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Pancreatic intraductal mucinous neoplasm: Case report

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Abstract
Pancreatic intraductal mucinous neoplasms are cystic lesions of the pancreas that have a potential to progress to pancreatic carcinoma, hence prompt and early recognition with surgical resection of high-risk lesions is of paramount importance. The differential diagnosis on imaging and histology includes pancreatic pseudocysts, mucinous cystadenomas of pancreas, pancreatic intraepithelial neoplasia, intraductal oncocytic pancreatic neoplasm (IOPN), intraductal tubulopapillary neoplasm (ITPN) and retention cysts. Diagnosis is mainly by clinical and radiological features. Cytology may be helpful if adequate sample is obtained. The clinical management of these tumours is a constantly evolving with current approach being surgical resection of tumours over 10mm and close radiological and tumour marker follow up for smaller lesions. Prognosis is highly dependent on main duct versus branch duct involvement, presence of high-grade lesions and associated invasive carcinoma component.

Keywords: pancreas, intraductal, mucinous, neoplasm, cyst

Introduction
Pancreatic intraductal mucinous neoplasms are cystic lesions of the pancreas which are grossly or radiologically visible, involving the main ducts or branch ducts or both [1]. They have a potential to progress to pancreatic carcinoma, hence prompt and early recognition with surgical resection of high-risk lesions is of paramount importance [2, 3]. We examine a case of a surgically resected intraductal papillary mucinous neoplasm in the tail of the pancreas, and its histological features.

Case report
A 38-year-old male was referred with vague abdominal pain. On imaging, was found to have a cystic lesion in the pancreas with duct and cyst connection, highly suggestive of intraductal papillary mucinous neoplasm, in the body and tail. A fine needle aspiration was attempted, however scanty inflammatory cells were only noted with lack of significant mucin. In view of the clinical and radiological features, surgical resection was performed, with distal pancreatectomy and splenectomy. A specimen of distal pancreatectomy and attached splenectomy weighing 220 grams was received. The pancreas measured 90x40x20mm and on sectioning the tail exhibited a well demarcated cyst with mucinous contents, measuring 15x11x8mm, with a wall thickness of 1mm. This appeared to be continuous with the main duct and lying 1mm away from the bare surface of the pancreas. The resection margin was 75mm away. On microscopy, multiple sections revealed pancreatic tissue with a large, dilated cyst involving main and branch ducts with low papillae lined by pseudostratified columnar cells with abundant mucin with intestinal differentiation. Focally cells show cuboidal morphology, however predominant population is of columnar mucin secreting epithelium with goblet cells. The stratification, with mild loss of polarity and nuclear hyperchromasia amounts to low grade dysplastic change. The cyst appeared to communicate with the terminal duct branches of the pancreatic ductal system. No features of high-grade dysplasia or invasive carcinoma were noted on extensive sampling. The adjacent pancreas exhibited features of chronic pancreatitis. The splenic tissue was histologically within normal limits. Two regional lymph nodes were noted with reactive changes. Based on these features, diagnosis of a low grade, mixed type, Intraductal pancreatic mucinous neoplasm (IPMN) with mixed histological combination of intestinal and pancreaticobiliary subtypes was confirmed. Resection margins were free of the lesion.

Gross mages

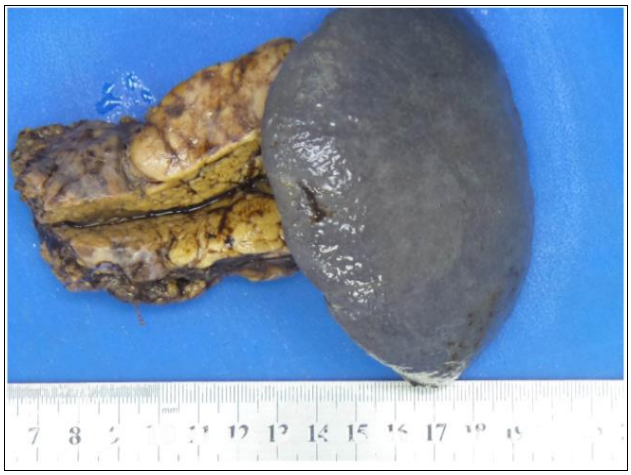

Fig 1: Gross specimen of distal pancreatectomy and splenectomy

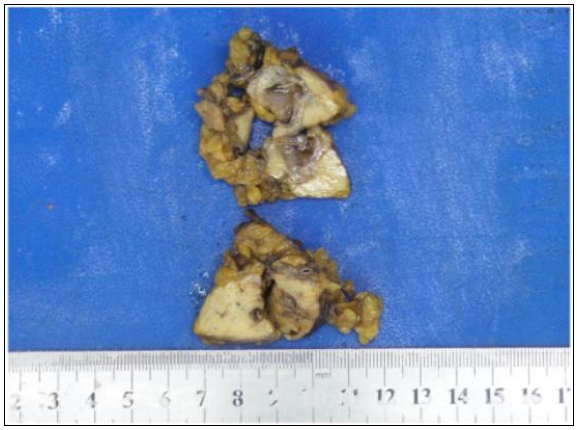

Fig 2: Serial sections of pancreas with cystic lesion in tail of pancreas involving main duct

Fig 3: Serial sections through the pancreas from body to tail with cystic lesion in tail of pancreas

Microscopic images

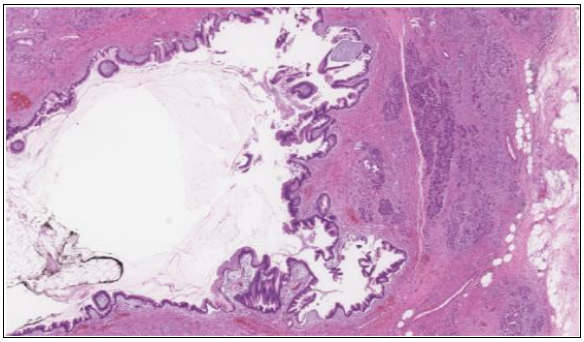

Fig 4: Dilated main duct with papillary projections lined by mucinous stratified cells. (H&E- 1X)

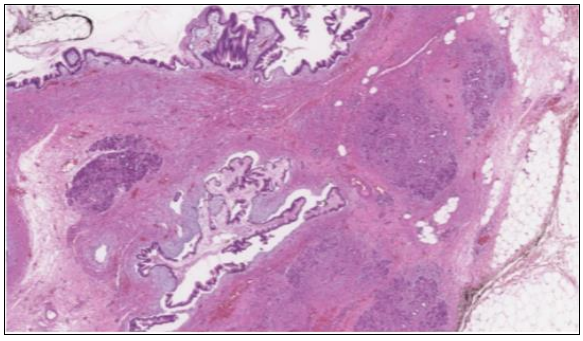

Fig 5: Main and branch duct involved by mucinous epithelial cells with stratification (H&E 1X)

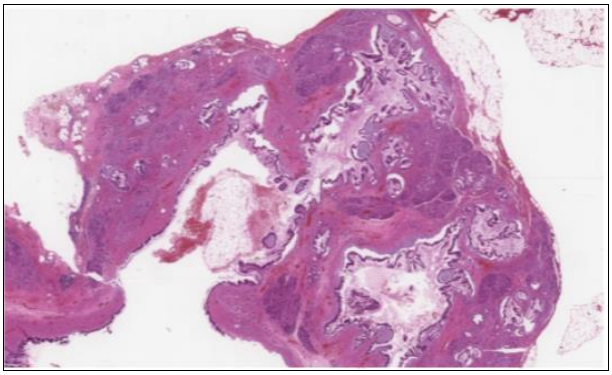

Fig 6: Main and branch ducts involved by mucinous cells with papillae and stratification. Adjacent pancreas with chronic pancreatitis (H&E 0.5X)

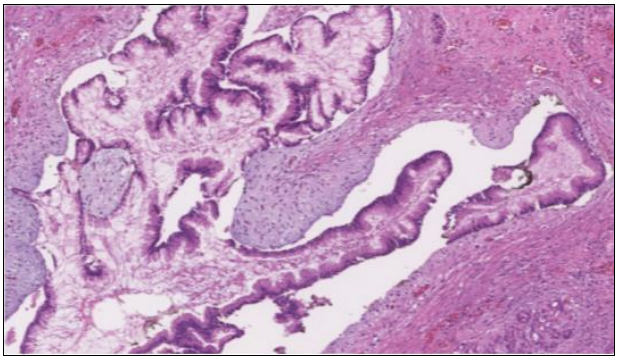

Fig 7: intestinal differentiation of lining cells with copious mucin within lumen (H&E 8X)

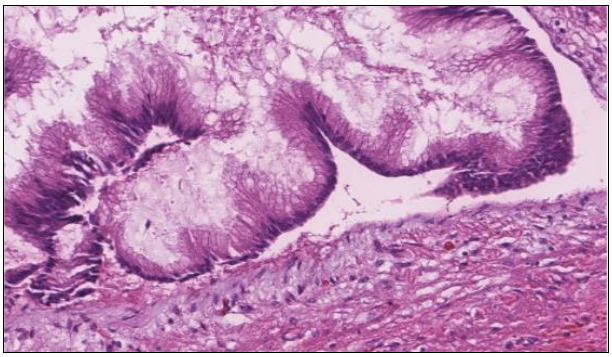

Fig 8: Mucinous cells with low grade dysplastic features. (H&E 20X)

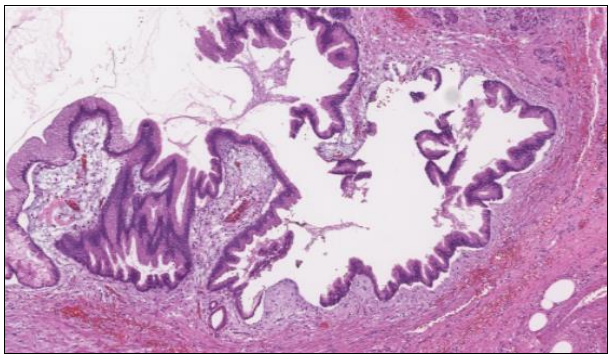

Fig 9: Main and branch duct involvement by neoplastic cells (H &E 8X)

Discussion

Intraductal papillary mucinous neoplasms are classically diagnosed as grossly visible lesions, more than 5mm, arising in the main duct or branches of the pancreatic ducts [1].

These are neoplastic and produce mucin. These neoplasms commonly occur in the elderly and in the head of the pancreas, and patients present with epigastric pain, diabetes mellitus, chronic pancreatitis, or jaundice [4, 5]. These lesions have been reported to have associations with syndromes like Peutz -Jeghers' syndrome, Mc Cune Albright Syndrome, Lynch Syndrome and Familial Polyposis [6, 7]. The pathogenesis behind these lesions has not been clearly elucidated yet and is under study. Associations with KRAS, RNA4, GNAS mutations have been studied [8, 9]. Three distinct types are recognised according to the involvement of the duct systems as 1) Main duct IPMNs, 2) Branch duct IPMNs or 3) Mixed IPMNs [1, 10]. These lesions are often associated with mural nodules and in situ or invasive carcinoma, identified in as many as 60% of main duct lesions. Lesions more than 30mm are more likely to harbour high grade lesions or associated carcinomas [11]. Histologically, the dilated duct/ducts are lined by intraductal proliferation of columnar to cuboidal mucin producing cells. These may be flat or arranged in microscopically or grossly visible papillae [1, 12]. The cytoarchitectural atypia is classified according to a two -tier system as low grade and high grade [1, 12]. The commonest lining epithelium is Gastric type, comprising 70% where the cells morphologically resemble gastric foveolar epithelium. These lesions are commonly low grade and involved branch ducts. The second commonest is Intestinal type, account for 10% of cases, with involvement of the main duct, and high-grade dysplasia. The least common, is Pancreaticobiliary type, involving the branch ducts and commonly with high grade lesions. Immunohistochemical markers like CK7, CK19, CEA and CA 19.9 are commonly expressed [1, 10, 13]. According to the type of differentiation, Gastric type IPMN expresses MUC5AC, MUC6 [13, 14]. Intestinal type IPMN expresses MUC2, CDX2, MUC5AC with a pattern of staining like invasive colloid carcinoma. Pancreaticobiliary type IPMN expresses MUC1, MUC6+ (focally) and MUC5AC [13, 14]. The differential diagnosis on imaging and histology includes pancreatic pseudocysts, mucinous cystadenomas of pancreas, pancreatic intraepithelial neoplasia, intraductal oncocytic pancreatic neoplasm (IOPN), intraductal tubulopapillary neoplasm (ITPN) and retention cysts [4]. Cytology may be helpful if adequate sample is obtained and range from hypocellular to hypercellular aspirates on a background of thick mucus [15].

The clinical management of these tumours is a constantly evolving field. Surgical resection is recommended for Main duct IPMNs with and main pancreatic duct diameter of greater than 10mm, or presenting with worrisome features as jaundice, or high-risk stigmata like mural nodules or solid areas as per the 2012 Fukuoka guidelines. Newer recommendations for management of asymptomatic patients and MPD diameters of 5 to 9mm include follow up with radiology and tumour marker levels [16, 17]. Prognosis is highly dependent on main duct versus branch duct involvement, presence of high-grade lesions and associated invasive carcinoma component. The 5-year survival rates of IPMN with low grade component is 100%, with high grade component is reported as around 85%. This drops between 36 to 90 % depending on the size of the tumour and the type of carcinoma [18, 19]. In the context of the current case, the presence of a 15mm cyst in a younger patient with clinical symptoms and classic radiology was noted. Curative treatment in the form of pancreatectomy was offered to the patient and performed. The patient is well and disease free on follow up.

Conclusion

Knowledge of the natural history and pathology of IPMN is still evolving, as is our understanding of the disease in terms of its management and molecular characteristics. While low grade IPMNs have an excellent prognosis, if left untreated, progression to higher grade lesions and invasive carcinoma is possible. In resected lesions, a close sampling of all suspicious areas, and mural nodules is essential so as not to miss incidental or lurking carcinomas. A long term follow up and monitoring of clinical symptoms is of paramount importance.

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