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Evaluation of EUS Guided Sampling for Hypervascular Pancreatic Masses

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Abstract

Background: Endoscopic ultrasonography (EUS) has gained an essential role in the detection, characterization, and sampling of biliopancreatic lesions or masses. Hypervascular solid pancreatic masses are frequently encountered secondary to a wide variety of pathologies, that can be benign or malignant, with subsequent broad differential diagnosis.

Aim of Study: The use of EUS guided fine needle aspiration (EUS-FNA) of pancreatic hypervascular lesions is not well standardized. The objective of our study was to evaluate-different techniques used in sampling this type of masses.

Patients and Methods: We identified patients who were referred for EUS examination for solid pancreatic masses detected by prior other radiological modalities, then we extracted EUS reports of hypervascular solid pancreatic masses as well as the details of EUS-FNA procedure. Finally, we joined the cytopathological examination.

Results: Data from a total of 388 patients were extracted from the EUS database during the study period. We included 11 patients in whom EUS confirmed the presence of hypervascular solid pancreatic mass. As the number of passes increases, the risk of blood contamination increases affecting the cellularity of slides p-value=0.013.

In our study, we noted degradation of the score of cellularity and an increase in blood contamination as the number of passes needed to acquire enough samples increases. This could be explained by the fact of the increase in the risk of trauma to the vascular network inside the lesion even after the application of color doppler.

Conclusion: In our study, we noted degradation of the score of cellularity and an increase in blood contamination as the number of passes needed to acquire enough samples increases. This could be explained by the fact of the increase in the risk of trauma to the vascular network inside the lesion even after the application of color doppler. Though the number of patients is limited, this is the first study to evaluate the impact of vascularity of solid pancreatic masses on the quality of specimen and impact on the final diagnosis. Further randomized case-control studies are needed to recommend the best methods to acquire samples in this sub-group of patients.

Key Words: *Endoscopic Ultrasound – Biopsy – Pancreatic Masses – Hypervascular.*

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Introduction

ENDOSCOPIC ultrasonography (EUS) has gained an essential role in the detection, characterization, and sampling of biliopancreatic masses due to the close vicinity of these structures to the gastrointestinal tract. It is now considered an indispensable tool forthe pre-operative evaluation of respectability through the accurate measurementof size, vascular encroachment to relevant blood vessels, and relation with surrounding organs. EUS examination has the advantage of proper evaluation of pancreatic neoplasms with high safety and superior diagnostic yield at the same time **[1]**.

Vascular-rich lesions can be evaluated using contrast-enhanced imaging modalities such as: Computerized tomography (CT) and magnetic resonance imaging (MRI) and positron emission tomography (PET) scan but the sampling procedure of these lesions is still challenging due to the risk of bleeding with a lack of accurate post-sampling diagnosis **[2,3]**.

Using endoscopic ultrasonography and color doppler sonography serves as a useful tool to recognize vascularity within the lesion and identify the internal echotexture with precise recognition of areas of central necrosis in large masses **[4]**.

Recent guidelines recommended histopathological examination of pancreatic tumors prior to initiation of chemotherapy. EUS guided fine needle-sampling (EUS-FNA) allowshisto-cytological as-

sessment of cells acquired from a lesion or a mass adjacent to the wall ofthe gastro-intestinal tract [5].

Conventional FNA methods have been applied for the aspiration of cells from pancreatic masses through different techniques. After puncturing the gut wall and expulsion of cells from the needle using the internal stylet. Concern has been rising that sampling vascular-rich lesions with Tru-cut needles may carry an increased risk of hemorrhage with subsequent complications [6].

Aim of the study:

The use of EUS guided sampling of pancreatic hypervascular lesions is not well standardized. The objective of our study was to evaluate different techniques used in sampling this type of masses. Our study aimed to identify factors affecting the quality of samples obtained after EUS-FNA of pancreatic masses in terms of cellular adequacy and blood contamination.

Patients and Methods

We reviewed the EUS database at three tertiary care referral centers in Egypt from January 2021 to January 2022. The availability of written informed consent was confirmed for all included patients. We identified patients who were referred for EUS examination for solid pancreatic masses detected by prior radiological modalities, then we extracted reports of EUS examination as well as details of the EUS-FNA procedure.

We selectedonly EUS reports of hypervascular solid pancreatic masses. Presence of vascular network inside the mass could be detected by applying color flow signal during the procedure. We reported masses with at least 1 blood vessel inside the tumor by doppler examination.

Two aspiration techniques were applied. These methods were defined as the following:

Capillary method - gradual slow withdrawal of the internal metallic stylet through a capillary mechanism to aspirate cells after the needle is confirmed inside the mass.

Suction technique - A negative pressure 10ml suction syringe is connected to the extremity of the needle and this is followed by aspiration through a maximal pressure load.

Both EUS sampling techniques were used in order and slides were labelled for each with adequate rinsing of the needle applied after each pass. ROSE (Rapid onsite evaluation) was available to confirm enough cellularity on the slides. The number of passes needed to reach cellular adequacy was documented.

Finally, we joined the final cytopathological examination conclusion. Clinical course, follow-up laboratory tests, and radiological evaluation were also recorded.

We confirmed our inclusion criteria by attaching reports of MRI or abdominal CT describing highly vascular pancreatic masses that were detected during the examination.

We identified exclusion criteria as follows: (1) Pregnant females, (2) Patients with no available informed consent for endoscopic examination, (3) EUS-FNA was not performed secondary to difficult accessibility of the mass, (4) bleeding tendency or coagulopathy: Low platelet count (<50,000 [illegible]) or high INR (>1.5).

Patients evaluation and EUS-FNA technique:

The 3 referral centers were equipped with same EUS machine. Endo-sonography was performed using a linear echoendoscope (Pentax UTK 3870 -Pentax, Japan) and an ultrasound machine (Hitachi Arietta, Tokyo). All patients received sedation withPropofol 1% (Baxter, USA). Procedures were performed by experienced endo-sonographers who had an experience in more than >1,000 EUS procedures. We used a disposable EUS-FNA needle 22-gauge (EchoTip; Cook Medical, IN, USA).

An integrated complete examination of all pancreatic masses was achieved from different stations depending on major vessels landmarks: (1) At the level of the cardia (after identification of the abdominal aorta) that allows for proper examination of the body and tail of the pancreas, (2) At the bulb and second part of the duodenum (after identification of the portal vein and superior mesenteric vessels) to assess the head of the pancreas as well as the uncinate process.

Once the lesion has been evaluated by EUS; color doppler imaging was applied to identify the vascularity and the surrounding vessels. The operator identified the best access to the pancreatic masses after evaluation of the pathway that avoids major intervening vessels.

The cellular material inside the lumen of the needle was expelled through the reintroduction of the metallic stylet. The acquired specimen was fixed on separate slides identified for each technique as well as cell block.

Cytological evaluation:

Half of the smeared slides were immediately fixed in 95% ethyl alcohol for a minimum of 15 minutes for later staining with H & E stain. The other half copy of slides was used to perform ROSE using Diff Quick stain to confirm adequacy for each sampling method before subsequent puncture in the same patient using other methods (up to five passes).

Lesions were classified according to the proportion of adequate clusters of cells for diagnosis to the amount of blood contaminating the examination field [7].

Experienced cytopathologists examined the study specimens. Blood contamination and cellular adequacy were graded. Cytopathologists were blinded to the fine needle aspiration cytology method used but were provided with the sociodemographic information and the clinical history of the patient.

Statistical analysis:

The Chi-square test was used to compare the difference in the distribution of frequencies among different groups. For continuous variables, an independent *t*-test analysis was carried out to compare the means of normally distributed data, while the Mann-Whitney U test was calculated to test the median differences of the data that do not follow the normal distribution. ANOVA test was calculated to test the mean differences of the data that follow normal distribution to detect the best aspiration method for diagnosis of hypervascular pancreatic lesions. A significant *p*-value was considered when it is equal to or less than 0.05. Data were analyzed using the SPSS statistical software version 20 (SPSS Inc, Chicago, USA).

Results

Sociodemographic characteristics of the included patients:

Data from a total of 388 patients were extracted from the EUS database during the study period.

We included 11 patients in whom EUS confirmed the presence of hypervascular solid pancreatic mass.

The calculated mean of age was 39.1 ± 16.4 years. Gender distribution was 7 women and 4 men. The leading symptoms werereported, and the most common documented symptom was vague diffuse abdominal pain. Other symptoms included: jaundice, weight loss, and persistent vomiting.

EUS features of hypervascular solid pancreatic masses:

EUS reports documented the full description of pancreatic masses in terms of size, location, echo pattern, and relation to surrounding organs as well as encroachment on surrounding vessels.

The average maximum diameter of reported masses was 3.7± 1.5cm as measured on still image during EUS examination. The lesions were distributed in location between the head, body, and tail of the pancreas. The used needle size was 22G by all experts.

The diagnoses of pancreatic masses attributed after cytopathological examination included: Solid pseudopapillary intra-pancreatic neoplasm (SPPN) (4 patients), neuroendocrine tumors (3 patients), malignant metastasis (2 patients), acinar cell carcinoma (1 patient) and accessory spleen (1 patient). Surgical specimen of SPPN and malignant resectable neuroendocrine tumor confirmed the diagnosis. Clinical and radiological follow-up confirmed non-progress of benign lesions (accessory spleen). The average number of passes 3.5 ± 1 was required to achieve enough cellularity on ROSE evaluation. Cytopathologists could attributea final opinion in all cases (1 1 case), all of whom received a definite diagnosis on their pathology report.

Fig. (1) illustrates cytological examination of EUS-FNA of pancreatic mass diagnosed as a solid-pseudopapillary neoplasm.

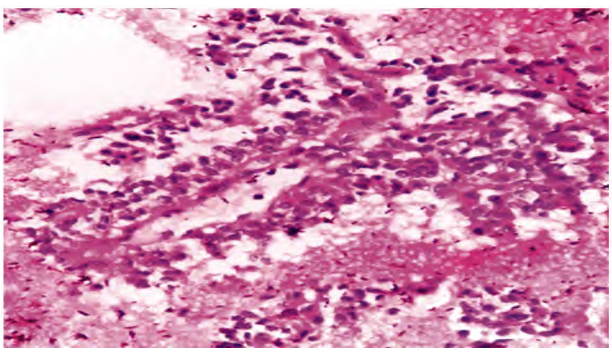

Fig. (1): Illustrates cytological examination of EUS-FNA of pancreatic mass diagnosed as a solid-pseudopapillary neoplasm of the pancreas using H&E stain of cell block preparation x400 power. Smears are showing adequate cellularity with a minimal amount of blood contaminating slide revealed a solid cellular smear pattern formed of cells with small round to oval, occasionally grooved nuclei with finely granular even chromatin and inconspicuous nucleolus with scant granular cytoplasm (Note tumor cells surround a vascular core with myxoid change).

Fig. (2) illustrates cytological examination of EUS-FNA of pancreatic mass diagnosed as a pancreatic neuroendocrine tumor.

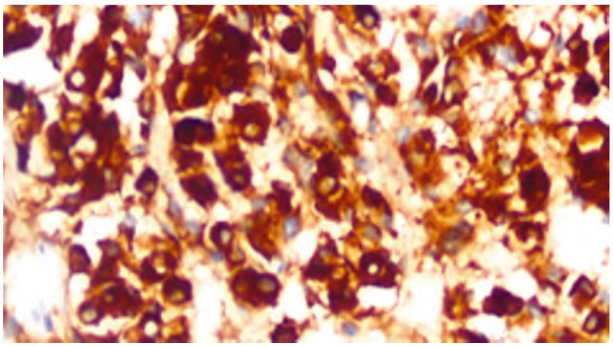

Fig. (2): Illustrates cytological examination of EUS-FNA of pancreatic mass diagnosed as a pancreatic neuroendocrine tumor, immunostaining with synaptophysin x400 power. Smears patterns formed of a uniform, monotonous population of cells with plasmacytoid features due to the eccentric, round nuclei.

The relationship between specimen cellularity and blood contamination with the number of needle passes through the lesion to acquire an adequate amount of cells for proper cytological reporting was studied. As the number of passes increases, the risk of blood contamination increases affecting the cellularity of slides p-value=0.013.

We compared slides performed through the capillary technique and slides performed through the suction technique. No difference between the 2 techniques in term of cellular adequacy or blood amount. No other direct relation could be shown with other factors (age, gender, site, or size of the masses).

Discussion

Hypervascular pancreatic masses are usually observed as a result of a broad range of pathologies.

The differential diagnosis is wide and ranges from benign conditions to aggressive malignancies including both primary neoplasms or secondary metastases **[8]**. Various pathologies may mimic hypervascular lesions in the pancreas, and it is essential to recognise these disorders to minimise unneccesary investigations **[9]**. Ability to classify these masses into their definitive pathology can be challenging, but it is crucial for guiding and directing proper clinical management **[10]**. Appropriate treatment is significantly dependent on the determination of the nature of these masses; hence, accurate and precise cytopathological reporting of acquired samples is essential.

In our study we describe variable entities of hypervascular solid pancreatic masses detected during EUS examination. Solid pseudo-papillary neoplasms of the pancreas (SPPN) have predominant solid component mixed with cystic papillary epithelial cells. They typically manifest in young females by abdominal pain and vomiting **[11,12]**. Pancreatic neuroendocrine tumors (PNETs) can present as solid hypervascular masses. However, there is no typical radiological appearance for all PNETs **[13,14]**. They still present less than 5% of pancreatic tumors. Metastases to the pancreas are uncommon and they usually follow primary from breast, lung, or kidneys. Acinar cell carcinoma is another malignancyseen in elderly men which tend to present as large vascular rich mass on CT examination **[15]**.

Proper differentiation should be clear from arteriovenous malformations, vascular anomalies (aneurysms) and developmental hypervascular lesions seen within the pancreas **[16]**.

Initial assessment of pancreatic masses can be performed by contrast enhanced CT or MRI **[17]**. They can also help to discriminate pancreatic cysts that may simulate hypervascular solid masses such as serous cystadenoma (SCN) alongside with EUS evaluation **[18]**. Crucial information about the site, size, localization, density as well as the vascular pattern of these lesions can be obtained. It can discriminate between intra and peri-pancreatic masses. Also, vascular anomalies (arterial and venous communication or pseudoaneurysm) can be clearly demonstrated **[19]**. Scanning can be conducted through a combination of phases: early arterial phase, parenchymal phase, and portal venous phase. Hypervascular masses are best illustrated at the pancreatic parenchymal phase (35-50 seconds after injection of the contrast) **[20,21]**.

Endoscopic ultrasound-guided biopsy usingfine-needle aspiration has become the technique of choice for sampling pancreatic masses **[22]**. Different types of needles and fine-needle aspiration techniques are used in clinical practice. Outcomes of EUS-FNA evaluation vary according to the type of the used needle, technique used to acquire the sample, and methods of specimen evaluation **[23]**. No consensus on the best technique is yet established.

The suction technique was reported to be associated with an increased risk of bleeding and gastroduodenal wall contamination with more slide smearing, time consumption, and more blood clots that hinder proper cytological evaluation **[24]**. In

contrast, the capillary method improve the adequacy and showed less blood and gastroduodenal contamination, less slide smearing, and proper cytological evaluation **[25,26]** . The suctiontechnique appears also to be associated with a greater number of passes needed to acquire enough cells on the slides **[27]** .

We demonstrated in our study that proper cytological reporting and diagnosis of hypervascular solid pancreatic lesions is directly dependenton adequate cellularity along with less blood contamination. This can be affected by the number of passes through hypervascular solid pancreatic masses. The number of passes required to confirm the nature of pancreatic masses on the cytopathology report is not exactly determined. The number of 4 passes of the EUS-FNA needle has been proposed as sufficient to obtain enough cellular material to detect malignancy. More passes did not increase the sensitivity of the biopsy **[28]** . No statistical difference appeared between the capillary and suction techniques that can affect the quality of the specimen. Other factors such asthe location, size of the lesion or the endoscopic approach (transgastric or trans-duodenal) did not appear to have impact on the interpretation by the cytopathologist.

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تقييم أخذ العينات الموجهة بمنظار الموجات فوق الصوتية من كتل البنكرياس الغنية بالأوعية الدموية

أكتسبت الموجات فوق الصوتية بالمنظار دوراً أساسياً فى إكتشاف وتوصيف وأخذ عينات من آفات أو كتل البنكرياس والقنوات المرارية. غالباً ما تصادف كتل البنكرياس الصلبة ذات الأوعية الدموية بشكل نتيجة لمجموعة واسعة من الأمراض، والتى يمكن أن تكون حميدة أو خبيثة، مع التشخيص التفريقى الواسع اللاحق.

لم يتم توحيد استخدام الشفط بالإبرة الدقيقة لأورام البنكرياس الغنية بالأوعية الدموية بشكل جيد. كان الهدف من دراستنا هو تقييم التقنيات المختلفة المستخدمة فى أخذ عينات من هذا النوع من الكتل.

حددنا المرضى الذين تمت إحالتهم لفحص الموجات فوق الصوتية بالمنظار بحثاً عن كتل البنكرياس الصلبة التى تم إكتشافها بواسطة طرق إشعاعية أخرى سابقة، ثم استخرجنا تقارير لكتل البنكرياس الصلبة المفرطة الوعائية بالإضافة إلى تفاصيل إجراء لعينة. أخيراً، احقنا تقارير الفحص الخلوى المرضى.

تم استخراج بيانات من إجمالى ٣٨٨ مريضاً من قاعدة البيانات خلال فترة الدراسة. قمنا بتضمين ١١ مريضاً أكدت فيهم نتيجة فحص الموجات فوق الصوتية بالمنظار عن وجود كتلة بنكرياسية صلبة مفرطة الأوعية الدموية. مع زيادة عدد التمريرات، يزداد خطر تلوث الدم مما يؤثر على الخلايا الخلوية للشرائح قيمة p=0.013.

فى دراستنا، لاحظنا تدهور درجة الخلوية وزيادة تلوث الدم مع زيادة عدد التمريرات اللازمة للحصول على عينات كافية. يمكن تفسير ذلك من خلال حقيقة زيادة خطر الإصابة بجرح على شبكة الأوعية الدموية داخل الآفة حتى بعد تطبيق دوبلر اللون.