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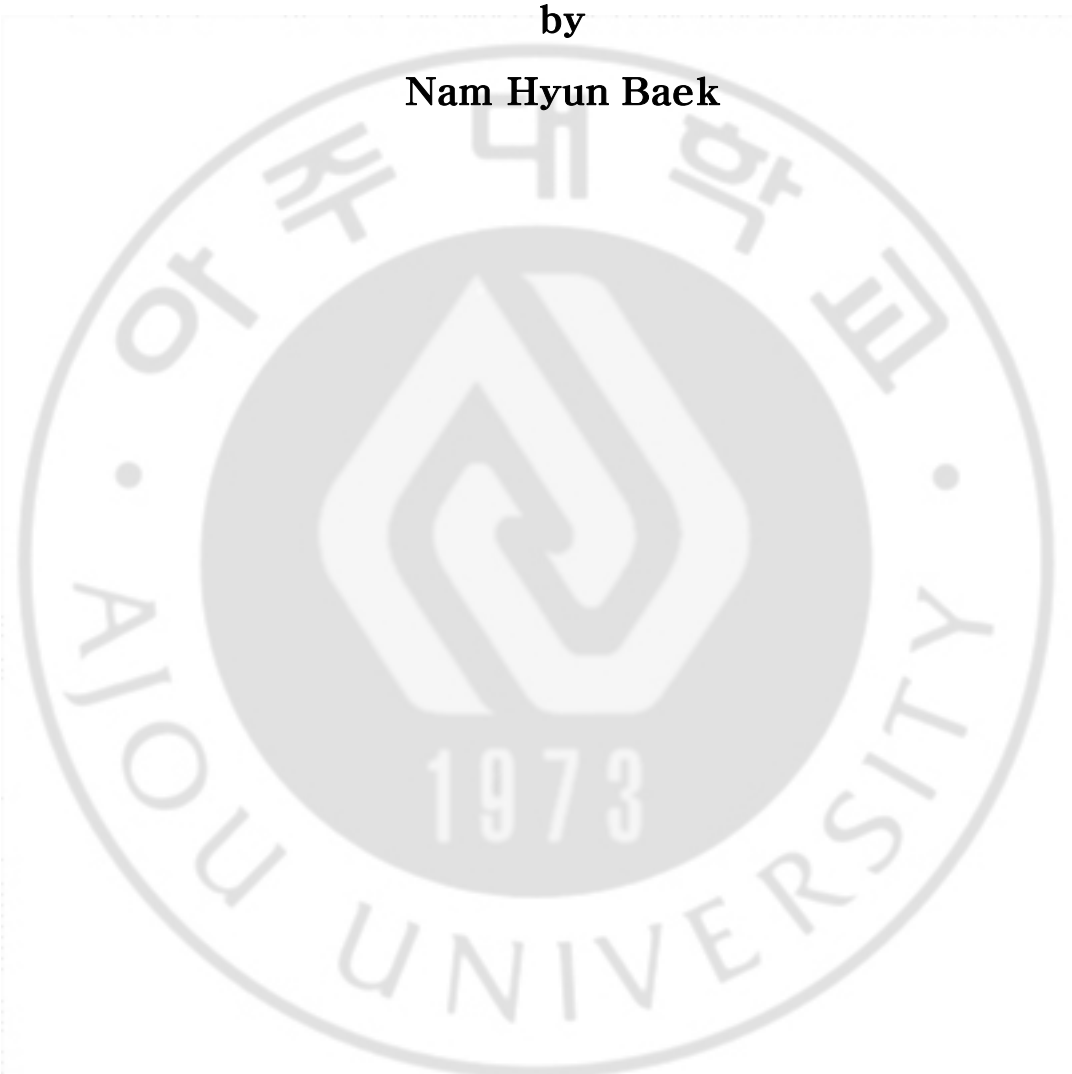
Surgical Outcomes for Solid Pseudopapillary Neoplasm of Pancreas

by

Nam Hyun Baek



Major in Medicine

Department of Medical Sciences

Surgical Outcomes for Solid Pseudopapillary Neoplasm of Pancreas

by

Nam Hyun Baek

A Dissertation Submitted to The Graduate School of
Ajou University in Partial Fulfillment of the Requirements
for the Degree of Master of Medicine

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-ABSTRACT-

Surgical Outcomes for Solid Pseudopapillary Neoplasm of Pancreas

Background/Aims: Solid pseudopapillary neoplasm (SPN) is a rare exocrine tumor of the pancreas with low malignant potential. This study was designed to evaluate surgical outcome of solid pseudopapillary neoplasm (SPN).

Methodology: From Between January 1994 to November 2013, 41 patients were diagnosed with SPN of the pancreas at Ajou University Medical Center and underwent surgical resection.

Results: Of the 41 patients, 33(80.5%) were female and 8(19.5%) were male with a mean age of 34.5 years (range, 12-63 years). The most common location of SPN was the tail (43.9%). Mean diameters of SPN was 5.5 cm (range, 1.2-14.5 cm). Nineteen patients (46.3%) had non-specific abdominal symptoms that had been investigated. Surgical treatment included distal pancreatectomy in 21, pancreaticoduodenectomy in 11, segmental resection of pancreas in 4, enucleation in 2, excision in 2 and surgical biopsy in 1. Thirty-nine of the 41 patients were disease-free at a median follow-up of 59 months (range, 1-125 months).

Conclusions: Patients diagnosed as SPN should receive surgical resection because of the excellent prognosis. Closed follow-up is recommended after surgery, even in patients without pathological malignant potential. For metastasis or recurrence, an aggressive surgical treatment is necessary because of the good possibility of long-term survival.

Keywords : Solid pseudopapillary neoplasm, Recurrence, Surgical treatment

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I. INTRODUCTION

Solid pseudopapillary neoplasm (SPN) is a relatively uncommon condition, with a reported incidence of 1% to 2% of all pancreatic tumors (Klimstra et al., 2000; Martin et al., 2002). SPN was previously known as solid and papillary epithelial neoplasm, and was first described by Frantz in 1959(Frantz, 1959). This is a tumor of the exocrine pancreas according to the World Health Organization (WHO) tumor classification system. SPN usually occurs in young women. Most patients with SPN are cured after surgical resection and have a favorable prognosis (Tipton et al., 2006).

Most reported cases of SPN are benign, but the low-grade malignant potential is 10% to 15% (Tang et al., 2005; Takahashi et al., 2006; Tipton et al., 2006; Suzuki et al., 2010). Some authors has reported that perineural invasion, vascular invasion, capsular invasion, or deep invasion into the surrounding tissue indicate malignant behavior (Tipton et al., 2006; Salla et al., 2007; Chung et al., 2009). However, none of these patients has been showed metastasis or recurrence during the follow-up period. Although SPN of the pancreas has been reported more frequently, reflecting its increased diagnosis and surgical treatment, the guidelines for this neoplasm remain unclear (Mao et al., 1995; Lam et al., 1999; Martin et al., 2002; Tipton et al., 2006). A few cases of SPN confined mainly to the liver, mesentery, and peritoneum have been reported in patients who survived for several years after surgery (Tang et al., 2005). Also, an aggressive surgical resection has been recommended for metastatic SPN (Tipton et al., 2006; de Castro et al., 2007; Machado et al., 2008). This study was designed to evaluate surgical outcome of solid pseudopapillary neoplasm (SPN) and to

describe the aggressive treatment of patients with locoregional or distant metastatic SPN.

II. MATERIALS AND METHODS

Between January 1994 to November 2013, the medical records of 41 patients who were pathologically diagnosed as pancreatic SPN by surgical resection at Ajou University Medical Center were retrospectively reviewed. Clinical data included sex, age, symptoms, preoperative radiologic findings, type of surgical treatment, postoperative complication, recurrence, metastasis, and survival. This study was approved by the Ajou University Institutional Review Board.

Computed tomography (CT) had been performed for preoperative diagnosis in all patients. Two board-certified abdominal radiologists reviewed the scans, which mainly showed the presence of a heterogenously enhanced solid and cystic mass. The diagnosis of SPN of the pancreas was based on the gross and microscopic appearance, as well as immunohistochemical staining. We assumed a malignant potential if a tumor was pathologically associated with was pancreatic parenchymal invasion, capsular invasion, perineural invasion, vascular invasion, and lymph node invasion.

For the primary pancreatic disease, two experienced hepatobiliary surgeons carried out operations. According to the International Study Group of Pancreatic fistula (ISGPF) [14], pancreatic fistula (PF) is defined as any measurable drainage from an operatively or subsequently percutaneous placed drain with an amylase content greater than three times the upper limit of normal serum amylase level. Three grades of PF severity were classified as described by the ISGPF clinical criteria. If the amylase concentration was less than three times the serum level, the drain was removed on day 4~7, regardless of the volume drained. Surgical mortality was defined as any death occurring during hospitalization or within 30

days postoperatively.

Patients were reviewed in the outpatient clinic 1 week after discharge from hospital. When the patient had any symptoms (abdominal discomfort, nausea, fever and chilling sensation), we recommended abdominal CT to identify intraabdominal fluid collection after surgery. Follow-up data were obtained from their outpatient clinical records. Patients were checked by abdominal CT 12 month after surgery and once per year thereafter. Survival was determined from the date of diagnosis to the date of death or to the date of last follow up. Patient survival data were obtained from the National Cancer Center in Korea. Categorical variables are expressed as frequencies (%), and continuous variables are presented as median and range.

III. RESULTS

A. Clinical findings

The clinical characteristics of the 41 patients with SPN are shown in **Table 1**. Of these patients, 33 (80.5%) were female and 8 (19.5%) were male with a mean age of 34.5±13 years (range, 12-63 years). The clinical presentation was nonspecific, comprising abdominal pain in 11 patients (26.8%), palpable mass in 5 (12.2%), back pain in 3 (7.9%), and abdominal discomfort in 2 (4.9%). 19 patients (46.3%) had non-specific abdominal symptoms found incidentally at routine examination. The mean diameter of SPN was 5.5±3.3 cm (range, 1.2-14.5 cm) and the most common location of SPN was the tail in 17 (43.9%), head in 15 (36.6%), neck in 4 (9.8%), neck and body in 2 (4.9%), and body in 2 (4.9%).

B. Surgical outcomes

40 of the 41 patients underwent complete pancreatic tumor resection by distal pancreatectomy (n=21), pancreaticoduodenectomy (n=11), segmental resection of pancreas (n=4), enucleation (n=2), and excision (n=2) according to SPN location (**Table 2**). Post-operative complications were evident in 9 (22%) of the 41 patients. Complications included grade A pancreatic fistula (n=4, 9.8%), intra-abdominal abscess (n=4, 9.8%; one treated by percutaneous drainage), and bleeding on the upper border of the pancreas with altered hemoglobin (n=1, 2.4%). The latter patient underwent a re-operation on postoperative day 1 to control bleeding occurring through previous incisions. Most of the patients were discharged without any symptoms for clinical observation. There was no postoperative mortality. Microscopic examination showed lymphatic invasion in 2 (4.9%), local invasion

of peripancreatic tissue in 13 (31.7%), perineural invasion in 10 (24.4%), capsular invasion in 11 (26.8%), and vascular invasion in 5 (12.2%). Thirty-nine patients were disease-free at a median follow-up of 59 months (range, 1-125 months). One patient who received non-surgery showed hepatic metastasis and regression of SPN of the pancreas 7 years later.

C. Recurrent case

A 38-year-old female underwent enucleation of 8.5cm mass located in the neck of the pancreas (first operation). The tumor showed no malignant potential and the lesion was completely resected. Radiologic findings after 6 months showed no residual lesion in the abdomen. The patient was subsequently lost to follow-up for 3 years. Radiology conducted 4 years later showed local recurrence in the head of the pancreas (**Figure 1A**). So, she had to undergo pancreaticoduodenectomy (**Figure 1B**). Five years later after second operation, follow-up CT scan revealed the tumors in the liver and mesentery (**Figure 2**). The patient underwent resection of all local recurrences and recovered well from the third surgery. More than 6 years after third surgical procedure, the patient remains alive with no evidence of recurrence or distant metastasis.

Table 1. Clinical characteristics of patients

	SPN (N=41)
Age, year, mean(SD)[range]	34(13)[12-63]
Gender (%)	
Female	33(80.5)
Male	8(19.5)
Symptom (%)	
Asymptomatic	19(46.3)
Abdominal pain	11(26.8)
Palpable mass	5(12.2)
Back pain	3(7.9)
Abdominal discomfort	2(4.9)
Weight loss	1(2.4)
Tumor location (%)	
Tail of pancreas	18(43.9)
Head of pancreas	15(36.6)
Neck of pancreas	4(9.8)
Neck and body of pancreas	2(4.9)
Body of pancreas	2(4.9)
Tumor size, median(range), cm	5.5(1.2-14.5)

SPN, Solid pseudopapillary neoplasm

Table 2. Surgical and pathological outcomes

	SPN (N=41)
Operations (%)	
Distal pancreatectomy	21(51.2)
Pancreaticoduodenectomy	11(26.8)
Central pancreatectomy	4(9.8)
Enucleation	2(4.9)
Excision	2(4.9)
Surgical biopsy	1(2.4)
Complications (%)	9(22)
Intraabdominal abscess	4
Pancreatic fistula	4
Postoperative bleeding	1
Mortality (%)	0(0)
Pathologic findings for malignant potential (%)	
Pancreatic parenchymal invasion	13(31.7)
Capsular invasion	11(26.8)
Perineural invasion	10(24.4)
Vascular invasion	5(12.2)
Lymphatic invasion	2(4.9)
Follow-up period, mo, mean(SD)[range]	58(36)[1-135]
Recurrence (%)	1(2.4)
Metastasis (%)	1(2.4)

SPN, Solid pseudopapillary neoplasm

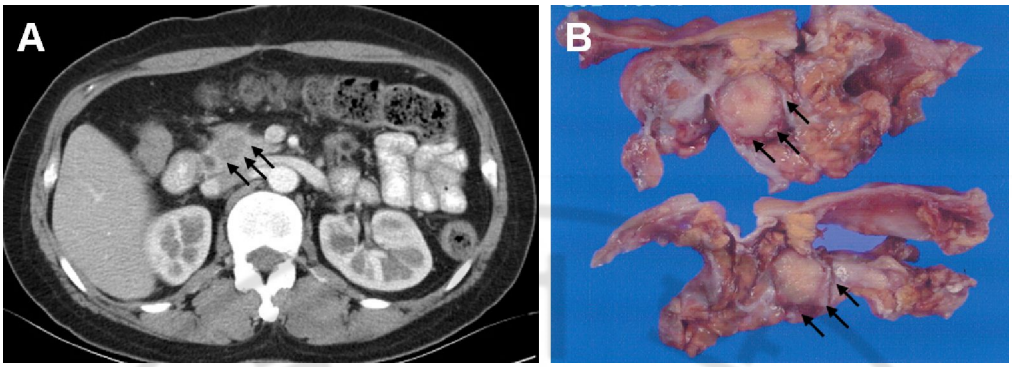

Fig 1. Local recurrence after enucleation (four years after first operation).

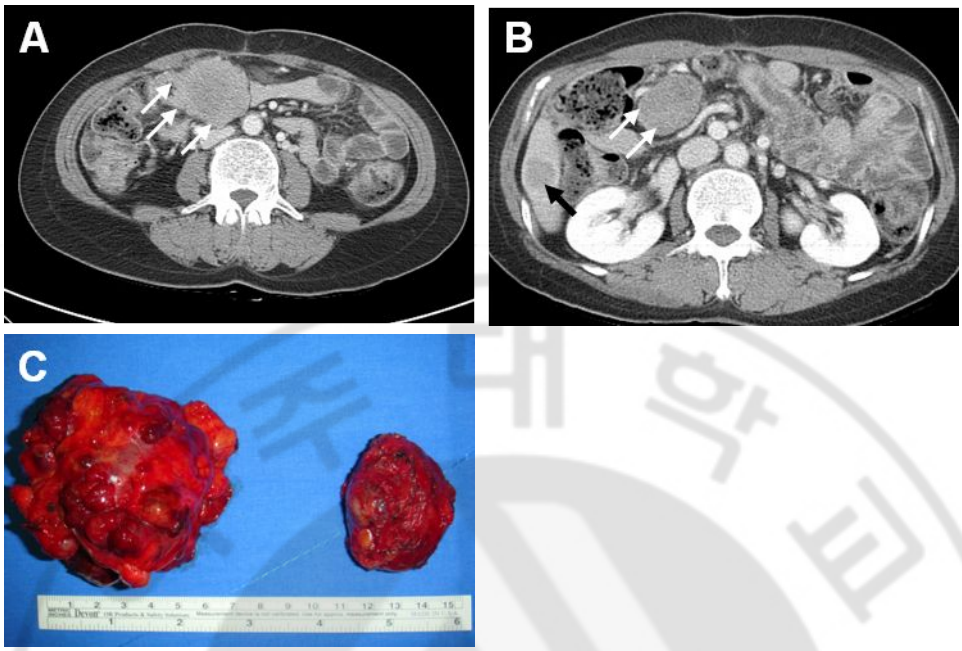

Fig 2. Peritoneal and hepatic metastases after second operation (nine years after first operation).

IV. DISCUSSION

Solid pseudopapillary neoplasm is a relatively rare pancreatic lesion with a low-grade malignancy potential that most commonly occurs in young females in their second or third decade of life. The age of patients with SPN ranges from 2 to 72 years (average 23.9 years) (Mao et al., 1995; Panieri et al., 1998; Jung et al., 1999; Lam et al., 1999; Tipton et al., 2006). The median age at diagnosis in our study was 34.5 years, which was older than in Asian reports (Hao et al., 2006; Patil et al., 2006). SPN presents with a variety of features of SPN. Papavramidis et al. (Papavramidis and Papavramidis, 2005) summarized the clinical findings of patients presenting with 718 SPN, reporting upper abdominal pain in 46.5% and non-tender abdominal mass in 34.8%. Asymptomatic cases accidently detected after routine examination have been reported in 15.5% of cases (Duff and Greene, 1985; Martin et al., 2002; Ng et al., 2003). These tumors can be discovered by chance during diagnostic imaging or may be suspected because of the presence of an asymptomatic palpable mass in young women. In our study, 19 patients were asymptomatic symptom and 14 patients presented with dull aching abdominal pain. Tumors can be located anywhere in the pancreas, but most cases tend to occur in the body and tail.

Preoperative diagnosis of SPN has been evaluated using CT, ultrasonography (US), endoscopic US (EUS), and magnetic resonance imaging (MRI). CT scan and EUS are more sensitive and specific, and are more accurate in diagnosing SPN (Stommer et al., 1991; Trivedi et al., 1999). Procacci et al. (Procacci et al., 1996) reported a 60% accuracy of CT in the diagnosis of pancreatic tumors. MRI, US, and endoscopic retrograde cholangiopancreatography have been used in diagnosing SPN. MRI was reportedly better

than CT in detecting the cystic or solid components of SPN (Yu et al., 2007). Recently, EUS-Fine needle aspiration biopsy is used for definitive preoperative diagnosis (Song et al., 2012).

Surgical resection is the treatment of choice, given its curative powers in patients with SPN (Tipton et al., 2006). Patients diagnosed as SPN mainly received distal pancreatectomy with/without splenectomy because the tumor was located in body and tail of the pancreas (21/41, 51.2%). Lymphadenectomy was not recommended in any of the recent major studies because relatively strong evidence exists that incidence of lymph node metastasis is extremely rare (Yoon et al., 2001; Adamthwaite et al., 2006; Kang et al., 2006). SPN has a low malignant potential, with a reported incidence of malignant transformation of around 15%, and has relatively favorable prognosis as compared with other pancreatic neoplasm (Mao et al., 1995; Tipton et al., 2006). A few cases of SPN confined mainly to the liver, mesentery, and peritoneum have been reported in patients who survived for several years after surgery (Tang et al., 2005). Although the criteria of malignancy have not yet been clearly established, many studies has reported that perineural invasion, vascular invasion, capsular invasion, or deep invasion into the surrounding tissue indicate malignant behavior (Tipton et al., 2006; Salla et al., 2007; Chung et al., 2009). But, none of these patients has been showed metastasis or recurrence during the follow-up period.

In our study, only a single patient who underwent resection as SPN had local recurrence on follow-up. This patient had no pathologic feature suggesting malignant potential. The present data indicate that regardless of the malignant potential, all patients with SPN must be observed closely. Even if there is metastasis, aggressive surgical procedure is justified because the prognosis after surgical treatment of SPN patients even with local recurrence and

metastasis or invasion is good (Canzonieri et al., 2003; Parelkar et al., 2013). One patient who received non-surgery showed hepatic metastasis and regression of SPN of the pancreas 7 years later. Although there have been few reports on the natural course of SPN, the regression of SPN of the pancreas recently have been reported in several pediatric cases (Hachiya et al., 2003; Nakahara et al., 2008; Suzuki et al., 2010; Yoon and Lim, 2012) 28]. The management of metastatic SPN is poorly defined in adults. Vollmer et al. (Vollmer et al., 2003) reported on a case with liver metastasis in an adult that was aggressively managed by surgical procedure. Such management was virtually impossible in the present cases, given tumor metastasis to the liver is most cases.

In conclusion, patients diagnosed as SPN should receive adequate surgical treatment because of the excellent prognosis. Close follow-up is recommended for patients who receive surgical treatment for SPN because the malignant potential of SPN is not related to pathological features. For metastasis or recurrence, surgical treatment should be done, since long-term survival is possible.

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– 국문요약 –

본원에서 시행한 췌장 고형 가성유두종의 수술적 결과

아주대학교 대학원의학과

백 남 현

(지도교수 : 김 욱 환)

목적: 고형 가성 유두종은 악성 변화를 가진 비교적 드문 췌장 질환으로 알려져 있다. 이에 저자는 고형가성 유두종의 수술적 결과에 대해 알아보고자 이 연구를 진행하였다.

방법: 1994 년 1 월부터 2013 년 12 월까지, 아주대학교 병원에서 고형 가성 유두중의 완치를 목적으로 수술한 41 명을 대상으로 연구를 진행하였다.

결과: 모든 환자 군의 평균연령은 34.5 세였고, 여자 환자는 33 명 남자환자는 8 명 이였다. 고형 가성 유두종의 가장 흔한 췌장 미부였으며, 종양의 크기는 5.5cm 였다. 고형 가성 유두종의 수술적 치료로써 원위부 췌장 절제술이 21 명으로 가장 많았으며 다음으로는 췌장-십이지장 절제술, 종양 제거술 순이였다. 41 명의 환자 중에서 1 례에서 재발을 보였으며 재발 후에도 수술적 치료가 시행되었다.

결과:고형 가성 유두종으로 진단된 환자는 수술 후 좋은 예후를 가지므로 반드시 수술적 치료가 필요하다. 그러나 고형 가성 유두종은 악성화 가능성이

있으므로 반드시 계속적인 추적관찰이 필요하며 우리 연구에 비추어 보았을 때 추적관찰 중 재발이 있다고 하더라도 환자의 예후를 위해서라도 반드시 수술적 치료가 필요하다.

핵심어 : 고형 가성 유두종, 재발, 수술적 치료