ANALYSIS

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Pancreatic Pseudo-Papillary Tumor: NCI experience over 17 years

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ABSTRACT

Background: Pseudo-papillary Tumor (SPT) or Frantz tumor is a rare type of pancreatic tumor with an incidence of only 0.5-5% of all pancreatic tumors. It was first described in 1959. SPT has a different behavior than pancreatic ductal adenocarcinoma (PDA) regarding its gender predilection, presenting symptoms, metastatic potentiality and survival. Preoperative diagnosis of SPT is also more difficult than PDA due to variety of findings, their presentation in imaging range from completely solid to completely cystic tumors, and biopsy is less accurate in SPT diagnosis than PDA. *Aim*: to review and present National Cancer Institute (NCI), Cairo University experience over the last 17 years in treating SPT, including diagnostic challenges and treatment outcome. Patients and *methods*: This is a retrospective case series study of all cases of pancreatic pseudo-papillary tumor that were treated in NCI, in the

period between January 2003 and December 2019. Demographic data of the patients, their presenting symptoms, investigations results, modality of treatment done and outcomes were collected from hospital records. *Results*: during this period 45 cases of SPT were treated. Most of them were females (41/45). Body of pancreas was the most common site of the tumor (18/45). Only one case had distant metastasis during initial presentation. Whipple procedure was done only in 12 cases. With follow up period ranged from 1-147 months, the 5 year disease free survival and overall survival were 86.4%, 92.1% respectively. *Conclusion:* SPT has a good prognosis, as regarding DFS and OS even in large tumor size, also SPT has low metastatic potential compared to PDA.

Keywords: Pseudo-papillary tumor, pancreatic tumor, whipple

1. INTRODUCTION

Pseudo-papillary pancreatic tumor (SPT) is a rare pancreatic tumor. It is also named Frantz tumor according to Dr. Virginia Kneeland Frantz who was the first one to describe it in 1959 (Frantz, 1959). The reported incidence of SPT In literature is 0.5-5 % of all pancreatic tumors (Yu et al., 2010). Controversy still exists about the cell of origin of SPT; some reports suggest it originates from pancreatic acinar cells; while others suggest it arises from a pluripotent cell that is still not differentiated to either exocrine or endocrinal cell (Klöppel et al., 1981). Unlike PDA which is more common in males; SPT is more common in females who represent about 85% of cases (Coelho et al., 2018). Although Kosmahl M et al. showed that up to 80% of SPTs expressed progesterone receptors (Kosmahl et al., 2000), It is still unclear if the female sex hormones have an influence on development of this type of tumor (Machado et al ., 2008).

SPT are known to rarely invade the surrounding tissue; and also to have low metastatic potential with about only 15 % of cases reported to have distant metastasis (Tang et al., 2005). Also it is known to have better prognosis compared to PDA with 5 year overall survival of up to 97% (Robert et al., 2002).

2. PATIENTS AND METHODS

A retrospective study where the hospital records in NCI, Cairo University were reviewed for all cases with pancreatic pseudo-papillary tumor treated in the period from January 2003 until December 2019. Demographic data of the patients, their presenting symptoms, investigations results, modality of treatment done and outcomes were collected and analyzed.

Statistical analysis

Data analysis was performed using Statistical Package for Social Sciences (SPSS) versions 21. Quantitave variables were described as mean±SD and or medians, and ranges. Qualitative variables were described as numbers and percentages. Survival analysis was performed by Kaplan-Meiermethod. Disease-free survivals were calculated from surgery date till the date of documented recurrence, death or last follow up. Overall survival was calculated from the date of diagnosis till the date of death or date of last follow up.

3. RESULTS

45 cases were found to have pancreatic pseudo-papillary tumor during the period of study. Most of them were females (41/45) and most common presentation was vague abdominal pain. Their features illustrated in table 1.

Table 1 Patients' demographic features and clinical presentation.

		Number (%) N=45
Age(years)	Mean ± SD	30.6 ± 11.26
	Range	9-61
Gender	Male	04 (8.9)
	Female	41 (91.1)
Symptoms	Pain	33 (73.3)
	Abdominal mass	23 (51.1)

	Jaundice	0 (0)
	Vomiting	0 (0)

All of the cases underwent CT abdomen, pelvis and chest, and all laboratory investigations needed including tumor markers (e.g. CA 19.9, CEA). In our center we don't perform guided biopsy for radiologically proven resectable pancreatic tumors; all the recorded biopsies (13 cases) were taken before the patients were referred to NCI. The results of investigations which were done to these cases illustrated in table 2.

Table 2 Preoperative radiological and biopsies results

		Number (%) N=45
CT results (tumor site)	Head	12(26.7)
	Body	18 (40.0)
	Tail	15 (33.0)
Size of tumor (cm)	Median(range)	7 (2-10)
Presence of metastasis	Yes	1(2.2)
	No	44(97.8)
Serum markers (CA 19-9)	Elevated	1(2.20)
	Not Elevated	44(97.8)
Guided biopsy taken	Yes	13(28.8)
	No	32(71.2)
Result of biopsy (N=13)	Pseudo-papillary tumor	8(61.5)
	Other pathology *	5(38.5)

*The other pathologies that were retrieved by guided biopsies were: 3 adenocarcinoma and 2 non conclusive

In this series, only one patient had liver metastasis during initial presentation. She received 7 cycles of FOLFIRIOX protocol and she was alive with a stable disease till the end of this study with follow up of 16 months. The other 44 cases underwent resection with the different surgical procedures done listed in table 3.

Table 3 Operative and complications results

		Number (%) N=44
Type of procedure	Whipple	12 (27.3)
	Distal pancreatectomy & splenectomy	21 (47.7)
	Central pancreatectomy	9 (20.5)
	Cystectomy	2 (4.5)
Other Organ resected	Left adrenalectomy	1 (2.3)
	Transverse colectomy	1 (2.3)
Hospital stay(days) Median (range)		8(3-43)
30 days postoperative complications	Pancreatic fistula	9 (20.5)
	Gastrointestinal Leakage	2 (4.5)
Mortality		1 (2.3)

All nine cases with pancreatic fistulae resolved with just conservative management. Regarding the two cases with Gastrointestinal Leakage; one of them underwent transverse colectomy and developed colonic fistula, which was managed by de-functioning ileostomy, the other case had leakage from the gastro-jejunostmy and was explored with drainage and revision of anastomosis was done but the patient died from septic shock.

Follow up period ranged from 1-147 months. At the end of this study, 4 cases developed recurrence; three of them had local recurrence and were managed by re-exploration and underwent surgical resection of the recurrence. The other one had irresistible liver metastasis and managed by chemotherapy and she died after 23 months. The median follow up time for DFS and OS was 15 and 21 months respectively with disease free survival (DFS) and overall survival (OS) rates of 86.4%, 92.1% respectively and are illustrated in fig.1, fig 2.

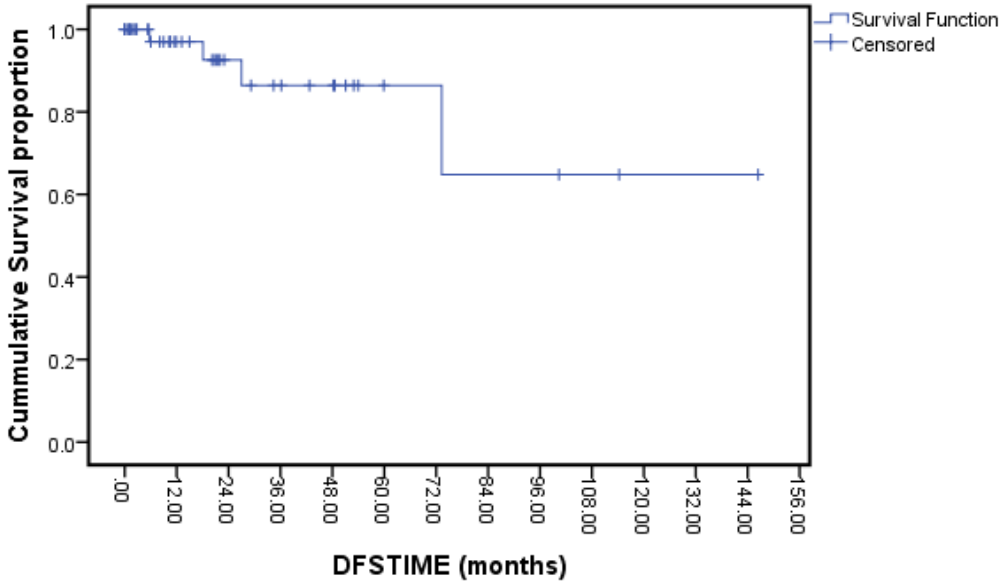

Figure 1 Disease free survival (Months)

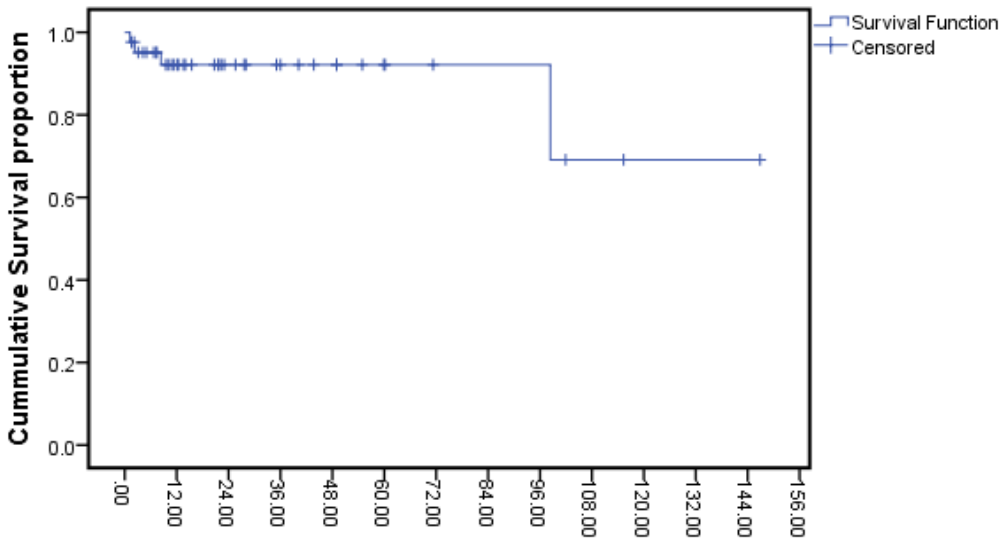

Figure 2 Overall survival (months)

4. DISCUSSION

According to Coelho JCU et al. females are more common than males to have SPTs, and they constitute about 85% of all cases (Coelho et al., 2018). Kosmahl M et al. illustrated that up to 80% of SPTs expressed progesterone receptors which may explain the

higher incidence of these tumors in female (Kosmahl et al., 2000). This was consistent to our study where we had 41 patients out of the 45 patients to be females (91.1%). Tang et al. Considered SPTs to have low malignant potential that rarely metastasize with only 15 % incidence to develop distant metastasis (Tang et al., 2005). This explains our results with only one patient had liver metastasis on presentation and another single patient developed liver metastasis after resection. Coelho et al., declared SPTs are usually non-invasive and thus the presenting manifestations occur mainly because of tumor compression rather than invasion, with pain being the most commonly encountered symptom with none of their study patients presented with jaundice even those who had large pancreatic head mass (Coelho et al., 2018), Cai et al. confirmed these results with only one patient out of their 115 patients presented with jaundice (Cai et al., 2014). This was the same as in our results with 73.3% of our patients presented with pain while none of them had jaundice despite that 23 of them (51.1%) had abdominal mass. PSTs can be accurately diagnosed preoperatively Due to their characteristic features with both CT scan and MRI; with accuracy ranges from18-82 % (Dong & Zhang, 2006). It can be differentiated from PDA and neuroendocrine tumors by their unique enhancement pattern (Dan et al., 2014). Shi et al. reported that calcifications occurred in much higher rates in male than female SPTs (Shi et al., 2019). Many other studies studied the use of endoscopic ultrasound (EUS) and EUS guided FNAC and they concluded that it is safe, and has about 82% accuracy (Jung et al., 2014; Law et al., 2014; Karsenti et al., 2020). In our study we didn't perform guided biopsy in our institute for our patients, but we had 13 patients who performed the biopsy prior to being referred to us with only 8 of them (61.5%) had accurate diagnosis while 5 (38.5%) had another pathology which was proven to be wrong after surgery and final pathology report was available.

Studies also concluded that surgical resection provides the best prognosis for SPTs; with 5 year overall survival of up to 97% (Yu et al., 2010; Robert et al., 2002). And with a low recurrence rate (Coelho at al., 2018). The disease also proved to have a protracted favorable course even in cases with metastatic dissemination (Tang et al., 2005), with resection of these metastatic deposits offers good prognosis; if possible (Ji et al., 2012). Our results fits with these studies with our 5 year survival was 92.1%., also the case who presented with liver metastasis was treated by chemotherapy and had stable disease till the end of this study with follow up of 16 months. The other case; that had irresistible liver metastatic recurrence was managed by chemotherapy and she died after 23 months.

5. CONCLUSION

SPTs are a rare type of pancreatic with different behavior than PDA being more common in females with low metastatic potential. Surgical resection provides the best prognosis with excellent overall survival even in large tumor size.

Abbreviations

PST: Pancreatic Pseudo-papillary tumor; PDA: pancreatic ductal adenocarcinoma; NCI: National Cancer Institute, Cairo University; DFS: disease free survival; OS: overall survival.

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Conflicts of Interest:

The authors declare no conflict of interest.

Ethical approval

This study was approved by our institutional cancer committee (Institutional Review Board, IRB #00004025), National Cancer Institute, Cairo University.

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