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Management of 100 Consecutive Cases of Pancreatic Serous Cystadenoma: Wait for Symptoms and See at Imaging or Vice Versa?

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Abstract. Pancreatic serous cystadenomas have a low malignancy rate. When nonsymptomatic, in selected patients, they can be managed without surgery; however, a high degree of diagnostic reliability is crucial. We admitted 100 consecutive cases (87 women with a median age of 51.86 years). Of these, 44 were symptomatic and 56 were diagnosed incidentally. Ultrasound correctly diagnosed 53% of the cases, incorrectly 31%, and was nondiagnostic in 16%. Computed tomography scan had similar rates (54%, 34% and 12%, respectively), while magnetic resonance imaging improved diagnostic accuracy to 74% and reduced incorrect diagnoses to 26%. In 21 cases, exploratory needle aspiration of the cyst was carried out; only 8 samples (38%) resulted in a diagnosis; in 12 patients (57%) insufficient material was acquired to allow for diagnosis, one case demonstrated epithelial dysplasia. In 1 patient an exploratory puncture resulted in a very serious bleeding. Sixty-eight patients were treated surgically, the 44 symptomatic cases and another 24 patients with ill-defined oligocystic lesions that could not be differentiated as serous or mucinous in the preoperative period. Two patients underwent resection because of frank tumor growth. In the two time periods analyzed (the first 7 years and the subsequent 6.5 years) the relationship between cases observed/operated on did not significantly change. Twenty-one (30.8%) distal pancreatectomies, 14 (20.5%) intermediate resections, 10 (14.7%) pancreaticoduodenectomies 4 (5.8%) enucleations, and 1 (1.4%) duodenum-preserving pancreatic head resection were carried out. Nine patients (13.2%), underwent exploratory laparotomy with a diagnostic biopsy. Another 9 underwent decompressive interventions with cystojejunostomies. The morbidity was 27.9%, with a reoperation rate of 7.3% and zero mortality. In general the patient's pain resolved in the postoperative period. Median follow-up was 43 months (range, 4–191 months). One patient died from other causes, and all others are currently alive. In the group of 32 patients who did not undergo operation, the median follow-up is 69 months (range, 8–164 months). Until more sophisticated technologies can be developed, the current diagnostic workup will not result in increased preoperative diagnosis of serous-cystic tumors of the pancreas. This is mainly relevant to the oligocystic forms, which account for about one fourth of all serous tumors observed.

Among the cystic neoplasms of the pancreas the serous cystic tumors (SCTs) are considered, with only ten exceptions reported in the literature [1–9], to have a benign biological and clinical course. The others, in particular the mucinous tumors, are either already malignant or tend to degenerate with time, and therefore surgical resection is the mandatory treatment of choice [10, 11].

The correct identification of clearly benign asymptomatic SCTs, and therefore the only possible indication for nonsurgical management of cystic neoplasm of the pancreas, is crucial. If the tumor type cannot be identified with absolute certainty in the diagnostic workup, laparotomy is inevitable, even for SCTs incidentally discovered, for no other reason than for a definitive and complete histological diagnosis [12–16].

The purpose of the present work was to analyze 100 consecutive cases of SCTs seen in our pancreatic unit. We present the general characteristics, clinical picture, and diagnosis. To verify the degree to which current techniques of imaging can influence management decisions, we paid particular attention to the various treatment options in two different periods, 1988–1994 and 1995–June 2001.

Patients

From 1988 until June of 2000, 599 patients affected with cystic lesions of the pancreas were admitted to our unit. Of these, 280 lesions (46.7%) were pseudocystic in nature, 102 (17%) were intraductal papillary mucinous, 100 (16.7%) were serous, 62 (10.3%) were mucinous, 39 (6.5%) mucinos cystadenocarcinoma and 16 (2.8%) solid papillary cystic tumors. All of the clinical findings were prospectively inserted into a computerized database. The patient's clinical history and perioperative course were then retrospectively selected and analyzed. Follow-up information was obtained via our pancreatic clinic or from patient physicians, or both. The 100 cases of SCTs are the object of the present work; the study group will be referred to using absolute numbers because of the obvious correlation of these with the percentage rates. In this group, 87 women with a median age of 51.86 years (range, 21–72 years) and 13 men with a median age of 53.76 years (range, 26–96 years) were treated; all of them underwent an ultrasound examination and computed tomography (CT) scan. Twenty patients were also studied with magnetic resonance imaging (MRI), 17 with endoscopic cholangiopancreatography, and 9 with endoscopic ultrasound. The cystic lesions presented with a median diameter of 3.7 cm (range, 1–10 cm).

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Table. 1. Symptoms of 44 patients affected with serous cystic tumors of the pancreas.

Pain[a]	33 (75%)
Anorexia and dyspepsia	7 (15.9%)
Weight loss and dyspepsia	6 (13.6%)
Obstruction of the upper GI tract[b]	3 (6.8%)

GI: gastrointestinal.
[a]Five patients (11.3%) suffered from pain associated with dyspepsia.
[b]One case with associated jaundice.

Results

In Table 1 the symptoms that led to radiological examinations in 44 of the 100 SCT patients are reported. The time lapse from the presentation of symptoms and diagnosis of the cystic lesions of the pancreas was, on average, 19.7 months (range, 5–50 months). In 56 patients the diagnosis of a pancreatic neoplasm was made incidentally during ultrasonographic exams performed for completely different reasons, usually for gynecological reasons. The mass was situated in the head of the pancreas in 31, the body in 27, the tail in 25, and the isthmus in 14 patients. Three patients were affected with von Hippel-Lindau (VHL) disease and presented with multiple pancreatic cysts, as expected. Typical characteristics (microcystic with a sponge-like "honeycomb" aspect or central scar, or both) led to precise diagnosis of SCTs in 74 patients (Fig. 1), and 26 others (Fig. 2) presented with a multiple macrocystic or unilocular aspect (oligocystic variant).

Ultrasound examination allowed for the correct diagnosis in 53% of cases, incorrect diagnosis in 31%, and was nondiagnostic in 16%; the results of CT scan were 54%, 34%, and 12%, respectively, and those with MRI were 74%, 26%, and nil, respectively.

In 21 cases a needle aspirate of the cystic contents was performed; only 8 samples (38%) were sufficient on the basis of the characteristics of the liquid and cytology to make a clear diagnosis of a serous tumor. In 12 patients it was not possible to acquire sufficient material for a definitive diagnosis; one case demonstrated an epithelial dysplasia, which necessitated analysis of a complete specimen. The resulting diagnosis showed a need for operation, but this patient was already a candidate for resection on the basis of symptoms alone. In another patient the needle aspiration injured the gastroduodenal artery resulting in a severe hemorrhage. We did not observe other complications related to this procedure (morbidity 4.7%). Sixty-eight patients were treated surgically; in the 44 symptomatic patients the principal indication for surgery was the presence of their symptoms. The other 24 patients who underwent operation presented with single cystic lesions that were not easily characterized preoperatively as serous or mucinous. Two patients underwent a resection, after a delay of 12 months and 13 months, respectively, after the cystic component of the lesion demonstrated a significant increase in diameter. For this purpose, significance was defined as more than 2 cm/year detected by the same operator. In Figure 3 the differences for the two time periods of the study (first 7 years and second 6.5 years) are summarized for patients who were observed and those who were operated on. There was a small decrease during the more recent period that was not statistically significant.

Surgical procedures in this series were as follows: 21 (30.8%) pancreatic tail resections (of which 8 "open" procedures were done with preservation of the spleen and 3 (recently) were performed laparoscopically); 14 (20.5%) intermediate resections; 10 (14.7%) pancreaticoduodenectomies; 4 (5.8%) enucleations, and 1 (1.4%) duodenum-preserving pancreatic head resection.

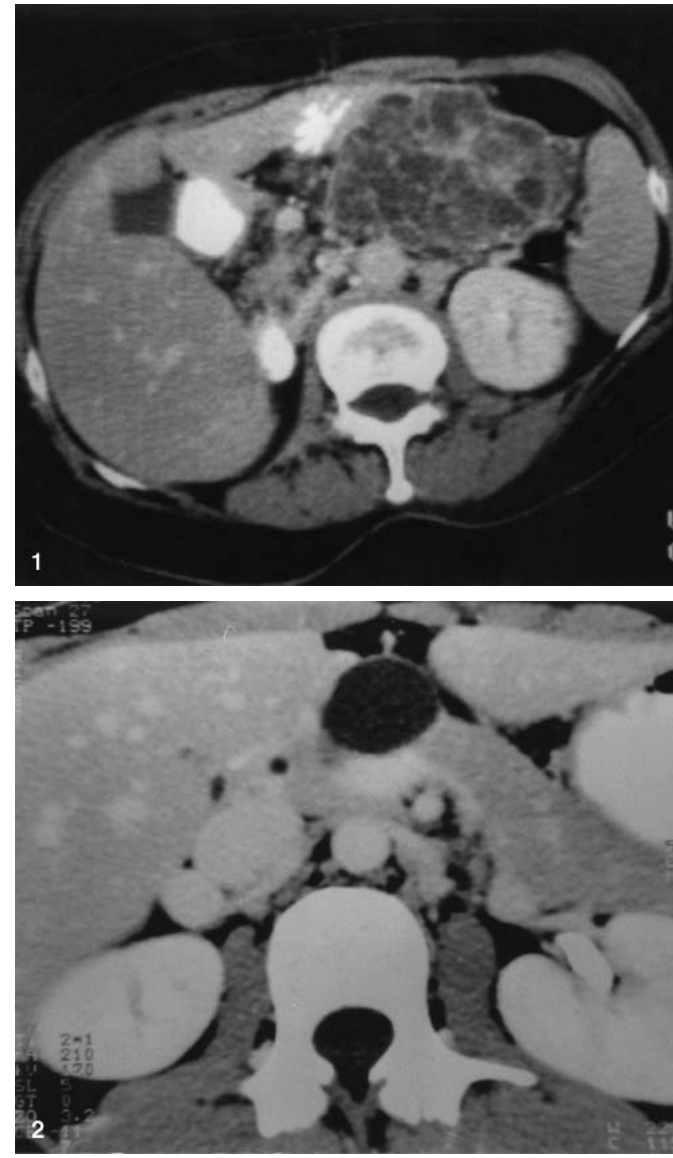

Fig. 1. Classic "honeycomb" aspect of the microcystic variant in a serous pancreatic tumor of the pancreatic body-tail.

Fig. 2. Unilocular aspect of a serous cystic tumor of the pancreatic neck (oligocystic variant). The computed tomographic findings cannot discriminate this lesion from a mucinous one.

All 11 patients who underwent resection of the pancreatic head were suffering from severe daily pain associated, in five patients, with severe dyspepsia and, in one, with obstructive jundice. Nine patients (13.2%), underwent exploratory laparotomy with a diagnostic biopsy. Palliative procedures (cystojejunostomies) were performed on 6 patients with elevated anasthesia risk (ASA 4) and in 3 patients with VHL. Comorbidity was mainly related to severe heart diseases in ederly patients.

Nineteen (27.9%) patients suffered surgical complications. In particular, the postsurgical database revealed 11 (16%) pancreatic fistulas (defined as output of, at least, 10 cc of liquid containing >

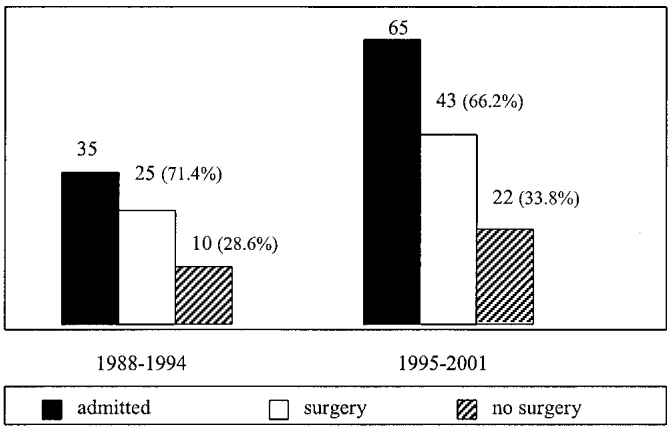

Fig. 3. Comparison of patients observed/operated in the two study periods.

1000 U/L of amylase after postoperative day 7). The complications were highest among those patients undergoing intermediate pancreatectomies (4/13 [30.7%]), while 27% of the pancreatic head resections (3/11), 25% of the enucleations (1/4), and 15.7% of the distal pancreatectomies (3/19) were associated with complications. Reoperation was necessary in 5 patients (7.3%), in 2 for hemorrhages, in 2 for abscesses, and in 1 for intestinal obstruction secondary to adhesions. In this series there have been no deaths. The median follow-up was 43 months (range, 4–191 months). One patient died from other causes, and all the others are currently alive and free of disease. All patients reported relief of symptoms in the immediate postoperative period.

In the 32 patients who did not undergo operation, the median follow-up is 69 months (range, 8–164 months), without any observed development of malignancy or any significant increase in the diameter of the lesion (> 2cm/year).

Discussion

Serous cystic tumors occur mainly in women; when symptomatic, they present with an aspecific and tricky clinical picture that usually results in a long lapse in time (about 18 months in the present study) before the diagnosis can be made [12–14]. The principal symptom is abdominal pain, but only 25% of our patients with symptoms had pain partially radiating to the flanks suggesting a possible pancreatic etiology; this is consistent with the experience of other authors [15–17]. Moreover, the clinical picture is not always correlated with the location and dimension of the neoplasm. In our opinion, the relative benignness of asymptomatic SCTs still permits, in selected cases, a conservative approach. This is even more true for patients of advanced biological age and comorbidity, those with an unfavorable clinical condition like VHL syndrome, and those with a tumor located in the head of the pancreas which makes the risk of surgery especially high. This management approach is only possible when the diagnosis is certain, and it clearly cannot be pursued when the only evidence is radiological demonstration of a single cystic lesion. Such lesions represent 26% of the variants in this series. In such cases the mass almost always consists of a capsule with a central unilocular or multilocular macrocystic component, and the radiographic images cannot discriminate these lesions from lesions caused by inflammation, peripheral mucinous or intraductal tumors, or papillary, cystic, or neuroendocrine tumors [18]. Fortunately, the "classic" microcystic variant is the most frequent of the SCTs, but in the presence of small tumors with significant connecting components, both ultrasound and CT can give the appearance of a solid neoplasm. However, MRI (carried out in the present series in only the more recent 20 patients, for whom further information was required after CT scan) can magnify the T2-weighted image of the liquid contents and the microcystic nature of the mass. Thanks to this technique, we have recently been able to make a definitive diagnosis in some patients who would otherwise have required a surgical procedure. The recently observed reduction in surgically indicated procedures, even if only limited from 71.4% to 66.2% of the total cases, seems to be due to improvements in the radiological work-up and to be deserved to future increasing rate.

Faced with a single cystic lesion, the possible utility of ultrasound or CT guided aspiration becomes a further problem in the diagnostic algorithm. The biochemical and cytological analysis of the intracystic liquid does not always directly correlate with the diagnosis [19–21]. Furthermore, there remains the disturbing unresolved problem of potential spread of malignant cells. In the case of a mucinous lesion, both the elevated percentage of superficial internal dysepithelialization and the coexistence of various degrees of dysplasia reaffirm that aspiration should be reserved only for selected cases. These considerations explain our limited number of aspirations (21%), which are further justified by the fact that only 38% of the aspirations were able to provide a definitive diagnosis.

Today a reliable decision not to undergo surgery for sero-cystic lesions of the pancreas must also take into account two additional elements recently stressed in the literature. The first is based on results of autopsies done in Japan [22] where 24% of cases analyzed revealed small sero-cystic lesions of the pancreas associated with a significant tendency to epithelial degeneration directly proportional to age. These data suggest a "natural history" of cystic tumors of the pancreas and correlates well with our sporadic observation of epithelial dysplasia. The second element is the documented, although still rare, potential malignant transformation of SCTs [1–9]. In particular, a recent report [9] appears to extend the present knowledge of SCTs, reporting a surprisingly high rate of malignancy (12%) and a strong association between SCTs and ductal cancer (8%).

Only "high volume" centers can guarantee the necessary surgical expertise to approach the "soft" pancreas with a cystic mass [23]. For example, in the present series, the rate of complications, particularly pancreatic fistulas, was higher than we usually report [24, 25]. It is wise that such resections are performed at major centers; in our experience, the complication rates can be limited, as can the clinical impact of related reoperations (7.3%) and mortality (nil).

Regarding the choice of resection, the gamut runs from classic pancreatic head and body-tail resections to more conservative operations with preservation of the spleen, sometimes performed laparoscopically. The finding of elevated pancreatic fistula rates after intermediate resections (30.7%), which is only partially influenced by our severe definition of this complication, suggests the need for more stringent evaluation to ascertain the real functional benefits of preservation of pancreatic parenchyma, the main reason for the procedure [26, 27].

In conclusion, 68% of the patients admitted to our unit with SCTs underwent a surgical procedure. Because of our particular experience as a referral center for pancreatic deseases, we have

reason to believe that this is not the same as that experienced at other centers, which are usually influenced by the decision of a family doctor or the direct diagnosis by a radiologist. Probably, at least in Italy, more than 30% of cases are never referred to a specialist. This is indirectly demonstrated by the long delay, even in symptomatic patients, from symptoms to diagnosis. The experience acquired in the sector of malignant cystic neoplasms of the pancreas indicates that the label "benign tumor" is often based on elements that are superficial, delaying in every case radical treatment, which could potentially heal the patient and instead condemns them [10]. As a result, all cystic lesions of the pancreas merit a specialist's consult.

In 44 patients the symptomatology mandated an intervention, whereas in 23 patients the work-up did not allow a definitive diagnosis regarding the benign or malignant nature of the cyst. The high number of surgical options, constant in the two contiguous analysis periods, is substantially correlated with the continued difficulty in preoperative identification of the serous character—benign oligocystic variant. Modern radiographic technology permits resolution in microcystic cases of small diameter, previously confused with solid masses; this seems to be the main factor responsible for the limited reduction in surgically managed cases.

Despite the fact that some reports of a high rate of malignant SCTs advocate oncological surgical resections as the only recommended options, in light of our very recent experience and that reported elsewhere [28], a synthesis of the management of SCTs can be attained by the time-honored surgical dictum "wait and see," in regards to the symptoms and radiological findings, becoming effectively "wait (for symptoms) and see (at imaging)."

Résumé. La malignité des cystadénomes séreux (CS) du pancréas est rare. Lorsque le CS est asymptomatique, on peut le traiter chez certains patients sans chirurgie; cependant, il faut une haute précision diagnostique. Nous avons analysé 100 cas consécutifs de CS (87 femmes d'une médiane d'âge de 51.86 ans), parmi lesquelles 44 étaient symptomatiques et 56 ont été diagnostiquées de façon fortuite. L'échographie a correctement fait le diagnostic dans 53% des cas, incorrectement dans 31% des cas, et n'a pas apporté de diagnostic dans 16%. La tomodensitométrie a produit des taux de succès similaires (rétrospectivement, 54%, 34% et 12%), alors que l'IRM a amélioré la précision diagnostique à 74% et a réduit le nombre de diagnostics incorrects à 26%. Parmi les 21 cas de ponction exploratrice du kyste, seulement huit échantillons (38%) ont produit un diagnostic, chez 12 patients (57%) le matériel acquis a été insuffisant pour permettre le diagnostic alors qu'un cas a montré une dysplasie épithéliale. Une hémorragie grave a été observée. Soixante-huit patients ont été traités chirurgicalement, dont 44 cas symptomatiques et 24 autres patients ayant des lésions pauvres en cellules («oligocytiques»), mal-définies que l'on ne pouvait différencier entre des lésions «mucineuses» ou «séreuses» en préopératoire. Deux patients ont eu une résection en raison d'une croissance tumorale franche. Dans les deux intervalles de temps analysés (les sept premières années et les 6.5 ans suivantes), on n'a noté aucune modification entre les cas observés ou opérés. On a rélisé 21 (30.8%) pancréatectomies distales, 14 (20.5%) résections intermédiaires, 10 (14.7%) duodénopancréatectomies, 4 (5.8%) énucléations et 1 (1.4%) duodénopancréatectomie avec conservation duodénale. Neuf patients (13.2%) ont eu une laparotomie exploratrice avec une biopsie à visée diagnostique. Neuf autres ont eu une anastomose kystojéjunale. La morbidité a été de 27.9%, avec un taux de réopération de 7.3% et aucune mortalité. En général, la douleur a disparu dans la période post-opératoire. La médiane de suivi a été de 43 mois (extrêmes 4–191). Un patient est décédé secondairement à d'autres causes alors que les autres patients sont toujours en vie. Dans le groupe de 32 patients qui n'ont pas été opérés, la médiane de suivi a été de 69 mois (extrêmes 8–164). Jusqu'à ce qu'il y ait des technologies plus sophistiquées, on ne pourra améliorer le diagnostic préopératoire des tumeurs kystiques séreux du pancréas. Ceci est principalement en raison des formes oligocytiques qui représentent environ un quart de toutes les tumeurs séreuses rencontrées.

Resumen. Los cistadenomas serosos del páncreas tienen una baja tasa de malignidad. Los no sintomáticos, en pacientes seleccionados, pueden ser manejados sin cirugía, pero se requiere un alto grado de precisión diagnóstica. El presente estudio se hizo sobre cien pacientes consecutivos (87 del género femenino, con edad promedio de 51.86 años), de los cuales 44 eran sintomáticos y 56 fueron diagnosticados en forma incidental. La ultrasonografía estableció el diagnóstico correcto en 53% de los casos, incorrectamente en 31% y fue no diagnóstica en 16%. La tomografia computadorizada exhibió resultados similares (54%, 34%, y 12%, respectivamente), en tanto que la resonancia magnética mejoró la certeza diagnóstica a 74%, y redujo el diagnóstico incorrecto a 26%. En 21 casos se practicó aspiración exploratoria del quiste con aguja; sólo en 8 muestras (38%) se pudo establecer el diagnóstico; en 12 pacientes (57%) el material resultó insuficiente para establecer el diagnóstico, y en uno se demostró displasia epitelial. En un caso la punción exploratoria produjo sangrado muy serio. Sesenta y ocho pacientes fueron tratados quirúrgicamente, los 44 sintomáticos y otros 24 con lesiones oligoquísticas no bien definidas que preoperatoriamente no pudieron ser diferenciadas entre serosas o mucinosas. En dos pacientes se hizo resección por franco crecimiento tumoral. En los dos periodos analizados (los primeros 7 años y los siguientes 6.5 años) no se observó cambio significativo en la proporción de los casos sometidos a observación frente a los casos operados. Se practicaron 21 (30.8%) pancreatectomías distales, 14 (20.5%) resecciones intermedias, 10 (14.7%) pancreatoduodenectomías, 4 (5.8%) enucleaciones y 1 (1.4%) resección de la cabeza del páncreas con preservación del duodeno. En nueve (13.2%) pacientes se efectuó laparotomía exploratoria con biopsia diagnóstica, y en otros nueve se practicaron intervenciones de descompresión con cystoyeyunostomías. La tasa de morbilidad fue 27.9%, con una tasa de reoperación de 7.3% y cero mortalidad. En general, el dolor desapareció en el periodo postoperatorio. El seguimiento mediano fue de 43 meses (rango 4–191 meses). Un paciente falleció por causa diferente, y todos los demás se encuentran vivos. En el grupo de 32 pacientes en que no se practicó operación, el seguimiento mediano fue de 69 meses (rango 8–164). Hasta cuando se disponga de tecnologías más sofisticadas, con el procedimiento diagnóstico actual no se logrará una mayor precisión diagnóstica de los tumores seroquísticos del páncreas; esto es especialmente pertinente en el caso de los tipos oligoquísticos, los cuales constituyen alrededor de la cuarta parte de todos los tumores serosos.

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