Pathology Unit, ASST Rhodense Garbagnate Milanese, Milan, Italy

ABSTRACT

Context Pancreatic lymphoma is a rare cause of pancreatic mass, accounting for 0.5% of all pancreatic neoplasms, frequently misdiagnosed as epithelial cancer thus leading to incorrect therapeutic management. In the last few years Endoscopic Ultrasound has emerged as the most cost-effective and safe procedure and it is now recognized as the first-line procedure in the management of solid and cystic pancreatic masses. However, endoscopic ultrasound-guided fine needle aspiration diagnosis of pancreatic lymphoma remains challenging for both endoscopists and pathologists. Case report Here we present an unusual case of secondary, pancreatic, nodular involvement in a patient who suffered from a diffuse large B-cell lymphoma 3 years earlier. To better characterize this radiological finding, an endoscopic ultrasound was performed, which showed in the uncinated process of the pancreas a hypoechoic mass measuring 17 mm in diameter. A fine needle aspiration was performed in order to rule out pancreatic involvement by the known lymphomatous disease. Both the direct smears and the cellblock sections displayed an abundant, scattered population composed by monomorphous large cells with round nuclei, with multiple nucleoli acting as lymphoid centroblasts. The immunocytochemistry analysis confirmed the cytological hypothesis showing expression of CD20 and CD79a and negativity for CD3 and cytokeratin AE1/AE3. Finally, a diagnosis of pancreatic B-cell lymphoma was achieved. Conclusion pancreatic malignant lymphomas are unusual, solid tumors categorized as non-epithelial neoplasms. Endoscopic ultrasound - fine needle aspiration appears a safe, useful and valuable diagnostic modality for diagnosing pancreatic lymphoma. Moreover an important role is played by the pathologist’s expertise to achieve an accurate diagnosis.

INTRODUCTION

Pancreatic lymphomatous involvement is a rather unusual event: primary pancreatic lymphoma represents a rarity, accounting for less than 2% of all lymphomas and approximately 0.5% of all pancreatic neoplasms [1]. Secondary pancreatic involvement during systemic disease can occur but cytological diagnosis is very rarely performed considering the multiorgan dissemination. Furthermore, pancreatic involvement may be misdiagnosed as pancreatic cancer thus leading to incorrect therapeutic management [2]. It is clear that tissue sampling is crucial for a correct diagnosis. While in the past pancreatic tissue sample was only achieved by performing percutaneous biopsy or exploratory laparotomy, recent studies have shown that fine needle aspiration (FNA) can be used to make the diagnosis of pancreatic lymphomas [3].

In the last few years Endoscopic Ultrasound (EUS) has emerged as the most cost-effective and safe procedure, and it is now recognized as the first-line procedure in the management of solid and cystic pancreatic masses [3]. Lymphomas can show different pattern of pancreatic involvement, the most common being the nodular, hypodense lesion at radiological investigations. Lymphomatous involvement of the pancreas is usually of the non-Hodgkin’s or B-cell type with diffuse large B-cell lymphoma being the most common histotype [4].

However, the diagnosis of pancreatic lymphoma with EUS-FNA remains challenging for both clinicians and pathologists.
Here we report an unusual case of secondary, pancreatic, nodular involvement diagnosed by EUS-FNA in a patient previously suffering from a diffuse large B-cell lymphoma.

CASE REPORT

An asymptomatic 68-years-old male patient was referred to our hospital for radiological follow-up of lymphoma. He had been diagnosed with diffuse large B-cell lymphoma 3 years earlier, and had obtained an excellent response to chemotherapy. At last evaluation, peripheral blood leukocyte count was normal and, at clinical evaluation, there was no evidence of palpable superficial lymph nodes. During the last follow-up, the patient underwent a CT scan showing no lymphadenopathies and no other neoplastic lesions at thoracic organs; however, a doubtful enlargement of the pancreatic head was seen (Figure 1). To better characterize this radiological finding, an EUS was performed, which showed in the uncinate process of the pancreas a hypoechoic mass measuring 17 mm in diameter characterized by infiltrative margins, with a central area of necrosis and ipoenhancement on evaluation after intravenous contrast agent administration (Sonovue) (Figure 2). Moreover, a peripheral rim of edematous pancreatic parenchyma was detected. The Endoscopist performed a FNA (3 passes, 25 G needle for direct smears and 3 passes, 22 G needle for cellblock) in order to rule out pancreatic involvement by the known lymphomatous disease. In the Pathology Unit direct smears were stained with May-Grunwald-Giemsa and with Papanicolaou stain. The 22 G needle and syringe were rinsed and the liquid obtained was later centrifuged. The sediment obtained was fixed in 10% buffered formaldehdy, routinely processed and paraffin-embedded as a cellblock. Two-micrometer-thick sections were cut, stained with hematoxylin and eosin (H&E). Other sections were cut and used for ancillary studies. Immunophenotypic profiles were determined according to standard immunoperoxidase methods. The panel of antisera for the cellblock sections included CD20, CD79a, CD3, and cytokeratin AE1/AE3. Both the direct smears and the cellblock sections displayed an abundant, scattered population composed by monomorphous large cells with round nuclei, with multiple nucleoli resembling lymphoid centroblasts. The immunocytochemistry analysis confirmed the cytological hypothesis showing expression of CD20 and CD79a and negativity for CD3 and cytokeratin AE1/AE3 (Figure 3). Finally, a diagnosis of pancreatic B-cell lymphoma was achieved.
DISCUSSION

Malignant lymphomas of the pancreas are unusual, solid tumors categorized as non-epithelial neoplasms, accounting for less than 1% of pancreatic tumors and less than 2% of extranodal lymphomas in case of primary lymphoma [1, 2]. On the contrary, secondary pancreatic involvement during systemic lymphoproliferative disease can occur in up to 30% of patients even if in this setting a predominant involvement of the pancreatic parenchyma is uncommon [5].

In recent years, EUS with FNA has shown an important role in the diagnosis of pancreatic lymphoma [3]. EUS provides detailed radiological information, especially about vascular and lymph nodes involvement by pancreatic malignancies particularly for lesions measuring < 20 mm, and has emerged as the most cost-effective and safe procedure.

Moreover it enables the Endoscopist to perform FNA in order to reach a cytological diagnosis: in this setting FNA achieved sensitivity and specificity for malignant cytology respectively of 85-91% and 94-98%. Despite its invasiveness, this technique is usually safe with a complication rate (perforation, pancreatitis, infections, tumor seeding and bleeding) of 0.28%-0.85% according to recent studies [1, 2].

Interestingly, most of reported cases of pancreatic lymphoma were diagnosed by EUS-FNB with 19 or FNA with 22-gauge needle, the last one obtaining poor results in the typization of the lymphomatous disease [4, 5, 6, 7, 8, 9]. In our case, we decided to perform FNA by using a 25 G needle for direct smears because of the angled position of the lesion located in the uncinate process and a 22 G needle for cellblock, obtaining an accurate diagnosis for both direct smears and cellblock, confirming that, in experienced hands, also a small needle is accurate and safe for a correct diagnosis of a pancreatic mass [2, 10, 11, 12, 13].

In conclusion, pancreatic malignant lymphomas are unusual, solid tumors categorized as non-epithelial neoplasms. Primary pancreatic lymphoma is an extremely rare entity but secondary pancreatic involvement can occur in up to 30% of patients, although extremely rare in case of lymphomatous remission since many years. EUS-FNA in experienced hands was a safe, useful and valuable diagnostic modality for diagnosing and subtyping pancreatic lymphoma in our case. Moreover an important non-Hodgkin lymphoma and is characterized by frequent extranodal involvement, which occurred in our case [1, 2]. Dissemination of lymphoma to the pancreas may display several patterns: nodular, diffuse and multinodular, with the nodular one being the most common form. In this contest, lymphomatous involvement of the pancreas is characterized by a nodular lesion visualized as hypodense at CT scan or hypoechoic at Ultrasound (US) evaluation. This kind of presentation poses major diagnostic challenges, especially if devoid of anamnestic information, since it may easily mimic the most common histotype of pancreatic neoplasm, adenocarcinoma. The distinction between pancreatic adenocarcinoma and primary or secondary pancreatic involvement by lymphoma is crucial to plan an appropriate therapeutic treatment: in fact, while for pancreatic adenocarcinoma surgery represents the most important strategy, in the setting of lymphomas chemotherapy alone can be administered [1, 2, 14].

In our case the cytological material, using a 25 G needle to perform an FNA, was adequate both qualitatively and quantitatively to formulate a diagnosis. The cytological smears were composed by large lymphoid cells resembling centroblasts. Therefore immunochemistry was applied on cellblock and centroblasts displayed positivity for B-cell markers as CD20 and CD79a and negativity for cytokeratin and T-cell marker CD3. Hence, integration of previous anamnestic, endoscopic-ultrasound, cytological and immunocytochemical data helped us to define this uncommon occurrence and a final cytological diagnosis of secondary pancreatic localization of diffuse large B-cell lymphoma was performed [15].

CONCLUSION

In conclusion, pancreatic malignant lymphomas are unusual, solid tumors categorized as non-epithelial neoplasms. Primary pancreatic lymphoma is an extremely rare entity but secondary pancreatic involvement can occur in up to 30% of patients, although extremely rare in case of lymphomatous remission since many years. EUS-FNA in experienced hands was a safe, useful and valuable diagnostic modality for diagnosing and subtyping pancreatic lymphoma in our case. Moreover an important
role is played by the pathologist’s expertise to achieve an accurate diagnosis applying ancillary techniques too, such as immunocytochemistry especially in deceiving cases.

Conflict of Interest
The authors declare that they have no conflict of interest.

References