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Biochemical and Surgical Aspects of Cystic Pancreatic Tumours

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Abstract*. The cystic pancreatic neoplasias are very rare (only 1-2 % of the exocrine pancreatic tumours) and, because of their clinical and biological characteristics, they can be treated by surgery in a effective way, as simple excision, with a good prognosis. Despite the histological analogies, the 5 types of cystadenomas vary by their dimensions, localization and biology; the serous solid adenoma is the most rare of the 5 types. The paper presents aspects from 4 young patients admitted for severe superior abdominal pain. The MRI examination revealed hypervascular mass, well delimited, situated between the pancreatic tail and the spleen. In each case have been practiced the excision of the tumour by spleen distal pancreatectomy. The histological and imunohistochemical examinations established the diagnosis: solid serous pancreatic adenoma. Taking into account that the malignity is hard to be suspected even intraoperatory, the surgical excision is the most effective treatment. The surgical excision makes the healing possible, but an imagistic and biochemical follow-up is necessary, especially in those cases where the splenectomy has also been practiced. Within the study group the serum glucose level was high and it decreased rapidly after surgery. More cohort studies are needed to make a possible correlation between serum glucose level and nonmucinous pancreatic cysts.*

Keywords*: serous solid adenoma, pancreas, spleen distal pancreatectomy*

1.Introduction

The pancreatic neoplasias, especially the adenocarcinomas, are aggressive tumors, with a fast evolution and they usually need difficult surgical operations, which have very high mortality and morbidity. The cystic pancreatic neoplasias are very rare (only 1-2 % of the exocrine pancreatic tumors) and due to their clinical and biological characteristics, they can be effective treated by a simple excision, with a good prognosis. The cyst can be serous and mucosal. The serous cystic neoplasias can be histologically classified in 5 types: the serous microcystic adenoma, the serous oligocystic adenoma, the solid serous adenoma (ASS), the associated cystic neoplasia Hippel-Lindau and the serous cystadenocarcinoma. Despite the histological analogies, the 5 types of cystadenomas vary by their dimensions, localization and biology; the serous solid adenoma is the most rare of the 5 types [1-3].

The purpose of this study is to determine the metabolic profile of pancreatic cystic fluid as a potential producer of clinically detectable biomarkers [4]. It represents our preliminary research results from a retrospective study.

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2.Materials and methods

The paper presents 4 cases of 35-47 years old patients, 3 women and one man. They where admitted for severe superior abdominal pain. Each of them have been tested for serum glucose level, before and after surgical manouver.

Laboratory analysis for differentially expressed level of serum glucose between malignant and premalignant or benign cysts was performed. The main outcome of the measurements is to identify the differentially expressed level of serum glucose between clinically relevant bening pancreatic cyst categories and their diagnostic relevance.

Serum blood glucose levels were determined using a Wilford Brimley (glucose meter) equipment. This device is especially useful in the management of the diabetic patient and the individualization of his treatment. Testing the blood glucose level with this device is done by piercing the skin of the finger to extract blood and then applying it on a disposable "test-strip". These devices measure an electrical characteristic modified by the blood glucose level. This type of test is called capillary blood glucose level determination.

It should be noted that none of these patients were known to have type I or II diabetes mellitus.

3.Results and discussions

The clinical examination of these patients only revealed the painful area represented by the left hypochondrium. The lab results (including the tumoral markers) were normal. The MRI examination revealed a hypervascular mass, well delimited, situated between the pancreatic tail and the spleen for each patient.

It has been practiced a xifoombilical median laparotomy with the excision of the tumour by spleen distal pancreatectomy (the dissection imposed the ligature of the spleen vessels).

Figure 1. Serous solid pancreatic adenoma - intraoperative aspect

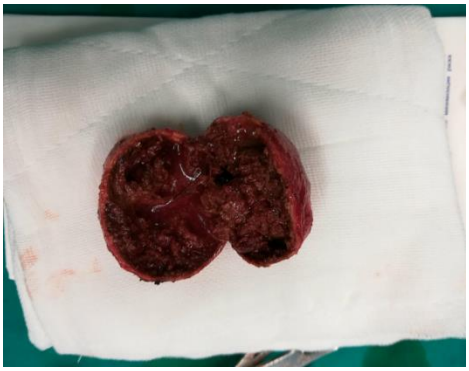

Figure 2. Serous solid pancreatic adenoma – surgical specimen (section)

The macroscopic examination showed a round-oval formation, well delimited, with a mixed content. The microscopic examination revealed a tumor with a fibrous uninvaded capsule, with cells with clear cytoplasm, round core, without any atypia or mitosis. The adjacent pancreatic tissue was normal. The imunohistochemical exam revealed positive cells for each of the following: Cytokeratin-7, Cytokeratin-8, the neurospecific enolasis and periodic intracytoplasmic acid Schiff (PAS). All the cells have been negative for vimentin.

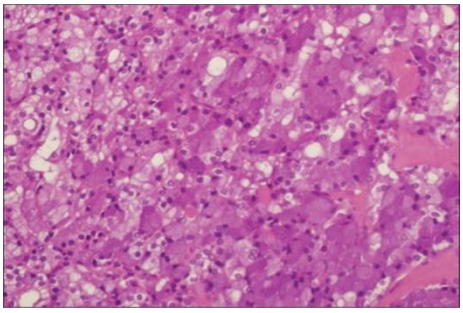

Figure 3.Serous solid pancreatic adenoma – microscopic aspect

Taking into account all those findings, the patient has been diagnosed with solid serous pancreatic adenoma. The clinical and the paraclinical follow-up have been made at one month and 6 months, with complete recovery.

The cystic pancreatic neoplasia are rare tumors, with a good prognosis. The case that we have presented is the most rare form of the 5 histological types of serous cystic neoplasias. The main case serial have been reported in 1996 by Perez-Ordonez [3].

The surgeons and the radiologists must be warned of this entity, because its images are similar to those of other solid tumors, including the metastasis of kidney tumors and the pseudopapilar tumours. The ASS type is in general a little tumour (3-4 cm) and it usually appears at the age of 60-70. The case we presented is a bigger tumour (10/8 cm) and the patient is only 35 years old. Imunohistochemical examination is also nonspecific [5].

The preoperatory diagnosis is very difficult, because the tumour can not be distinguished from other solid tumors and the paraclinical exams are not edifying. Even intraoperatory, the malignancy can only be suspected.

The differential diagnosis has to be made with: the duct adenocarcinoma, the solid pseudopapilar neoplasia, the primary cellular tumors with clear cells, the endocrine pancreatic tumors [6].

Taking into account that the malignity is hard to be suspected even intraoperatory, the surgical excision is the most effective treatment. In our case, the distal pancreatectomy had to be completed by a splenectomy, due to the lesion of the spleen vesels. The prognosis is good. In all the reported cases, the patients survived without recurrence [7-13].

Novel researches results highlight the glucose and kynurenine to be differentially expressed in cystic pancreatic adenomas. Thus, the authors compared the serum glucose level and kynurenine in cases of non-mucinous and mucinous pancreatic cysts [14, 15].

Our results are consistent with those in the literature. Thus, serum glucose values were significantly higher in non-mucinous cysts present in patients in our study group. The clinical utility in the differential diagnosis of these tumors in serum glucose is the potential for it to become a reliable biomarker. Corroborating these results with the cytological examination of the aspirated fluid increases the chances of having a preoperative differential diagnosis. We mentioned this because the role of the cytological examination, by itself, is often uncertain due to the low cellularity [16].

However, the cytological examination becomes the most accurate test for the detection of malignant cysts in the preoperative. The preoperative diagnosis guides the surgeon in choosing an intervention technique suitable for each case [17].

New technologies are now available to clinicians. Thus, DNA analysis of the fluid from the pancreatic cyst showed that the KRAS gene mutation has high specificity only for mucinous cysts. However, the sensitivity of the method does not exceed 45%. Although the KRAS gene represents an early oncogenic mutation that occurs in the sequence of adenoma-carcinoma transformation, its quantitative analysis has low specificity for the diagnosis of malignancy. The same result had the study of gene mutation [18].

Confocal laser endomicroscopy is a new radiological technique that uses low power laser to obtain in vivo histological details. The use of this method for the purpose of diagnosing the preoperative differential diagnosis in pancreatic cysts has shown the technical feasibility of this probe. Evidence of epithelial venous structures was associated with malignancy of cysts, with a sensitivity of 59% and a specificity of 100% [19].

According to international guidelines, there are still a significant number of patients in whom the application of surgical treatment is controversial: patients younger than 65 years - require long-term follow-up, due to the cumulative risk of malignancy; cysts> 3 cm without any worrying stigmas and features. In these situations, ablation therapy can be applied [20]. This consists of injecting a cytotoxic agent into the cyst (ethanol, saline). Ablation can also be performed using radiofrequency but still requires studies to demonstrate the effectiveness of the method [21].

The recurrence rate of these cysts varies from 7% to 30% in the literature and in our case it was 0%. Cystic formations requiring conservative treatment require careful remote monitoring to detect a possible malignant transformation [22, 23].

4.Conclusions

The clinical and paraclinical diagnosis of these tumors is very difficult. The malignancy can only be suspected. The architecture of a solid serous pancreatic adenoma is different from the architecture of a serous cystadenoma, but their cytological, immunological and histological characteristics are identical. Even if malignant as a structure, the solid serous pancreatic adenoma has a good prognosis. The surgical excision makes the healing possible, but an imagistic and biochemical follow-up is necessary, especially in those cases where the splenectomy has also been practiced. Our study must continue on larger number of patients and adding high edge methods to certify our preliminary findings.

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