CLINICOPATHOLOGICAL STUDY OF SOLID PSEUDOPAPILLARY TUMOR OF PANCREAS

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ABSTRACT

Objective: To study the morphological and immunohistochemical features of solid pseudopapillary tumor of pancreas.

Study Design: Retrospective study.

Place and Duration of Study: Shaukat Khanum Memorial Cancer Hospital and Research Centre from Jun 2016 to Mar 2017.

Material and Methods: Sixty-four patients (n=64) including 61 females and 3 males with pathological diagnosis of solid pseudopapillary tumor were selected from archives of Shaukat Khanum Memorial Cancer Hospital and Research Center for the period of 2000-2017. For the sample selected, their morphological features and immunohistochemical profile were reviewed and analyzed. The morphological features are considered as gold standard for the diagnosis.

Results: The mean age was 33 years (range 8-50 years). Immunohistochemical stains were performed on formalin fixed paraffin embedded section of 55 cases. Pancytokeratin was performed on 8 cases, out of which only 2 cases showed positivity. CD10 was performed on 14 cases, out of which only 12 cases showed positivity. Neuron specific enolase (NSE), CD56, vimentin, progesterone receptor (PR) and β catenin were performed on 8,5,3,13 and 16 cases respectively and showed positivity in majority of cases. Neuroendocrine markers (chromogranin and synaptophysin) were performed on 25 and 6 cases, from which it showed weak positivity in 3 cases. CD99 was performed on 19 cases and showed characteristic dot like staining.

Conclusion: Among the immunohistochemical stains, CD99 had a specific dot like staining pattern and was used as a first line marker in diagnosis.

Keywords: CD99, Immunohistochemistry, Pancreas, Solid Pseudopapillary tumor.

INTRODUCTION

Solid pseudopapillary tumor of the pancreas is an uncommon pancreatic tumor and represents 1-2% of exocrine pancreatic tumors[1]. The tumor occurs predominantly in young females[2-4]. However, occurrences in children and elderly have also been reported[5,6].

Solid pseudopapillary tumor was first described by Dr. Frantz in 1959[4]. Later on the World Health Organization (WHO) in 1996 defined it as low-grade malignant neoplasm of exocrine pancreas[7].

Patients with solid pseudopapillary tumor (SPT) have an excellent prognosis after surgical resection[8]. Pathogenesis is related to E cadherin/β catenin mutation due to abnormality in wingless-type mouse mammary tumor virus integration site (WNT) signal transduction pathway[9].

The diagnosis of solid pseudopapillary tumors on trucut biopsies and excision biopsies poses a great difficulty for the pathologist, as due to their similarity with other endocrine and exocrine pancreatic tumors including pancreatic neuroendocrine tumor, Pancreatoblastoma and acinar cell carcinomas. These tumors have similar morphological and few immunohistochemical features, including clinical presentation and radiological appearance but with different prognosis and treatment[10,11].

Immunohistochemically, these tumors show positivity for neuron specific enolase (NSE),

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vimentin, CD10, progesterone receptor (PR) and β catenin, variable positivity for synaptophysin and cytokeratin and negativity for chromogranin[4,8,11,12]. However, recently a unique dot-like staining pattern of CD99 in solid pseudopapillary tumor was evident which has been described in these three studies[10,13,14].

The rationale of this study was to demonstrate the morphological and immunohistochemical features as well as the diagnostic utility of CD99 in solid pseudopapillary tumor diagnosed at Shaukat Khanum Memorial Cancer Hospital and Research Centre.

MATERIAL AND METHODS

It was a retrospective study done at the department of histopathology Shaukat Khanum Memorial Cancer Hospital and Research Centre. Medical records of all 64 patients with pathological diagnosis of solid pseudopapillary tumor were obtained from archives of Shaukat Khanum Memorial Cancer Hospital and Research Center who presented during period of 2000-2017 by non probability purposive sampling. For the sample selected, their morphological features and immuno-histochemical profile were reviewed and analyzed. The morphological features are considered as gold standard for the diagnosis. Immunohistochemical staining was done in 55 cases on formalin-fixed, paraffin-embedded sections. The sections were stained for the following markers: Pancytokeratin (Leica Bond AE1/AE3), NSE (Leica Bond 22C9), CD56 (Leica Bond CD564), Vimentin (Leica Bond V9), CD10 (Leica Bond 56C6), progesterone receptor (Leica Bond 16), β catenin (Leica Bond 17C2), chromogranin (VENTANA), synaptophysin (Leica) and CD99 (VENTANA O13). The sections for leica and VENTANA were respectively deparaffinized in bond de-wax solution and EZ prep solution. Antigen retrieval was performed in bond ER2 (Ph. 9.0) and cell conditioning 1 (Ph. 8.0) in automated stainer (Bond 111) and VENTANA benchmark XT. staining was performed with bond polymer detection kit and ultra view 3,3'-diaminobenzidine (DAB) detection kit and the sections were developed with diaminobenzidine tetrahydrochloride and counterstained with hematoxylin. The prepared slides were reviewed by two histopathologists including myself. For NSE, chromogranin, synaptophysin and vimentin cytoplasmic staining in tumor cells was considered as positive. Membranous staining for Pan Cytokeratin, CD56 and CD10 and nuclear staining for PR and β catenin was taken as positive. For CD99 dot like staining in tumor cells was considered to be positive.

Statistical analysis was done using SPSS–20. Mean and standard deviation for tumor size (In centimeters) and age were calculated. Categorical variables like location of tumor, clinical details

Table: Results of Immunohistochemical stains (n=55).

	Pattern of staining	Total no of cases	No of positive cases	No of negative cases
Pancytokeratin	M + C	8 (14.54%)	2 (25%)	6 (75%)
NSE	C	8 (14.54%)	8 (100%)	Nil
Chromogranin	C	25 (45.45%)	2(8%)	23 (92%)
Synaptophysin	C	6 (10.90%)	1 (16.66%)	5 (83.34%)
CD56	M	5 (9.09%)	5 (100%)	NIL
Vimentin	C	3 (5.45%)	3 (100%)	NIL
CD10	M	14 (25.45%)	13 (92.85%)	1 (7.15%)
PR	N	13 (23.63%)	13 (100%)	NIL
β catenin	N	16 (29.09%)	16 (100%)	NIL
CD99	Dot like	19 (34.54%)	19 (100%)	NIL

M= membranous, C= cytoplasmic, N= nuclear

and gender are given in form of frequency and percentage.

RESULTS

Of the 64 patients, 61 (95.3%) were female and 3 (4.6%) were male. Their mean age was 33.26 ± 7.32 years (range 8-50 years). The average tumor size was 9.4 ± 4.07 centimeters (range 2.2-20 cm). The clinical details regarding tumor size and location were not provided in 20 cases. In remaining 44 cases, 17 (38.63%) cases the tumor was located in the pancreatic head, in 5 (11.36%) it was located in the body and in the remaining 20 (45.45%) patients it occurred in the tail. Of the 64 patients, 10 (15.6%) patients were admitted in Shaukat Khanum Hospital, of which preoperative FNAC diagnosis was done in 9/10 (90%) patients (7/10 through endoscopic ultrasound (EUS) guided and 2/10 through ultrasound guided Fine needle aspiration cytology (FNAC).

The histopathological and cytological features of the cases are described. Sixteen (25%) cases were either fragmented or referred blocks for which gross details were not available. In remaining 48 (75%) cases, grossly the tumors were well-encapsulated or circumscribed, solid and cystic in 26/48 (54.16%) cases, predominantly cystic in 7/48 (14.58%) and entirely solid in 15 (31.25%). Microscopically the tumors were arranged in pseudopapillary architecture with areas of solid, cystic and trabecular pattern. The papillae show hyalinized fibrovascular cores and lined by round to polygonal cells with clear to eosinophilic cytoplasm, monomorphic nuclei and eosinophilic nucleoli. Hemorrhage, necrosis, foci of calcification, cholesterol clefts and hyaline globules were also seen in some cases. On cytology, the smears were cellular with small loose clusters and few intact papillary structures with fibrovascular cores. The cells show fine chromatin and grooved nuclei. The immunohistochemical stains were applied on 55 (85.9%) cases and remaining 9 (14.1%) cases were diagnosed on morphological basis and pattern of staining has been shown in table.

The fig-1 shows the histopathological and cytomorphological features of solid pseudopapillary tumor and fig-2 shows the characteristic staining pattern of CD99 on paraffin and cell block respectively. Fig-3 shows the results of immuno histo chemical stains.

The result in table shows that CD99 applied on 19 cases was positive on all cases with dot-like staining pattern. All the usual

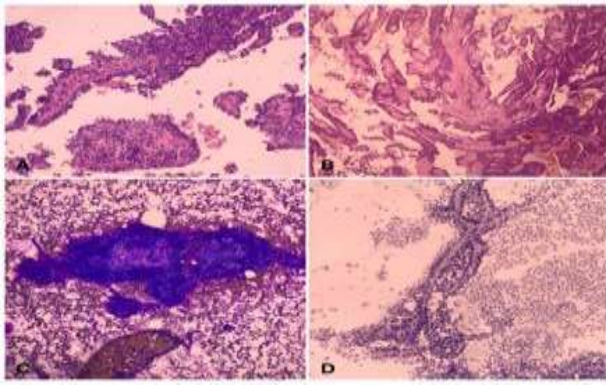

Figure-1: A & B) Hispathological features of solid pseudopapillary tumor (H & E400x and 200x) respectively. C & D). Cytomorphological features (GIEMSA and PAP Stains 200x) respectively.

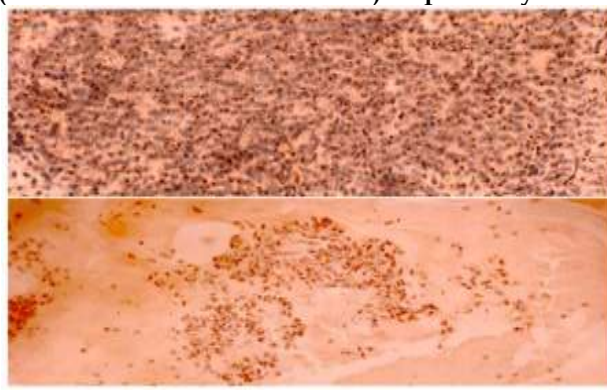

Figure-2: A) Paranuclear dot-like staining (IHC, CD99, 400x) on paraffin block. B) Paranuclear dot-like staining (IHC, CD99 , 200x) on cell block.

immunohistochemical stains for solid pseudopapillary tumor showed diverse pattern of expression from positive to focal positive with negativity for neuroendocrine markers.

DISCUSSION

Solid pseudopapillary tumors comprise 1-2% of pancreatic tumors[15]. Their occurrence in young adolescent girls and progesterone positivity

describe their relation with sex hormone receptors[15]. In our study, 61 of 64 patients were female and 3 were male with a mean age of 33 years.

The first case of solid pseudopapillary tumor was described by Lichtenstein[16] as papillary cystadenocarcinoma of pancreas in pancreatic tail, however the detailed pathological description with three case series was than described by Frantz in 1959. The incidence of solid pseudopapillary tumor has been increasing due to advances in imaging modalities[2,3,17]. Our study shows that majority of the tumors are located in pancreatic head and tail and it is supported by many case studies[3,13,17].

Differential diagnosis of solid pseudo-papillary tumor of pancreas includes pancreatic neuroendocrine tumors, pancreatoblastoma, acinar cell carcinoma and pancreatic pseudocyst[3,18]. Histologically these tumors are characterized by alternating cystic and solid areas of polygonal epithelial cells. The characteristic pseudopapillary appearance results from degenerative changes resulting in tumor cell discohesion.

The morphological and immuno-histochemical features of solid pseudopapillary tumors and pancreatic neuroendocrine tumors are quite overlapping, so it is difficult to differentiate between them[7]. The neuroendocrine tumors have a high malignant potential (40-90%) with gross invasion or metastasis in 20% of the cases. The 5 years survival rate is 65% of neuroendocrine tumors and 95% in case of solid pseudopapillary tumors[19]. Histologically both tumors have cystic and solid areas with monomorphic tumor cells. However, pseudopapillary architecture and discohesive appearance of cells is usually not observed in neuroendocrine tumors[15]. Immunohisto-chemically solid pseudopapillary tumor of pancreas can show overlapping expression of pan CK, synaptophysin, CD56, chromogranin, CD10 and vimentin with neuroendocrine tumors[19,20], the expression of neuroendocrine markers with pancreatoblastoma and pancreatic enzymes with acinar cell carcinoma[18].

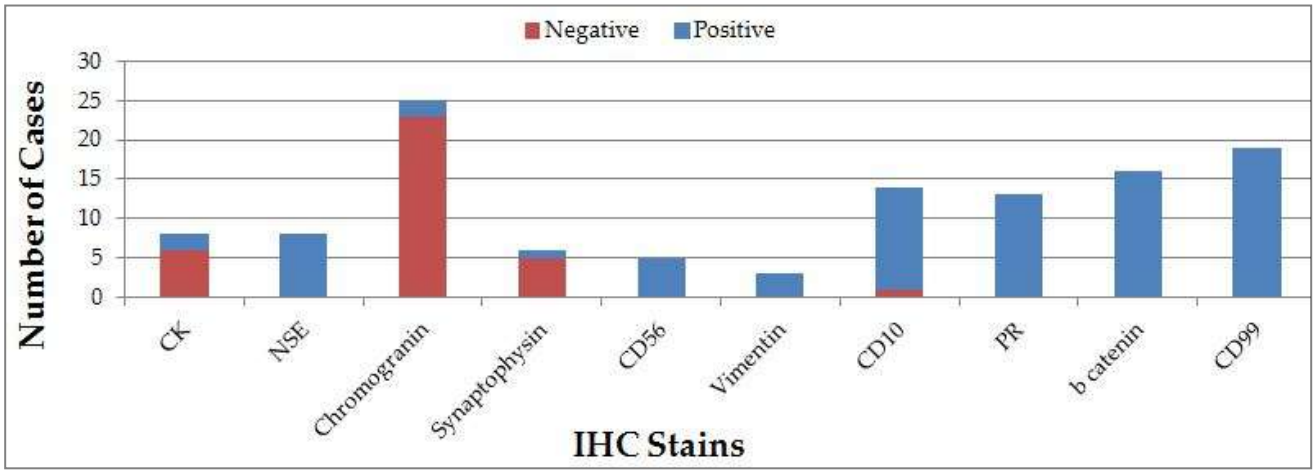

Figure-3: Results of IHC stains.

Recently a study by Ohara et al[19] published the nuclear expression of β catenin with loss of E cadhenin in solid pseudopapillary neoplasm and membranous plus cytoplasmic expression of β catenin without loss of E cadherin on neuroendocrine tumors. However, the interpretation of staining of β catenin and E cadherin is difficult. Moreover, the nuclear staining of β catenin can also be seen in other pancreatic tumors[10,11,20].

CD99 immunohistochemical stain unique staining pattern in solid pseudopapillary tumor compared with complete absence in neuroendocrine tumors has been described recently in three studies. CD99 is

atransmembrane glycoprotein encoded by MIC2 gene and is expressed in Ewing's sarcoma, PNET, acute lymphoblastic lymphoma, leukemia, acute myelogenous leukemia, myeloid sarcoma, synovial sarcoma and mesenchymal chondrosarcoma. It is found in pseudo autosomal region of x and y chromosomes[14].

It is also useful to differentiate ependymomas from nonependymal neoplasms[21]. It has a characteristic diffuse membranous pattern of expression, however in solid pseudopapillary tumor it shows a dot like staining pattern[10].

In our study we retrospectively analyzed the morphological and immunohistochemical features of solid pseudopapillary tumors of our institution from 2000-2017. We found a unique staining pattern of CD99 and our results are also supportive of other studies in the literature. However, the exact pathophysiology for this characteristic staining pattern is still under investigation.

CONCLUSION

We have concluded that the diagnosis of solid pseudopapillary tumor is primarily based on morphological features. The pattern of staining of CD99 is quite a consistent finding. Therefore, it can be used as a first line marker, an adjunct to morphology for definitive diagnosis and to differentiate it from other pancreatic tumors. Moreover, if used alone it can be cost effective as compared to an extensive panel of Immunohistochemical stains used in the past for the diagnosis.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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