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Solid and Papillary Neoplasms of the Pancreas

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Solid and papillary neoplasms of the pancreas, a rare tumor usually found in young female patients, seldom presents with metastasis since it is a tumor with low potential for malignancy. The prognosis for this lesion is much more favorable than that for other pancreatic neoplasms. In an attempt to understand the characteristics and prognosis of this lesion, we reviewed twenty cases treated at the Department of Surgery, Severance Hospital, Yonsei University from 1985 to 1994. The mean age of the patients was 25.6 years(range: 13 to 39 years), and 19(95%) were women. Chief complaints were palpable mass(50%), pain(45%), and indigestion(5%). In laboratory studies, tumor markers, including CEA, CA125, CA19-9, and aFP were studied in eight patients, and found negative. Other laboratory findings were also nonspecific. These tumors may occur anywhere in the pancreas. In our studies, the tumor was most often located in the tail(45%), and the head(40%) of the pancreas. These were treated by distal pancreatectomy and splenectomy(55%), Whipple's operation (20%), pylorus preserving pancreatoduodenectomy(10%), enucleation(10%) or excision(5%). Significant morbidity or mortality was not observed during hospitalization, and no recurrence or malignant degeneration occured during the mean follow-up period of 4 years(range: 1 month to 9 years). In conclusion, this study has suggested that the patients with a solid and papillary neoplasm of the pancreas have a good prognosis for successful treatment, if the disease is diagnosed early and the tumor is completely resected. A higher index of suspicion, and more aggresive diagnostic workups are needed in dealing with this disease entity.

Key Words: Solid and papillary neoplasms of the pancreas

INTRODUCTION

Primary tumors of the exocrine pancreas are numerous, and many different histological types are known(Cubilla and Fitzgerald, 1979). They are often highly malignant. The prognosis of these tumors is usually poor, since they are often diagnosed at a later stage, and when discovered, involvement of the pancreas proper and other adjacent organs is frequent. Solid and papillary neoplasms of the pancreas, a rare tumor usually found in young female patients, seldom presents with metastasis because of its less aggressive nature. The prognosis for this lesion is much more favorable than that for other pancreatic neoplasms. It arises at the tail or the body of the pancreas, usually forming an encapsulated large mass. However, local and distant metastasis is rare, and when radical excision is performed, favorable prognosis can be expected, which distinguishes this tumor from the other more aggressive pancreatic tumors. Since the initial report by Frantz of 3 cases in 1959(Frantz, 1959), sporadic reports have been available in the literature(Hamoudi *et al.* 1970; Compagno and Oertel, 1979), and in Korea, a total of 10

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cases have been reported by Bae *et al.*(1984), Jung *et al.*(1985), Hong *et al.*(1988). and Ahn *et al.*(1990). In an attempt to understand the characteristics and prognosis of this lesion, and emphasize the necessity of an early and more aggressive diagnostic workup, we hereby report twenty cases treated at the Department of Surgery, Severance Hospital, Yonsei University from 1985 to 1994, along with a review of the literature.

MATERIALS AND METHODS

20 pathologically confirmed cases of solid and papillary neoplasms of the pancreas treated at the Department of Surgery, Severance Hospital, Yonsei University, from 1985 to 1994 were retrospectively reviewed. The selection and data collection were based on the hospital records, and the follow up status was evaluated, based on recent outpatient clinic records or telephone interviews. The follow up information was available in all 20 cases, and the follow up periods were between 1 month to 9 years postoperatively.

RESULTS

Distribution of age and gender

Among 20 patients, 19(95%) were women, and the mean age was 25.6 years(range: 13 to 39 years).

Clinical manifestations and physical examination

A palpable abdominal mass was the most commonly encountered clinical manifestion(50 %) of this lesion, and other common symptoms were abdominal pain(45%) and indigestion(5%)(Table 1). An abdominal mass was palpable at the left upper quadrant(5 cases), epigastrium(3 cases), right upper quadrant(1 case), and periumbilical area(1 case). Abdominal pain was felt at the left upper quadrant(4 cases), epigastrium(4 cases), and right upper quadrant(1 case). In most patients, the abdominal mass and pain were felt at the left upper quadrant and epigastrium(Table 2 & 3).

Other associated symptoms were postprandial abdominal discomfort, general weakness, nausea, vomiting, weight loss, diarrhea, flank pain, and constipation. Jaundice was not observed in any of the cases.

Duration of infliction

A duration of symptoms ranged from 2 days to 2 years(mean 4 months), but most were less than 1 month in 12 cases(60%). Symptoms lasting more than 6 months comprised 5 cases (25%).

Laboratory findings

Peripheral blood smear, urinalysis, and serum electrolytes were normal in all 20 cases.

Table 1. Chief complaints

Chief complaints	No. of cases(%)
Palpable mas	10 (50)
Pain	9 (45)
Indigestion	1 (5)

Table 2. Location of palpable mass(N=10)

Location	No. of cases
LUQ	5
Epigastrium	3
RUQ	1
Periumbilical	1

-LUQ; left upper quadrant
RUQ; right upper quadrant

Table 3. Location of pain(N=9)

Location	No. of cases
LUQ	4
Epigastrium	4
RUQ	1

-LUQ; left upper quadrant
RUQ; right upper quadrant

One patient had elevated liver enzymes which was attributed to the history of chronic hepatitis. All tests were also normal after surgical exploration. Serum amylase was elevated in one case. The level was 596 IU/L(N:60-180 IU/L), and serum lipase was elevated to 340 IU/L (N:0-190 IU/L) in the same case, but among 11 cases evaluated, no other elevations were noted. The elevated amylase and lipase were attributed to concomitant postoperative pacreatitis.

Tumor markers, such as CEA, CA19-9, CA125, aFP were evaluated in 8 patients, without revealing any abnormality. In three patients, all markers were evaluated.

Radiological findings: Abdominal ultrasonography or abdominal computerized tomography were performed in all 20 cases, with 17 patients having both. 2 cases were diagnosed by abdominal ultrasonography, and 1 case was diagnosed by abdominal computerized tomography. In the radiological evaluations, the mass was well demarcated from the surrounding tissues and the margins were smooth and well encapsulated. Internally, cystic and solid components were seen simultaneously(Fig. 1 & 2). In two cases, the surfaces were lobulated. In five cases, calcifications were noted. Local and distant invasions were observed in none of the cases.

Among the 19 cases where preoperative abdominal ultrasonographic evaluations were performed, 11(58%) were correctly diagnosed with a solid and papillary neoplasm of the pancreas. Other diagnoses were pancreatic pseudocyst, cancer, and pancreatic tumor. All patients exhibited abnormalities on ultrasonography. Among the 18 cases where abdominal computerized tomography(CT) was performed, 17 revealed abnormalities. 11(61%) were diagnosed with a solid and papillary neoplasm of the pancreas. Other diagnoses included cancer and lymphadenopathy(Table 4).

On endoscopic retrograde cholangiopancreatography(ERCP), displacement or obstruction of the pancreatic duct was noted(Fig. 3). On the upper gastrointestinal series(UGI), performed in 8 cases, there was no invasion of the gastrointestinal tract. However, the stomach, duodenum or other parts of the small in-

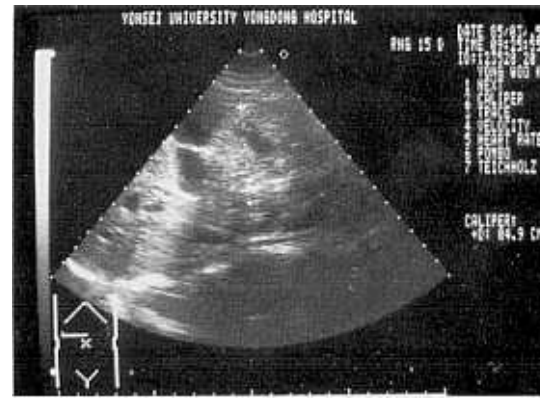

Fig. 1. Pancreatic mass which was composed of solid & cystic portions.

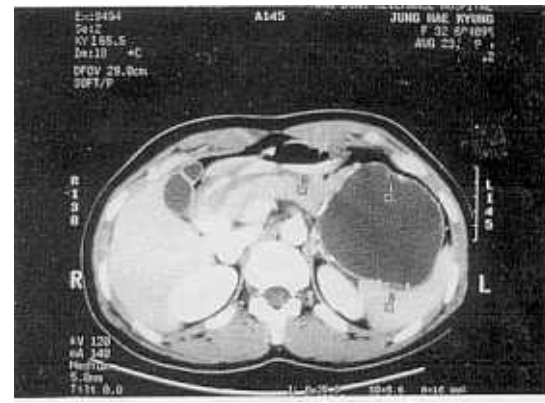

Fig. 2. Well capsulated, homogenous, huge mass undergoing central necrosis & subcapsular calcification. Contrast study did not show any central enhancement.

Table 4. Diagnostic study

Study	Tested positive (No. of cases)	(%)
Ultrasonography	19/19	(100)
CT scan	17/18	(94)
ERCP	10/11	(91)
NAB	5/5	(100)
UGI	4/8	(50)

−CT; computed tomogram

ERCP; endoscopic retrograde cholangipancreatography

NAB; needle aspiration biopsy

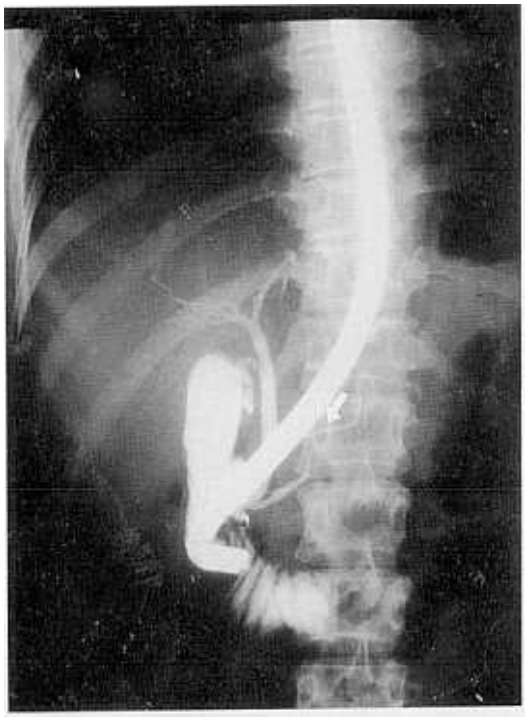

Fig. 3. ERCP showing that pancreatic duct was upward displaced, but not obstructed (arrows).

testine were compressed or displaced according to the various locations of the pancreatic mass.

In 5 cases, needle aspiration was performed. 4 cases were diagnosed with solid and papillary tumor, and 1 case was reported to be a malignant papillary adenocarcinoma, which was confirmed to be a solid and papillary neoplasm on surgical excision.

Other diagnostic tools used were fiberoptic gastroscopy, barium enema, MRI and arterial angiography. All gave nonspecific results.

Surgical exploration and operative findings

The time elapse from hospital admission to surgery, ranged from 3 to 33 days with a mean of 8.6 days. 16 cases(80%) were explored within 10 days of admission. The most commonly utilized types of skin incision were the right paramedian(4), and the left paramedian (4). The lengths of the skin incision ranged

Table 5. Location of tumor & type of operation

Location	Type of operation	No. of cases
Head(n=8)	Pancreatoduodenectomy	4
	PPPD*	2
	Enucleation	
	Excision & end to end anastomosis of panc. duct	
Body & Tail (n=12)	DP** & Splenectomy	11
	Enucleation	

*PPPD: pylorus preserving pancreatoduodenectomy
**DP: distal pancreatectomy

from 10 to 30 cm, with a mean of 18.9 cm.

The mass was located at the pancreatic tail in 9 cases(45%), tail and body in 2 cases(10%), body in 1 case (5%), and head of the pancreas in 8 cases(40%). In 11 of 12 cases when the tumor was located at the pancreatic tail, tail and body, or body of the pancreas, distal pancreatectomy with splenectomy was employed. One remaining patient received enucleation of the tumor mass. Among 8 cases in which the tumor was located at the head portion of the pancreas, Whipple's operation was performed in 4 cases, and a pylorus preserving pancreatoduodencetomy was done in 2 cases. In the other two cases, tumor enucleation alone and enucleation with pancreatic duct anastomosis were done(Table 5 & 6).

Severe adhesion to the adjacent organs was noted in 7 cases on surgical exploration. No infiltration of the tumor mass was grossly found, but in one case a capsular invasion to the spleen was reported on histologic evaluation. No distant metastasis was seen. Lymph node enlargements were suspected on palpation in 8 cases, but pathologic review confirmed all to be benign reactive hyperplasia.

The diameter of the mass ranged from 2 to 13 cm, with the mean diameter of 7.8 cm. The weight of the resected lesion was reported in 7 cases, which ranged from 24 to 750 gm, with the mean of 288 gm.

The duration of hospitalization ranged from 8 to 51 days(mean : 14.6 days). 4 patients who received Whipple's operation stayed considera-

Table 6. Case review(20 patients)

No.	Sex/Age	Duration (year)	Tumor		Operative methods
			Location	Size(cm)	
	F/31	10/12			DP & SP
2	F/28	2/365			DP & SP
3	F/27	2			DP & SP
4	F/15	1			DP & SP
5	M/13	10/365			DP & SP
6	F/18	10/365			Excision & end to end anastomosis of panc.duct
7	F/21	1/12	head	10×10×12	Whipple's OP.
8	F/33	1/12	tail	10×8×5	DP & SP
9	F/34	1/12	body, tail	4×3×4	DP & SP
10	F/34	4/12	head	2×3×2	Whipple's OP.
11	F/25		tail	11×9×7	DP & SP
12	F/29	1/12	head	7×5×5	PPPD
13	F/25	6/12	head	13×12×5	Whipple's OP.
14	F/39	3/12	tail	4×5×3	Enucleation
15	F/32	1/12	head	2×2×1	Whipple's OP.
16	F/24	6/12	head	7×7×5	PPPD
	F/23	10/365	head	7×5×4	Enucleation
18	F/23	1/12	tail	7×8×10	DP & SP
19	F/13	10/365	tail	4×5×4	DP & SP
20	F/24	15/365	body	6×6×5	DP & SP, Incidental appendectomy

(DP: distal pancreatectomy, SP: splenenctomy PPPD: pylorus preserving pancreatoduodenectomy)

bly longer, which is understandable in light of the wide field of dissection required for this procedure. One of these patients had a wound infection and postoperative leak from choledochojejunal anastomosis which was managed conservatively. The remaining 16 patients were discharged within 2 weeks of the operation without complications.

Pathological findings

Gross findings: The mass was usually round or oval and multinodular. The surfaces were smooth and covered with a fibrous capsule. On the cut section, the mass was omposed of numerous cysts, within which dark bloody necrotic tissue was found. Solid whitish yellow components were found between the cystic structures(Fig. 4).

Histological findings: Large cystic tumors

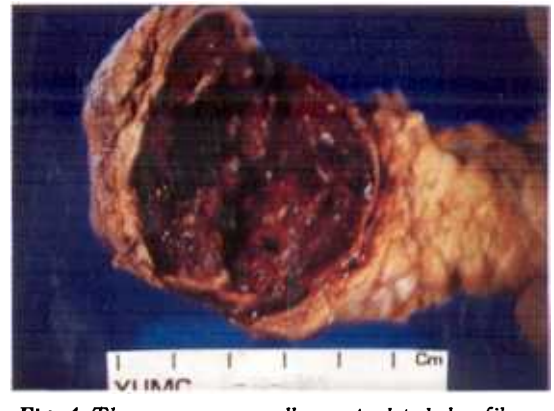

Fig. 4. The mass was well encapsulated by fibrous capsule, and it was composed of numerous cysts, within which dark bloody necrotic tissues were found.

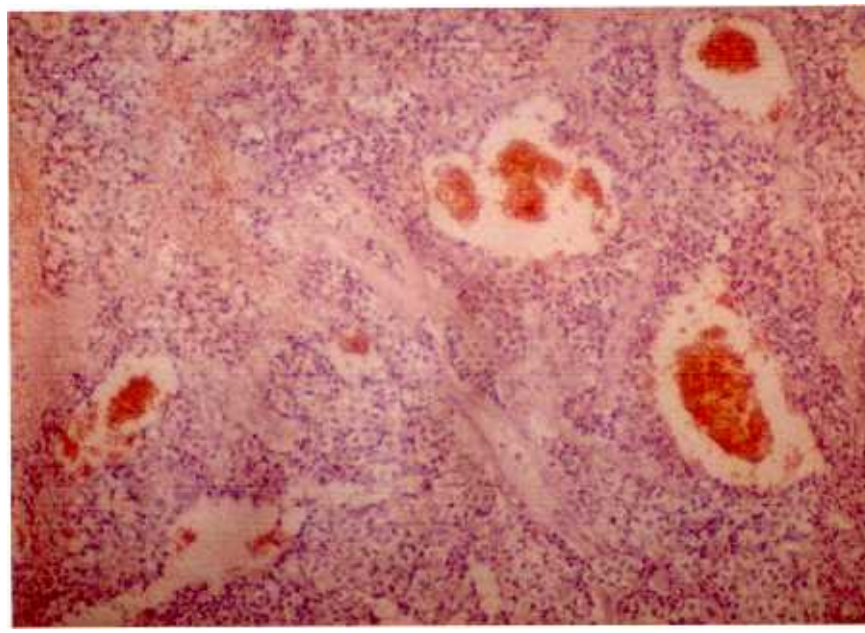

Fig. 5. *Solid area with microcystic spaces containing amorphous eosinophilic material and fibrous septa (H & E, ×100).*

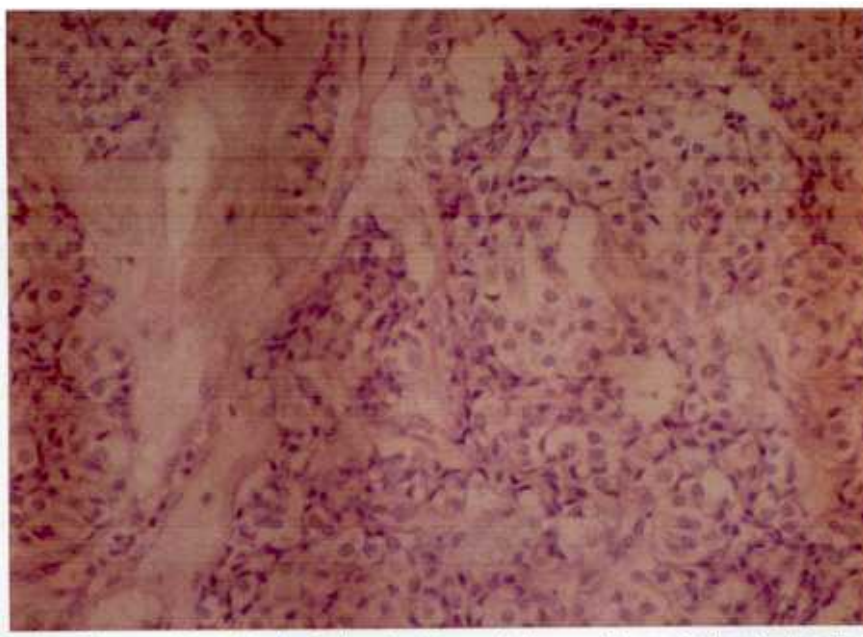

Fig. 6. *Small uniform oval shaped cells of abundant clear cytoplasm with rounded and relatively clear nuclei Multiple microcystic area & fibrous septa were noted (H & E, ×200).*

were composed of various small sized cystic and solid papillary components. The compositions were variable among the specimens but both components were present in all cases. Multiple septa were found in the solid compartment. Fine fibrovascular stroma divided the celluar mass into nests. Cells were oval or rectangular with eosinophilic cytoplasm and oval nucleus. The size and shape of individual cells were rather uniform. No active mitosis or celluar pleomorphism were noted. Small cysts were filled with amorphous, eosinophilic materials(Fig. 5 & 6).

Follow up

Postoperative status after discharge was evaluated based on recent outpatient clinic records or telephone interviews. Information was available in all 20 cases, and follow up periods were between 1 month to 9 years postoperatively. 9 cases were followed under 2 years, 4 cases between 2 to 5 years, and 7 cases were followed for more than 5 years. Among the 7 patients currently visiting outpatient clinics, 3 do not have any signs and symptoms. 4 patients complain of indigestion or abdominal pain. Common symptoms during the immediate postoperative periods were epigastric discomfort or pain, vomiting, right upper quadrant pain, wound paresthesia, and indigestion, which were observed in 10 patients. However only 4 patients still complain of similar symptoms but state that there is less severity.

Radiological monitorings after operations were ultrasonography, computerized tomography(CT), UGI and fiberoptic gastroscopy in 11 cases. Ultrasonography was performed in 8 cases. Common findings on ultrasonography were abdominal fluid collection(2 cases), atrophic changes in the pancreas(1 case), dilated pancreatic ducts(1 cases), and no abnormality (4 cases). CT was done in 2 cases, and one patient had abdominal fluid collection, atrophic pancreas, and dilated pancreatic ducts. The other patient had no demonstrable abnormality on the CT scan(Table 7). On other tests, no abnormalities were found. Except for one patient, the above findings were found to be normal in the follow up serial evaluations.

Two patients were readmitted to our center; one patient with alkaline reflux gastritis was admitted one month after excision and was managed conservatively to health. The other patient was admitted for a total of 4 times after surgery. At first, two years after the initial operation, liver abscess developed and a pigtail catheter drainage was done. Two months later, CHD, IHD stones developed, so a choledocholithotomy, operative cholangiogram, and T-tube choledochostomy was done. Upon the third year, CBD stones developed and a PTBD was done. One month after the PTBD catheter insertion, recurrent IHD stones developed, and the patient was treated conservatively. The patient is being followed on an OPD basis.

No mortality or recurrence was observed

Table 7. Follow-up radiologic study

Study	Findings	Previous OP. name	No. of cases
Sono	Fluid collection	DP & SP	1
		Whipple	1
	PD dilatation	DP & SP	1
	Pancreas atrophy	Whipple	1
	Nomal		4
CT	Fluid collection, PD dilatation & Pancreas atrophy	Whipple	1
	Normal		1

(PD: pancreatic duct, DP: distal pancretectomy, SP: splenectomy)

after operation in all cases.

DISCUSSION

Solid and papillary neoplasm of the pancreas is a rare entity, both clinically and pathologically. Although the mass is usually huge at diagnosis, it is surprisingly benign clinically and rarely metastasizes. The origin of this tumor is controversial, but seems most likely derived from tubular structures, based on the morphologic studies of intercellular space, desmosome and the cellular configurations(Hamoudi *et al*, 1970; Boor and Swanson, 1979; Compagno and Oertel, 1979; Alm *et al*, 1981). However the presence of the granules containing neurotransmitters or endocrine substances and annulate lamellae also suggests paratubular origin(Bombi *et al*, 1984). Some suggest that both theories are only different expressions of the same hypothesis(Bae *et al*, 1984; Jung *et al*, 1985), since pancreatic paratubular or endocrine components all originate from tubules(Bockman, 1981). Kloppel *et al.* demonstrated intracellular alpha-1-antitrypsin from the tumor cell, thus supporting the paratubular origin, and since the tumor is prevalent among young females, the genetic or endocrine predispositions are suspected in the development of the tumor. There are many terms describing this entity, mostly based on histologic characteristics. For example, papillary cystic neoplasm(Boor and Swanson, 1979; Bombi *et al.* 1984), solid and cystic acinar cell tumor(Kloppel *et al*, 1981), papillary epithelial neoplasm(Hamoudi *et al*, 1970), and papillary cystic epithelial neoplasm(Bombi *et al*, 1984) are some of the terminologies used. It is very likely that this tumor has been classified or diagnosed under other types of pancreatic tumor(Compagno and Oertel, 1979; Sanfey *et al*, 1983). Porter has used the term "low grade papillary neoplasm", reflecting its benign clinical nature.

Compagno *et al.* have reported the mean age of 24 years, which was similar to our findings of 25.6 years.

The most common presenting symptoms were a large abdominal palpable mass with or without tenderness(Compagno and Oertel, 1979; Friedman *et al*, 1985). Among the 20 patients, 10(50%) who presented with a palpable abdominal mass, most were at the left upper quadrant (5 cases). Tenderness was noted in 9(45%) cases, at the left upper quadrant and epigastrium (4 cases each)(Table 1,2 and 3). Sometimes patients were asymptomatic and the tumors were found during other abdominal operations, but rarely, they were found due to hemoperitoneum from the rupture of the tumor(Kloppel *et al*, 1981; Bombi *et al*, 1984). Generalized symptoms such as jaundice or multiple joint pain are also among the encountered complaints(Mullin *et al*, 1968; Ahn *et al*, 1990), and occasionally skin induration similar to erythema nodosum is also noted(Mullin *et al*, 1968; Friedman *et al*, 1985). The joint pain is explained by the elevated level of serum lipase, as in pancreatitis, pancreatic ductal carcinoma, and acinar cell tumor, which cause fat necrosis at subcutaneous tissues around joints(Mullin *et al*, 1968; Ahn *et al*, 1990). In our series, no jaundice, multiple joint pain, or skin nodules were observed. Indigestion, nausea, vomiting, weight loss, flank pain, and constipation were other commonly encountered symptoms.

Peripheral blood smear, urinalysis, serum electrolytes, and serologic liver profiles are usually normal(Kuo *et al*, 1984; Ahn *et al*, 1990). In our series, one patient had an elevated level of liver enzymes which was later attributed to chronic hepatitis B.

Tumor markers such as CEA are usually nonspecific, which was confirmed in our patients. Eosinophilia has been reported(Kuo *et al*, 1984; Friedman *et al*, 1985) but we did not observe this.

On simple abdominal radiological evaluations, secondary defects or calcifications caused by the tumor could be seen(Bombi *et al*, 1984; Friedman *et al*, 1985). On the upper gastrointestinal series, surrounding organs compressed or displaced by the huge tumor mass could be observed, and on ERCP, deformed pancreatic ductal configurations, usually ductal structures within the tumor mass, could not be seen, and no communica-

tion with the pancreatic duct was noted. The obstruction of the main pancreatic duct is reported to be rare(Sanfey *et al*, 1983), but we have observed such obstruction in two patients. ERCP is a useful diagnostic modality in differentiating pseudocyst, pancreatic ductal carcinoma, and solid and papillary neoplasm of the pancreas(Samuel *et al*, 1994).

On abdominal ultrasonography and CT, solid and papillary tumor is seen as a huge encapsulated, well demarcated, tumor with both solid and cystic components. Differentiating it from the mucoid cystic tumors is difficult when the cystic component predominates (Friedman *et al*, 1985), but the measured Hounsfield units(HU) were around + 40 HU - + 50 HU which suggests that hemorrhagic necrosis is a key in differentiation(Alm *et al*, 1981; Choi *et al*, 1988). Calcification within or around the tumor is an infrequent finding, and should be differentiated from the other tumors with calcification, such as microcystic adenoma, mucinous cystic tumors, or nonfunctioning islet cell tumors. However the presence of calcification alone does not significantly aid in differentiating between these tumors(Friedman *et al*, 1985; Choi *et al*, 1988; Hong *et al*, 1988). In our series, calcific infiltration of subcapsular portion was seen in 5 patients(Fig. 2).

Arterial angiography revealed hypovascular tumor with displacement of surrounding vessels. On a contrast enhanced CT scan, the tumor could be differentiated, because acinar carcinoma shows total or partial increase in density, but only peripheral enhancement is seen in solid and papillary tumor(Alm *et al*, 1981; Balthazar *et al*, 1984; Hong *et al*, 1988).

Fine needle aspiration of the tumor is indicated when the mass should be differentiated from mucoid cystic tumor, pseudocyst, or pancreatic carcinoma(Tatsuta *et al*, 1986; Jones *et al*, 1987; Katoh *et al*, 1989; Samuel *et al*, 1994). CEA, CA19-9, pancreatic enzymes, presence of mucus, and cytological evaluation should be performed with the aspirate. We have performed 5 cytologic examinations, and in 4 cases, the information was helpful in preoperative diagnosis.

According to the location of tumor, distal pancreatectomy with splenectomy, pylorus preserving pancreatoduodencetomy, Whipple's operation or enucleation can be chosen. Surgery should be performed even if local infiltration is present(Kim *et al*, 1985), and in selected cases when complete excision is not possible, excision combined with postoperative radiotherapy on residual mass is feasible(Dales *et al*, 1983). In our series, 8 head portion tumors and 12 tail or body tumors were treated. In 11 of 12 cases, when the tumor was located at the pancreatic tail, tail and body, or body of pancreas, distal pancreatectomy with splenectomy was employed. One remaining patient received enucleation of the tumor mass. In 8 cases, where the tumor was located at the head portion of pancreas, Whipple's operation was performed in 4 of them, and pylorus preserving pancreatoduodencetomy in 2 of them. In the other two cases, tumor enucleation alone and enucleation with pancreatic duct anastomosis were done. On surgical exploration, no local or regional infiltration of tumor mass was found grossly, and no case of distant metastasis was seen. The average resected weight of the tumor was 288 gm and many of them were quite massive.

On microscopic analysis of solid and papillary neoplasms of the pancreas, central capillaries surrounded by papillary epithelial cells, small cysts of various sizes and intervening plated patterns of solid components are seen. It should be differentiated from acinar cell tumor, mucoid cystic carcinoma, carcinoid tumor, and tubular carcinoma. Mucoid tumor can easily be diagnosed by the presence of mucoid content within the tumor. Tubular tumor can be differentiated grossly without difficulty on the basis of capsule formation and low incidence of local infiltration.

Compagno and Oertel reported one death attributable to recurrence among 52 patients who were operated on due to solid and papillary neoplasm of the pancreas, with the mean follow up of 7.1 years. In the remaining 51 patients, no recurrence was observed. Sporadic cases of metastasis to the liver, abdominal cavity, or lymph nodes(Compagno and Oertel, 1979; Choi *et al*, 1988) and recurrence after several years are found in the literature

(Cubilla and Fitzgerald, 1979), but even in the face of recurrence or metastasis, the pathologic type of tumor is the same as the primary tumor, so when resected, good prognosis can be expected. On this study, the follow up periods ranged from 1 month to 9 years and no recurrence was found. 10 patients complained of epigastric discomfort or pain, vomiting, right upper quadrant pain, wound paresthesia, or indigestion. However only 4 patients still complain of similar symptoms and do so with less severity. In five patients, abdominal fluid collection, atrophic pancreas, and dilated pancreatic ducts were found on CT scan and ultrasonography. Among these patients, 3 had received pancreatoduodenectomy, and the findings on imaging studies were attributed to benign postoperative changes. Except for one patient, above findings were later found to be within physiological limits, and the remaining one patient is still in the process of being evaluated.

This tumor is rare, but if it is diagnosed and treated early, the prognosis is good. So a higher index of suspicion and more aggressive diagnostic efforts are recommended for this pancreatic disease.

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