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ORIGINAL ARTICLE

Retrospective analysis of clinicopathological features of solid pseudopapillary neoplasm of the pancreas

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Abstract Solid pseudopapillary neoplasm (SPN) of the pancreas is a rare neoplasm that accounts for 2–3% of all primary pancreatic neoplasms. This study aimed to characterize clinicopathological features associated with SPNs and to retrospectively evaluate the relationship of these features with predictive parameters associated with aggressive behavior. We reviewed 16 cases of SPN of the pancreas that had been diagnosed between 2005 and 2014 at our pathology department. A total of 16 cases, 15 female and one male, were evaluated in this study. The patient age ranged from 13 years to 63 years with a median of 35.70 years. The mean tumor diameter ranged from 2 cm to 18 cm with a mean diameter of 5.90 cm. We identified a significant association between the presence of clear cells and perineural invasion ($p = 0.019$), which was considered to be a predictive factor for aggressive behavior. Other features (i.e., localization, nuclear grooves, central hyalinization, myxoid stroma, eosinophilic bodies, foamy histiocyte aggregates, multinucleated cells, and calcification) were not significantly associated with predictive factors for aggressive behavior. One patient died as a result of a pancreatic fistula that developed as a postoperative complication. The remaining 15 patients are alive and have not demonstrated any signs of recurrence or metastasis. The current study suggested that the presence of clear cells might serve as a possible prognostic indicator of perineural invasion, which is a predictive parameter associated with aggressive behavior in SPN.

Conflicts of interest: All authors declare no conflicts of interest.

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Introduction

Solid pseudopapillary neoplasm (SPN) of the pancreas is a type of pancreatic neoplasm with low malignant potential, and it represents 0.17—2.70% of all cases of pancreatic tumors [1]. This tumor type was first reported by Frantz [2] and was initially referred to by multiple names, including solid papillary cystic tumor, cystic epithelial neoplasm, and papillary cystic tumor, until the World Health Organization (WHO) designated and reclassified them as SPNs in 2010 [3]. The nature and clinical behavior of these tumors remains elusive. Pancreatic SPN is primarily observed in women and has a peak incidence in patients aged 20—40 years [4]. Most patients are asymptomatic and present incidentally with an abdominal mass that is detected by radiological imaging, and they exhibit levels of tumor markers within normal limits. WHO reported that perineural invasion, pancreatic paranchymal invasion, or lymphovascular invasion do not remark increased malignant behavior, but predictive factors for aggressive behavior [3]. SPN metastasis is rare, and in a recent study, some clinicopathological factors, such as male gender, younger age, large tumor size (>5 cm), and elevated mitotic rate are suggested to result in increased malignant behavior [5—7]. The main objectives of this study were to characterize clinicopathological features associated with SPNs and to retrospectively evaluate the relationship of these features with predictive parameters associated with aggressive behavior.

Materials and methods

We reviewed the cases of 16 patients diagnosed with SPN of the pancreas between the years 2005 and 2014 at our pathology department (Bursa, Turkey). Two pathologists reviewed and evaluated all the slides using light microscopy. Information regarding histological and pathological features, such as tumor size, presence of calcification, central hyalinization, multinucleated cells, histiocytes, nuclear grooves, clear cells, eosinophilic body, necrosis, myxoid stroma, mitotic activity, presence of perineural, lymphovascular, pancreatic parenchymal invasion, lymph node involvement, and metastasis were collected.

Immunohistochemical study

Furthermore, for differential diagnosis (i.e., pancreatic neuroendocrine neoplasms, adenocarcinoma, acinar cell carcinoma) immunohistochemical study was performed. Immunohistochemistry was carried out for a panel of markers, including progesterone receptor (PR), CD10, CD56, synaptophysin, CD57, chromogranin, epithelial membrane antigen (EMA), cytokeratin AE1/AE3, and Ki67 on a Leica Bond Max automated slide stainer system (Leica, Bannockburn, IL, USA). The primary antibodies used were NCL-L-PGR-312 (Novocastra, Newcastle, UK; 1:150 dilution) against PR, NCL-L-CD10-270 (Novocastra; 1:80 dilution) against CD10, NCL-L-CD56-1B6 (Novocastra; 1:100 dilution) against CD56, NCL-L-SYNAP-299 (Novocastra; 1:200) against synaptophysin, Clone-NK1 (Lab Vision, Fremont, CA, USA; 1:100) against CD57, NCL-L-CHROM-430 (Novocastra; pre-diluted) against chromogranin, NCL-L-EMA (Novocastra; 1:400) against EMA, NCL-L-AE1/AE3 (Novocastra; 1:200) against cytokeratin, and Clone SP6 (Lab Vision; 1:250) against Ki-67.

Statistical analysis

Variables were expressed as the median (minimum—maximum) or frequency. Between group comparisons were performed using Fisher's exact test. SPSS for Windows version 21.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis, and $\alpha = 0.05$ was considered statistically significant.

Results

Clinical data

We evaluated a total of 16 patients, 15 female and one male, who were diagnosed with SPN of the pancreas at our pathology department. The patient age ranged from 13 years to 63 years, with a median of 35.70 years. The most frequently observed age range was 20—40 years. Nine patients were asymptomatic, and seven patients presented with symptoms of abdominal pain or vomiting. Four patients had a medical history of diabetes mellitus and hypertension. The tumors were located in the body or tail of the pancreas in 10 patients (62.50%) and in the head of the pancreas in six patients (37.50%). Serum tumor markers, such as carbohydrate antigen 19.9, carcinoembryonic antigen, and α-fetoprotein, were assayed. One patient with a tumor located in the head exhibited elevated levels of carbohydrate antigen 19-9 (73 U/mL; normal range $\leq$ 37 U/mL). A preoperative diagnosis of SPN was made in four patients (28.60%) based on the characteristic features revealed by radiological imaging. Surgical procedures included partial pancreatectomy in seven patients, distal pancreatectomy in six patients, and pancreaticoduodenectomy (Whipple procedure) in three patients. Abdominal ultrasonography computed tomography was used to evaluate patients during routine follow-up visits. The patients were followed for a median of 28 months (range 10—72 months). One patient died as a result of a pancreatic fistula that arose as a postoperative complication. The other 15 patients are living and have not demonstrated signs of recurrence or metastasis.

Pathological features

On a gross level, all of the tumors evaluated in this study were encapsulated and well demarcated from adjacent pancreas tissue. The mean diameter of the tumors was 5.9 cm, ranging from 2 cm to 18 cm. A tumor diameter $>$ 5 cm was observed in seven (43.70%) cases, and tumors $<$ 5 cm were observed in nine cases (56.30%).The cut surfaces of the tumors exhibited a reddish-white, spongy appearance and demonstrated signs of hemorrhaging.

Most tumors were composed of solid, cystic, and pseudopapillary components. The nuclei of all tumor cells were uniformly round and characteristic nuclear grooves were