ORIGINAL RESEARCH PAPER

Pathology

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RARE SOLID PSEUDO-PAPILLARY NEOPLASM OF PANCREAS DIAGNOSED ON ENDOSCOPIC ULTRASOUND GUIDED FINE NEEDLE ASPIRATION, WITH HISTOPATHOLOGICAL AND IMMUNOHISTOCHEMICAL CONFIRMATION - SERIES OF FOUR CASES.

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ABSTRACT

Solid pseudo papillary neoplasm of pancreas is very rare tumor and accounts for 0.17-2.7 % of all neuroendocrine tumor of pancreas. We report four cases of this neoplasm, which presented to our department within one year duration. Our first case is a 19 year old female who developed abdominal pain of two days duration and CECT abdomen revealed heterogeneously enhancing mass in the pancreatic duodenal groove (head of pancreas). Second patient, was an 18 years old female who also presented with diffuse abdominal pain. CECT revealed heterogeneously enhancing pancreatic head mass. Third patient, a 45 years old female known case of Sheehans syndrome and hypothyroidism presented with intermittent pain abdomen from last three months. Computed tomography revealed large hypodense lesion in right lumbar region measuring 12x12 cm with calcification within the mass along with a hypodense lesion in segment 5 of liver measuring 2 cm. Fourth patient a 17 years old female presented with chief complaints of abdominal pain intermittent in nature for fifteen days. The routine laboratory tests revealed no deviation from the normal values. A computed tomography scan was performed which showed a heterogeneously enhancing mass in the uncinate process of pancreas which measured 2x3 cm. These lesions were excised and sent for histopathological examination which revealed features which were consistent with the diagnosis of solid pseudo papillary neoplasm of pancreas in all four cases. Subsequent immunohistochemistry evaluation was carried out which confirmed the diagnosis in all four cases.

Introduction

Solid pseudopapillary neoplasm of pancreas is relatively uncommon low malignant potential pancreatic neoplasm with many pseudonyms, which occur most exclusively in young women under the age of 20 years[1]. It is rare in childhood[2,3], in older women and in men[4]. It was first described by Frantz in 1959, so also known as Guber-Frantz tumor[5]. These tumors behave in benign manner but 10-15 % of cases show spread or metastasis[6]. Still considered to be of uncertain histogenesis the tumor is thought to be hormone dependent[7]. Occurring anywhere along the length of pancreas, the mass is usually sizable at presentation, averaging 8 cm, although tumors are detected at a smaller size with advanced radiographic techniques. Patients present with few non- specific digestive type symptoms including abdominal discomfort or pain, dyspepsia and bloating accompanied by enlarging mass[8].

Case Reports

Case 1: A 16 year old female was admitted to our institute with history of occasional diffuse abdominal pain for last 4-5 months. The routine laboratory test results were in normal range. Abdominal ultrasound revealed pancreatic tail mass. Computed tomography identified 15 x 16 cm well defined soft tissue density with central cystic areas in the tail of pancreas (fig. 1).

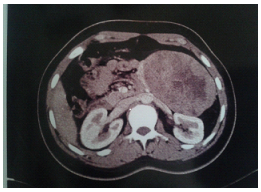

Fig. 1: Contrast enhanced CT of solid pseudopapillary neoplasm of pancreas with central cystic change in the tail of pancreas

The endoscopic ultrasound guided fine needle aspiration EUS-FNA revealed the presence of monotonous population of tumor cells, several layers of which covered the central fibrovascular stalks and formed papillary like structures (fig. 2).

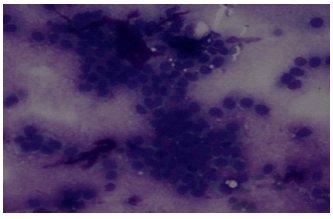

Fig. 2: cytomorphological appearance of solid pseudopapillary neoplasm of pancreas revealing pseudopapillary pattern of monomorphic cells.

The patient underwent pancreaticoduodenectomy and histopathological examination demonstrated small to medium sized polygonal cells exhibiting grooving and indentation of nuclei. Nuclei were inconspicuous and these cells were poorly supported by tiny vessels and more aligned around central fibrovascular stalks, myxoid stroma and fibrosis was also seen focally producing pseudopapillary cystic pattern. Groups of foamy macrophages were also seen but no necrosis or mitotic figures were seen.

Immunohistochemistry was performed which showed strong positivity for PR and CD 10. Overall features were consistent with solid pseudopapillary tumor of pancreas.

Case no 2: A 17 years old female presented with chief complaints of abdominal pain intermittent in nature for fifteen days. The routine laboratory tests revealed no deviation from the normal values. A computed tomography scan was performed which showed a heterogeneously enhancing mass in the uncinate process of pancreas measuring 2 x 3 cm. The endoscopic ultrasound guided fine needle aspiration EUS-FNA showed a cellular aspirate with hyalinized vascular stalks lined by neoplastic cells having delicate granular cytoplasm, indistinct cell borders round to oval nuclei, distinct nuclear grooves and inconspicuous nucleoli. The lesion was excised by pancreaticoduodenectomy (fig.3)

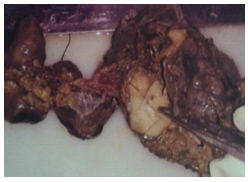

Fig. 3: Macroscopic appearance of solid pseudopapillary neoplasm of pancreas. Cut surface demonstrates tan gray soft tissue lesion.

and sent for histopathological examination which revealed tumor cells arranged in pseudopapillary pattern around vessels with hyaline core. Foci of neuroendocrine differentiation were also seen. No necrotic areas were identified. However occasion mitotic figures were seen. All the resection margins were free of tumor. Eleven lymph nodes were resected from the specimen, which showed features of non specific reactive lymphadenitis. Sections from the gall bladder and duodenum were unremarkable.

Immunohistochemistry was performed which showed strong positivity for PR and CD 10.Overall features were consistent with solid pseudopapillary tumor of pancreas. No adjuvant therapy was offered in any of the four cases we studied and no residual tumor or metastasis was identified on follow up period.

Case no 3: A 45 years old female a known case of Sheehan's syndrome and hypothyroidism presented with intermittent pain abdomen for three months. Computed tomography revealed large hypodense lesion in right lumbar region measuring 12 x 12 cm with calcification within the mass along with a hypodense lesion in segment V of liver measuring 2 cm. Intra operative findings were chronic inflammatory cyst arising from the pancreatic head measuring about 12 x 11 cm and was seen to be adherent to the surrounding tissues. The endoscopic ultrasound guided fine needle aspiration EUS-FNA showed highly cellular smears composed of a monotonous population of cuboidal cells arranged in loosely cohesive groups, as isolated cells, and as a single and multiple layers around vascular cores. The tumor cells had delicate granular cytoplasm with indistinct cell borders. The nuclei were round to oval with finely dispersed chromatin, grooved nuclear contours, and indistinct nucleoli. Mitotic figures were inconspicuous. Histopathological findings revealed small polygonal tumor cells with oval nuclei arranged in branching pseudopapillary fragments, nests and sheets, separated by thin fibro connective tissue. The supportive fibro connective tissue exhibited tiny vessels and areas of hyalinization. Myxoid connective tissue was also identified producing pseudomicrocystic pattern in sections. No necrosis or mitosis was identified (fig. 4).

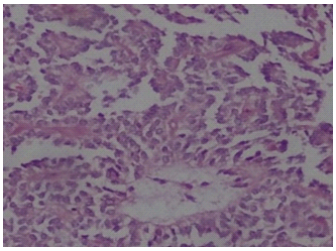

Fig. 4: Histological appearance of solid pseudopapillary neoplasm of pancreas revealing pseudopapillary pattern with collection of hyaline globules

On immunohistochemistry tumor cells showed strong nuclear reactivity for PR and CD 10. Overall features were consistent with solid pseudopapillary neoplasm of pancreas.

Case no 4: A 19 year old female presented with two days history of pain abdomen. All the routine laboratory tests were within normal limits. Contrast enhanced computed tomography revealed heterogeneously enhancing mass in pancreatico-duodenal groove 5 cm in maximum diameter.The endoscopic ultrasound guided fine needle aspiration EUS-FNA revealed cellular smears composed of monotonous cells arranged in loosely cohesive clusters, and around vascular cores. Individual tumor cells showed granular cytoplasm and round to oval nuclei with indistinct nucleoli. Mitotic figures were inconspicuous. The lesion was excised by pancreaticoduodenectomy. On gross examination the tumor was yellowish with cystic, hemorrhagic and degenerative changes. Microscopically the monomorphic tumor cells were arranged in cords and nests with oval to round nuclei which were eccentrically located. The remaining tumor was solid with foci of cystic and showed pseudopapillary change. Immunohistochemistry was performed which showed strong positivity for PR (fig. 5)

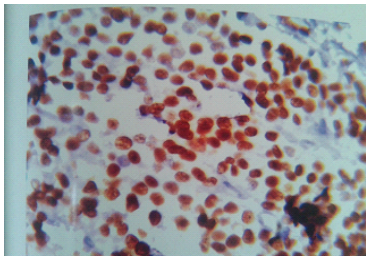

Fig. 5: Immunohistochemical appearance of solid pseudopapillary neoplasm of pancreas, revealing nuclear positivity for progesterone receptor

and CD 10 (fig. 6). Overall features were consistent with solid pseudopapillary tumor of pancreas.

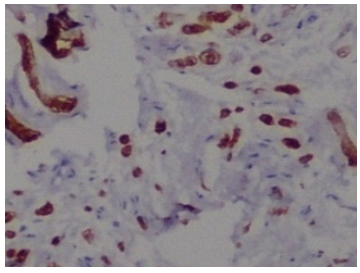

Fig. 6: Immunohistochemical appearance of solid pseudopapillary neoplasm of pancreas revealing nuclear positivity of Cd10.

Discussion

Solid pseudopapillary neoplasm is a rare neoplasm with low malignant potential usually affecting young women in second or third decade of life with female male ratio of 10: 1[9].The pathogenesis of tumor is unknown although its tendency to affect young women has suggested that sex hormones may be involved in the origin of solid pseudopapillary tumor. Also solid pseudopapillary tumor has been postulated to arise from primitive pancreatic cells (e.g. acinar cells, ductal epithelium or endocrine cells)[10] or from cell lines of female genital bud[11].

The clinical presentation is nonspecific including abdominal discomfort, mild abdominal pain or palpable abdominal mass[12]. Due to its slow growth solid pseudopapillary tumor often remains asymptomatic until tumor has enlarged considerably. The most common localization of solid pseudopapillary is tail of pancreas followed by head and body. Unusual presentations include multicentric tumor in pancreas and extra pancreatic sites such as

mesocolon, retroperitoneum, omentum, liver and duodenum possibly representing synchronous tumor spread[13,14]. The key histological hallmarks are solid and pseudopapillary proliferation of monomorphic cells without increased mitosis or cytological atypia[15,16]. Beta catenin mutations, alteration in Wnt pathway and disorganization of E-cadherin have been implicated in the development of solid pseudopapillary neoplasm.[17, 18] Cyclin D is over expressed in most cases16. The common expression of progesterone receptor and the strong predilection for females suggest that it might be a hormone dependent tumor18. However estrogen receptors have not been demonstrated.

Regarding diagnostics routine laboratory data and tumor markers are of no help. Ultrasound and CT, MRI show large well circumscribed heterogeneous mass with varying solid and cystic components demarcated by peripheral capsule and occasional calcification. MRI is superior to CT to suggest correct diagnosis and it helps to distinguish certain tissue characteristics such as hemorrhage cystic degeneration and presence of capsule. The diagnosis can be confirmed by an endoscopic ultrasound scan with fine needle aspiration biopsy[19,20] or percutaneous core needle biopsy with ultrasound and CT guidance[20].

Histologically solid pseudopapillary neoplasm are commonly well circumscribed and well encapsulated with irregular degenerative cystic cavities and hemorrhages. The tumor contains a mixture of solid cystic and pseudo papillary patterns in various proportions[5]. The diagnosis can be confirmed by immunohistochemical analysis[25].

Unlike most other pancreatic neoplasms solid pseudopapillary neoplasms mostly behave in an indolent fashion and has low malignant potential and excellent prognosis. Malignant behavior is observed in 10-15 % cases. Metastasis has been described in regional lymph nodes, liver and peritoneum and omentum[13]. Surgical resection is the standard care in the management of solid pseudopapillary neoplasm. Tumor enucleation and incomplete excision should be avoided due to risk of tumor dissemination, development of pancreatic fistula[21] and high recurrence rate. Extensive lymphatic dissection or resection of adjacent structures is not warranted as lymph node metastasis is seen in less than 2 % cases[22,23]. In our cases all histologically examined lymph nodes were negative for any metastatic disease. Tumor size should not be regarded as a predictor of resectibility because very big lesions of the size of 30 cm may be resected without any problem[24]. Unlike other pancreatic tumors stage of the disease does not play any role in the treatment of solid pseudopapillary neoplasm[22].

Overall 5 year survival approaches 97% patients undergoing surgical resection[22]. Features that may indicate an aggressive clinical behavior are diffuse infiltrative growth, extensive tumor necrosis, significant nuclear atypia, high mitotic rate, venous invasion, dedifferentiation, aneuploidy, double loss of x-chromosome, trisomy of chromosome 3 and unbalanced translocation between chromosome 13 and 17[25]. Solid pseudopapillary neoplasms, affecting elderly males has been associated with increased likelyhood of malignancy[16,26].

Conclusion

Solid pseudopapillary neoplasm is a rare pancreatic neoplasm of uncertain malignant potential and unclear histogenesis typically affecting young females without any significant symptoms. Imaging may suggest diagnosis but in unclear cases preoperative diagnosis should be accomplished by percutaneous CT guided core needle biopsy or the endoscopic ultrasound guided fine needle aspiration (EUS-FNA) in order to avoid otherwise indicated preoperative chemotherapy or radiotherapy. Complete surgical resection is the treatment option and solid pseudopapillary neoplasm should be considered in the differential diagnosis of any solid or partly cystic pancreatic or upper abdominal mass lesion, especially in young female having non-specific symptomatology.

Conflict of interest: None

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