Case report

Mixed neuroendocrine-non-neuroendocrine tumour of pancreas mimicking groove pancreatitis: Case report

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ABSTRACT

Introduction: Mixed neuroendocrine-non-neuroendocrine neoplasm (MiNEN) is a rare tumour of the pancreas which can mimic groove pancreatitis.

Case report: We present a 49-year-old Indian male presented with constant, dull-aching epigastric pain for last 6 months radiating to back, not associated with jaundice, gastrointestinal bleed, fever or weight loss. He also had history of alcohol abuse for last 15 years. Physical examination was unremarkable. Laboratory investigations were within normal limits. Contrast enhanced computed tomography (CT) of the abdomen was suggestive of groove pancreatitis. CA 19.9, CEA and IgG4 levels were normal. Upper gastrointestinal endoscopy revealed an oedematous mucosa with narrowing of second part of duodenum. Endoscopic ultrasound (EUS) showed bulky pancreas with ill-defined heteroechoic head with periduodenal soft tissue thickening. EUS guided fine needle aspiration revealed chronic inflammatory cells. Based on the endoscopic findings and imaging, we suspected the diagnosis to be groove pancreatitis. He underwent open Whipple’s pancreaticoduodenectomy. Histopathological evaluation revealed well differentiated neuroendocrine tumour and immunohistochemistry revealed features which was consistent with mixed neuroendocrine-non-neuroendocrine tumour (MiNEN). Post-operative period was uneventful and he was discharged on post-op day 7. A PET-CT scan was done to look for any silent metastasis and it was negative. He received 4 cycles of cisplatin-based chemotherapy. He was symptom free and doing well on 12 months follow up with no evidence of recurrence in surveillance CT imaging.

Discussion: Pancreatic MiNEN is characterised by presence of two malignant tissues, adenocarcinoma and NET, with one constituent involving at least 30% of the tumour. We report the pitfalls in diagnostic work-up which can lead to misdiagnosis of this rare entity. Specially due to admixture of different kinds of tissue, radiological investigations can be misleading.

Conclusion: Our case highlights the fact that MiNEN of pancreas can mimic a benign condition like groove pancreatitis. If routine histopathological and immunohistochemical evaluation is not done on the resected samples, relying on radiological and fine-needle aspiration cytology evidences, the actual diagnosis could be missed.

1. Introduction

Pancreatic mixed neuroendocrine non-neuroendocrine neoplasms (MiNEN) is an extremely rare clinical entity. WHO redefined it in 2017 as the association of both neuroendocrine and epithelial components [1]. It shows features of either acinar or ductal adenocarcinoma with neuroendocrine tumour (NET), and either component should account for at least 30% of the tumour [2]. Although, MiNEN can involve any part of gastrointestinal tract, rarely has it been found in pancreas [3,4]. Existing medical literature is sparse, clinical management is not standardized and little is known about survival outcomes. Herein, we present a novel case of MiNEN of the pancreas which presented as groove pancreatitis and created a diagnostic dilemma. This case report was realised following SCARE guidelines [5].

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2. Case report

A 49-year-old Indian male presented with constant, dull-aching epigastric pain for last 6 months radiating to back, associated with post-prandial nonbilious vomiting. It was not associated with jaundice, gastrointestinal bleed, fever or weight loss. He also had history of alcohol abuse for last 15 years. Physical examination was unremarkable. Laboratory investigations such as complete hemogram, electrolytes, liver function test, serum amylase and lipase were within normal limits. Ultrasonography of the abdomen was unremarkable. Contrast enhanced computed tomography of the abdomen revealed a subtle parenchymal hypo-attenuation involving pancreatic head with effaced pancreatico-duodenal groove, showing tracking fluid density. There was no arterial phase abnormal hyper enhancement. Main pancreatic duct was 7 cm, common bile duct was 9 mm with intrahepatic biliary radicle dilatation. Overall this was suggestive of groove pancreatitis (Fig. 1). CA 19.9, CEA and IgG4 levels were normal. Upper gastrointestinal endoscopy revealed an oedematous mucosa with narrowing of second part of duodenum. Endoscopic ultrasound (EUS) showed bulky pancreas with ill-defined heteroechoic head with periduodenal soft tissue thickening (Fig. 2). EUS guided fine needle aspiration was performed which revealed chronic inflammatory cells. Based on the endoscopic findings and imaging, we suspected the diagnosis to be groove pancreatitis. Although malignancy could not be ruled out without histopathological evaluation of the resected specimen. In view of the provisional diagnosis of groove pancreatitis with clinical symptoms of gastric outlet obstruction, he underwent open Whipple’s pancreaticoduodenectomy. Operative time was 234 min and blood loss was 190 ml. Resected specimen (Fig. 3) was sent for histopathological evaluation. On cut section a periamputary growth measuring 2.5 × 2.0 × 1.8 cm was found. Microscopic evaluation revealed well differentiated neuroendocrine tumour (Fig. 4) with mitotic rate <2mitosis/2 mm² (Grade G1) which was extending through the sphincter into the duodenal submucosa. All the resection margins were free and no lymph nodes (0/12) were involved. Overall pathological staging was pT2N0Mx. On further characterisation with immunohistochemistry (Fig. 5), it stained positive for CK 7, EMA, synaptophysin, and negative for CK 20 which was consistent with mixed neuroendocrine-non-neuroendocrine tumour (MiNEN). Post-operative period was uneventful and he was discharged on post-op day 7. A PET-CT scan was done to look for any silent metastasis and it was negative. He received 4 cycles of cisplatin-based chemotherapy. He was symptom free and doing well on 12 months follow up with no evidence of recurrence in surveillance CT imaging.

3. Discussion

Pancreatic MiNEN is characterised by presence of two malignant
tissues, adenocarcinoma and NET, with one constituent involving at least 30% of the tumour. Furthermore, acinar adenocarcinoma is reported to more common compared to ductal adenocarcinoma [6]. In the neuroendocrine component, MiNEN commonly contains neuroendocrine carcinoma (poorly differentiated, Ki67 > 20%), however, NET (well differentiated, low Ki67) can also be present, as in our case. Morphologically it can be subcategorized into collision tumour and mixed variety depending on the admixture of the constituent components in the transition zone [2]. It is usually seen in elderly patients with a median age of 60 years, located variably in all parts of the pancreas [7].

In our case the tumour was nonfunctional and the atypical location in cross-sectional imaging; endoscopic findings and cytological analysis pointed more towards the diagnosis of groove pancreatitis (GP). The strong history of alcohol addiction and presentation with epigastric pain radiating to back in the absence of weight loss also pointed towards an inflammatory etiology of the pancreatitis. However, later we realised that insertion of EUS was restricted due to narrowing of the duodenal lumen which might lead to inadequate sampling of the tissue. Moreover, EUS has high negative predictive value and cannot access the whole tumour to diagnose MiNEN especially [2]. The accuracy of the EUS is also dependent on the operator [8]. In our case pre-operative evaluation for functional status of the tumour was not done as we did not think of NET in our differential diagnosis. Although markers for pancreatic adenocarcinoma (CEA and CA 19.9) and autoimmune pancreatitis (IgG4) were done as these two are known differentials for GP [8]. Moreover presence of hyper-attenuation on arterial phase of CECT due to rich capillary network is highly suggestive of NET. But this was not the case for us as there may be varied proportion of the neuroendocrine component in MiNEN. Considering the preoperative diagnosis as GP, Whipple’s pancreaticoduodenectomy was considered as the treatment of choice. Resected specimen on histopathological and immunohistochemical (IHC) examination confirmed the diagnosis to be MiNEN. Hence histopathology along with IHC stays the gold standard for diagnosis of this rare entity. Although this procedure along with R0 resection is the treatment of choice for MiNEN also. The biological behaviour and overall outcome is unclear due to its low incidence [9]. Adjuvant chemotherapy is usually given even after R0 resection, however, it is not clear whether to deal with both components of the tumors or with the major component only. La Rosa et al. proposed that adjuvant chemotherapy should focus on the dominant component because the outcome of such mixed tumour follows that of a more aggressive cell type [4]. The overall prognosis for MiNEN is poor [3,4,10]. Due to its paucity of follow-up data, the actual prognosis is yet to be defined. The purpose of reporting this rare clinical entity was to highlight the challenges in diagnostic work-up in our case and to make the clinicians aware that MiNENs can mimic GP. Moreover, it is important to report such anecdotal cases to get knowledge about their clinicopathological behaviour and standardise optimal treatment options.

4. Conclusion

Our case highlights the fact that MiNEN of pancreas which is an extremely rare form of malignancy with poor outcome, can mimic a benign condition like groove pancreatitis. If routine histopathological and immunohistochemical evaluation is not done on the resected samples, relying on radiological and fine-needle aspiration cytology evidences, the actual diagnosis could be missed. This would be disastrous the patient in terms of prognosis. So clinicians should be aware of MiNEN while listing differentials for groove pancreatitis.

Declaration of competing interest

None declared.

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Ethical approval

Not required in our institution to publish anonymous case reports.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

Arkadeep Dhali: Conception, design of the study, acquisition of the data, drafting the manuscript, final approval of the version to be submitted.

Sukanta Ray: Conception, design of the study, acquisition of the data, drafting the manuscript, final approval of the version to be submitted.

Sujan Khamrui: Acquisition of the data, final approval of the version to be submitted.

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Gopal Krishna Dhali: Acquisition of the data, final approval of the version to be submitted.

Registration of research studies

Not applicable.
Guarantor

Dr. Sukanta Ray act as guarantor for the report and accept responsibility for the work.

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