The solid and cystic pseudopapillary neoplasm, also known as Gruber-Frantz tumour, of the pancreas is a rare primary pancreatic neoplasm of unknown etiology, occurring most commonly in young women. It may often cause few symptoms and may reach a large size by the time they are detected. Degenerative cystic changes and hemorrhagic areas are common, and the clinical presentation is that of a cystic pancreatic tumor. This unusual tumour was first described by Frantz in 1959 in a report of three cases. The tumour was further characterized by Hamoudi et al. in 1970 and proposed as a distinct tumour entity in 1981 by Kloppel et al. Patients with papillary cystic and solid tumours of the pancreas have very good prognosis. It is important to distinguish this tumour from other pancreatic growths. Metastases to liver and peritoneum are uncommon and most patients have fared well after limited resection become its indolent growth. Papillary cystic tumor possibly originates from primordial pancreatic cells and lack definite evidence of endocrine or exocrine differentiation. It has been mistaken for endocrine neoplasm or a cystic tumour. Pathological features include cellular, hyper vascular regions without gland formation, and degenerative pseudopapillae. Immunophenotyping does not indicate any specific line of differentiation and ultra structure studies do not disclose a particular finding. However, it is possible to at least suspect the diagnosis of Gruber-Frantz tumour on cytology specimen in the light of clinical and radiological findings.

Two cases of Gruber Frantz neoplasm were diagnosed in cytology section of the department of histopathology, Liaquat National Postgraduate Medical Centre, Karachi Pakistan. One of those cases had subsequent histological confirmation of the diagnosis.

**CASE REPORTS**

**Case 1:** A 32 years old female presented with complaint of vague abdominal pain for 2 to 3 months. The general physical examination was unremarkable except for mild pallor. Jaundice was absent. On abdominal examination, a mass was palpable. Routine laboratory tests were within normal range except mild anemia. Ultrasound examination revealed a circumscribed heterogeneous mass in the tail of pancreas with solid and cystic components. Focal hemorrhage was also noted. No lesion was seen in liver. Chest X-ray was normal. After aspiration cytology, resection of the tumor mass was performed with uneventful postoperative period.

**Case 2:** A 27 years old pregnant woman with complaint of epigastric discomfort had a palpable lump on abdominal examination. Baseline investigations revealed anemia. Liver function tests were also performed and showed elevated liver enzymes. She underwent sonographic examination. The ultrasound showed well-defined heterogeneous mass measuring 11.4 x 9.5 cms, with areas of cystic degeneration just below the left lobe of liver. FNAC was performed with no complication thereafter. The subsequent details are not available as the patient did not follow in the same hospital.

Aspirations of both the abdominal masses were performed, using a disposable 22-gauge needle and
10-ml syringes, under ultrasound guidance. In each case, aspirated material was spread onto the glass slides, immersed in 95% ethanol for fixation and then air-dried. Material from the biopsy was put in 10% buffered formalin. The smears after fixation were subjected to staining. One was stained with papanicolaou stain and three with routine hematoxylin-eosin (H&E) stain. In each case, cell block was prepared from tissue fragments in the syringe and needle hub. After processing and paraffin embedding, 4 um sections were prepared and stained with H & E. In first case resected tumor mass was grossly examined thoroughly, sections submitted for light microscopy. The immunohistochemistry was performed by DAKO ENVISION method.

The hematoxylin -eosin and pap stain examination of the smears of both the cases revealed proteinaceous and hemorrhagic background along with many macrophages, some foamy macrophages and leukocytes. Many clusters and papillary fronds of atypical epithelial cells were seen. The cells showed mildly enlarged eccentric nuclei with some nuclear grooving, but even chromatin and small inconspicuous nucleoli. Mitoses were rare (Figure 1).

Cell block preparation revealed multiple small and large tissue fragments with papillary structures covered by one to many layers of atypical cells arranged around blood vessels. Immunohistochemical studies were performed. Tumour cells stained focal positive with cytokeratin AE1/AE3 and were strongly positive with vimentin. Staining with chromogranin was negative. A diagnosis of papillary neoplasm was made with strong suggestion of solid-cystic papillary epithelial neoplasm.

The excised tumor of the first case comprised of a large well-circumscribed mass measuring 12.5 x 10 x 8.5 cms. Cut surface was spongy and hemorrhagic. Light microscopic examination revealed an encapsulated neoplasm composed of many layers of monomorphic cells surrounding tiny blood vessels, forming pseudo papillae, pseudomicrocystic and trabecular patterns (Figure 2). Nuclear morphology was same as seen in cytology. Cytoplasm was pale with some eosinophilic globules. The fibro-vascular core contained foci of mucin. Hemorrhage, cystic degeneration and necrosis were also present. Mitotic figures were rare.

DISCUSSION

Solid and papillary epithelial neoplasm, also known as papillary cystic neoplasm, is a rare, low-grade pancreatic malignancy that usually affects young women, often in their twenties. It can rarely be seen in old age or in men. A predilection for blacks and East Asians has been suggested. It accounts for less than 3% of all non-endocrine pancreatic tumors. Clinically, most patients present with vague upper abdominal pain accompanied by an enlarging abdominal mass. Jaundice is rare even if lesion is located at head of pancreas. Occasionally, these tumors are asymptomatic and picked up at imaging, physical examination or laparotomies performed for other reasons. Clinical diagnosis and histopathological findings of this pancreatic tumor may be unrecognized due to difficult differentiation between endocrine and exocrine pancreatic neoplasm, such as acinar cell carcinoma or islet cell tumor and cystadenoma of the pancreas. However, surgeons should be aware of this benign but rather uncommon lesion because the biologic behaviour of Gruber-Frantz tumour is indolent and complete excision is successfully possible.

The papillary cystic and solid tumor of pancreas is a primary pancreatic neoplasm of unknown etiology. A role for sex hormones in the pathogenesis is suggested by its predilection for young fertile women. Controversial data have been provided for the presence of Progesterone Receptors (PR) and for estrogen receptors.
The diagnosis of this interesting neoplasm can be made on cytology in most of the cases, performed by ultrasound-guided fine needle aspiration. The cytological features i.e. uniform cells forming sheets and pseudo papillae along with the help of immunohistochemistry enables the pathologist to reach the diagnosis. These express positivity for vimentin, keratin along with alpha–1–antitrypsin, neuron - specific enolase, chromogranin and other neuroendocrine markers. None of 20 cases by Pettinato et al. revealed pancreatic hormones, opioid peptides or neuroendocrine markers reactivity. Electron microscopic examination was also performed with five cases showing oval nuclei, moderate amount of rough endoplasmic reticulum and many mitochondria. No diagnostic secretory granules were found. A study by Notohara et al. revealed a panel of immunohistochemical stains. Solid-cystic pseudo papillary tumors show strong and diffuse positivity for CD10, CD56 and vimentin, and focal weak reactivity with synaptophysin and Pan-CK and negativity for chromogranin. However, despite characteristic microscopic appearance, the immunophenotype is not specific and does not define a line of differentiation corresponding to any normal pancreatic cell type.

The biologic behaviour is benign with indolent course but with the potential for aggressive behaviour and infrequent metastasis to liver or peritoneum. The aggression may be in the form of local recurrence or infiltration to adjacent organs or vessels. Metastases to liver are reported in 7% of patients. Lung and skin may also be recipients of metastasis of this tumour. Survival is usually long, even if disseminated disease is present.

In view of favourable prognosis, pathologist as well as clinician should be aware of this indolent uncommon neoplasm and diagnosis should be at least suspected on cytology and be persuaded in the light of clinical information. Immunohistochemistry may be helpful and thus complete excision of the tumour mass is possible.

REFERENCES


