CASE REPORT

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

Germana de Nucci[1], Nicola Imperatore[1,2], Enzo Domenico Mandelli[1], Marta Nicola[3], Franca Di Nuovo[3], Gianpiero Manes[1]

[1]Gastroenterology and Digestive Endoscopy Unit, ASST Rhodense Garbagnate Milanese, Milan, Italy

[2]Gastroenterology, Department of Clinical Medicine and Surgery, School of Medicine Federico II of Naples, Italy

[3]Pathology 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 hystotype [4].

However, the diagnosis of pancreatic lymphoma with EUS-FNA remains challenging for both clinicians and pathologists.

Received May 02nd, 2018 - Accepted June 28th, 2018
Keywords Pancreatic Lymphoma, Familial; Endoscopic Ultrasound-Guided Fine Needle Aspiration
Abbreviations EUS endoscopic ultrasound; FNA fine needle aspiration
Correspondence Germana De Nucci
Gastroenterology and Digestive Endoscopy Unit
ASST Rhodense, Viale Forlanini 98, 0024
Garbagnate Milanese, Milan, Italy
Phone +39 02994302937
Fax +39 02994302905
E-mail germanadenucci1@gmail.com

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 formaldehyde, 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.

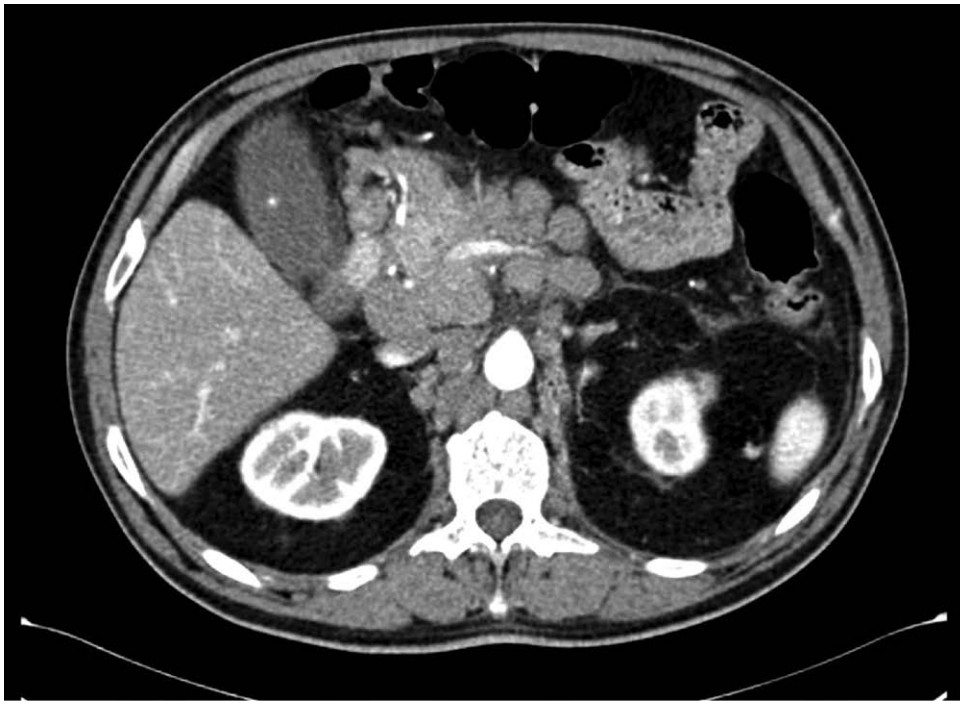

Figure 1. Computed Tomography scan imaging showing the presence of a pancreatic mass in the head of pancreas.

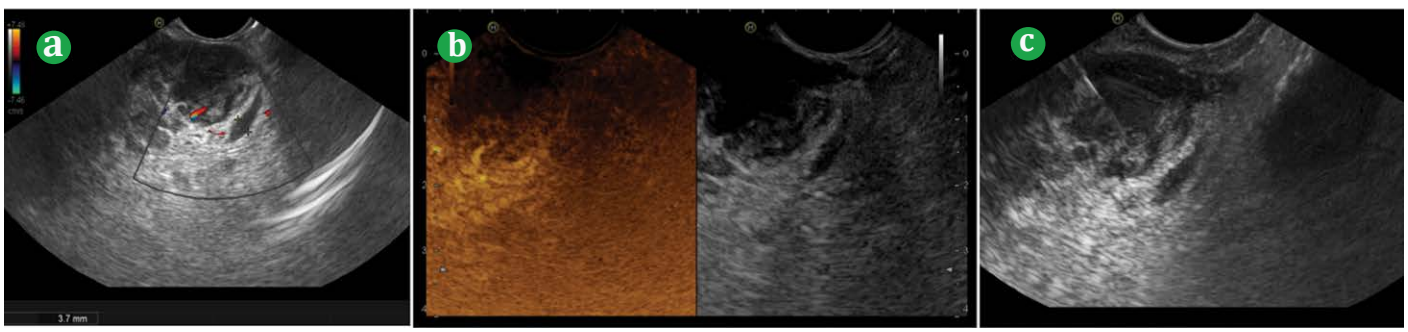

Figure 2. (a, b). Pancreatic Mass at EUS and after the administration of intravenous contrast agent. **(c).** Fine needle aspiration (FNA) of pancreatic mass.

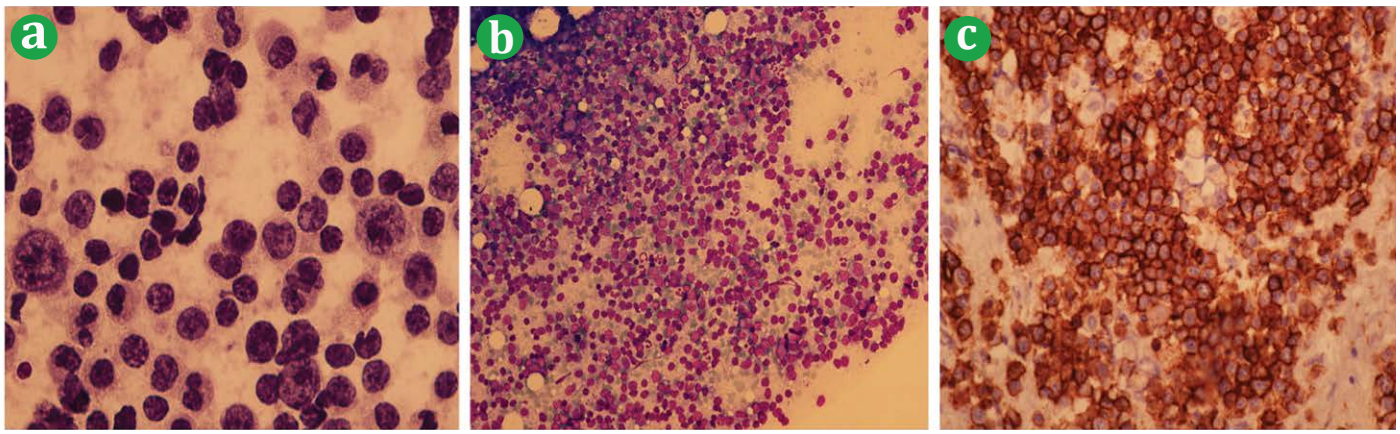

Figure 3. (a). Direct smears stained with Papanicolaou stain (100x) and **(b).** May-Grunwald-Giemsa (20x). **(c).** Expression of CD20 at immunocytochemistry analysis (40x).

DISCUSSION

Malignant lymphomas of the pancreas are unusual, solid tumors categorized as non-epitehelial 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 carried out by EUS achieves 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 our case report, the patient was discovered with an asymptomatic pancreatic mass after a remission of lymphoma since 3 years. From an epidemiological point of view, diffuse large B-cell represents the most common 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 hystotype 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 cytocheratin 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

1. Johnson EA, Benson ME, Guda N, Pfau PR, Frick TJ, Gopal DV. Differentiating primary pancreatic lymphoma from adenocarcinoma using endoscopic ultrasound characteristics and flow cytometry: A case-control study. Endosc Ultrasound 2014; 3:221-5. [PMID: 25485269]

2. Rossi ED, Larghi A, Verna EC, Martini M, Galasso D, Carnuccio A, et al. Endoscopic ultrasound-guided fine-needle aspiration with liquid-based cytologic preparation in the diagnosis of primary pancreatic lymphoma. Pancreas 2010; 39:1299-302. [PMID: 20944491]

3. Chang KJ. State of the art lecture: endoscopic ultrasound (EUS) and FNA in pancreatico-biliary tumors. Endoscopy 2006; 38 Suppl 1:S56-60. [PMID: 16802226]

4. Khashab M, Mokadem M, DeWi J, Emerson R, Sherman S, LeBlanc J, et al. Endoscopic ultrasound-guided fine-needle aspiration with or without flow cytometry for the diagnosis of primary pancreatic lymphoma — A case series. Endoscopy 2010; 42:228-31. [PMID: 20101569]

5. Sadaf S, Loya A, Akhtar N, Yusuf MA. Role of endoscopic ultrasound-guided-fine needle aspiration biopsy in the diagnosis of lymphoma of the pancreas: A clinicopathological study of nine cases. Cytopathology 2017; 28:536-541. [PMID: 28737285]

6. Mohamadnejad M, Khosravi P, Khani M, Nikmanesh A, Eloubeidi MA. Primary pancreatic Hodgkin's lymphoma diagnosed on EUS-guided FNA. Gastrointest Endosc 2016; 83:844-5. [PMID: 26422973]

7. Nakaji S, Hirata N, Shiratori T, Kobayashi M, Fujii H, Ishii E, et al. A case of primary pancreatic lymphoblastic lymphoma diagnosed by endoscopic ultrasound-guided fine-needle aspiration. Clin J Gastroenterol 2014; 7:180-4. [PMID: 26183638]

8. Ramesh J, Hebert-Magee S, Kim H, Trevino J, Varadarajulu S. Frequency of occurrence and characteristics of primary pancreatic lymphoma during endoscopic ultrasound guided fine needle aspiration: a retrospective study. Dig Liver Dis 2014; 46:470-3. [PMID: 24560534]

9. Larghi A, Iglesias-Garcia J, Poley JW, Monges G, Petrone MC, Rindi G, et al. Feasibility and yield of a novel 22-gauge histology EUS needle in patients with pancreatic masses: a multicenter prospective cohort study. Surg Endosc 2013; 27:3733-8. [PMID: 23644834]

10. Zhou J, Wu H, Lin J, Wang X, Zhang S, Cramer H, et al. Fine needle aspiration evaluation of pancreatic lymphoma: A retrospective study of 25 cases in a single institution. Diagn Cytopathol 2018; 46:131-138. [PMID: 29143491]

11. Fukuba N, Moriyama I, Ishihara S, Sonoyama H, Yamashita N, Tada Y, et al. Primary Pancreatic Malignant Lymphoma Diagnosed from Endoscopic Ultrasound-guided Fine-needle Aspiration Findings. Intern Med 2016; 55:31-5. [PMID: 26726082]

12. Gandhi NS, Feldman MK, Le O, Morris-Stiff G. Imaging mimics of pancreatic ductal adenocarcinoma. Abdom Radiol (NY) 2018; 43:273-284. [PMID: 29038855]

13. Nakaji S, Hirata N, Shiratori T, Kobayashi M, Fujii H, Ishii E, et al. A case of primary pancreatic lymphoblastic lymphoma diagnosed by endoscopic ultrasound-guided fine-needle aspiration. Clin J Gastroenterol 2014; 7:180-4. [PMID: 26183638]

14. Abedi SH, Ahmadzadeh A, Nikmanesh A, Mohammad Alizadeh AH. The role of endoscopic ultrasound in primary pancreatic lymphoma presented with acute pancreatitis: a case report. JOP 2014; 15:493-6. [PMID: 25262719]

15. Sadaf S, Loya A, Akhtar N, Yusuf MA. Role of endoscopic ultrasound-guided-fine needle aspiration biopsy in the diagnosis of lymphoma of the pancreas: A clinicopathological study of nine cases. Cytopathology 2017; 28:536-541. [PMID: 28737285]