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Diagnosis and management of small bowel neuroendocrine tumours: A state-of-the-art

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Abstract

This article is an extensive review that provides an update on the epidemiology, pathophysiology, symptoms, diagnosis, and treatment of small bowel neuroendocrine tumours. Neuroendocrine tumors (NET) are a group of neoplasms that derive from neuroendocrine cells. The small intestine is the most frequently affected site of the gastrointestinal tract. NETs are currently the most common primary tumors of the small intestine, mainly involving the ileum. Small intestine (SB) NETs by definition are located between the ligament of Treitz and the ileocecal valve. They are characterized by being small and inducing an extensive fibrotic reaction in the small intestine and mesentery, resulting in narrowing or twisting the intestine. Clinical manifestations depend on the location of the primary tumor and its functionality. The majority of them are non-functional NETs and usually asymptomatic; in an advanced stage, NETs present symptoms of mass effect by non-specific abdominal pain, or carcinoid syndrome (CS) which develops in patients with liver metastasis (around 10%). The manifestations of CS specifically are facial flushing (94%), diarrhea (78%), abdominal cramps (50%), heart valve disease (50%), telangiectasia (25%), wheezing (15%) and edema (19%). Diagnosis is made by imaging or biochemical tests, which order of

request will depend on the initial diagnostic hypothesis, while confirmation always will be histological. All patients with localized SB NET with or without regional metastasis in the mesentery should be considered for curative resection. Locoregional and distant disease may be susceptible to several therapeutic strategies within a multimodal treatment concept, as chemotherapy, somatostatin analogs, and palliative resection.

INTRODUCTION

The first description of a small bowel NET was made by Langhans in 1867, who described a polypoid tumour of the small intestine[1].Nowadays, Neuroendocrine neoplasms (NEN) are a heterogeneous group of neoplasms derived from neuroendocrine cells. The term NEN encompasses well-differentiated neuroendocrine tumours (NETs) and poorly differentiated neuroendocrine carcinomas (NECs)[2]. NEN most commonly arise from the gastrointestinal tract[3,4].

NENs can develop throughout the Gastrointestinal tract (GI-NEN) in the following areas: small intestine (45%), rectum (20%), appendix (16%), colon (11%), pancreas (5-10%) and stomach (7%)[5] **(Figure 1).**

NEN account for 1.0–1.5% of all gastroenteropancreatic (GEP) neoplasms[6]. Small bowel neuroendocrine tumours (NETs) are increasing in incidence and are now the most common primary malignancies of the small intestine[2]. The incidence of NETs in general, and small bowel (SB) NETs specifically, are increasing steadily since the 1970s, possibly owing to detection of early-stage disease [7,8].

The aim of this manuscript is to carry out an updated narrative review on the diagnosis and treatment of small bowel neuroendocrine tumours.

CONCLUSION

Neuroendocrine tumours are neoplasms that can be found in any part of the body. This review is focused on those with its location or origin of the digestive tract at the level of the small intestine because of its variable form of presentation and difficulty to

diagnose, as well as on the treatment approach, emphasizing a multidisciplinary effort. We observe that reports of current series place them in some cases as one of the most frequent tumours in the small intestine. As their incidence is increasing, the importance of understanding their behavior and how to approach them correctly increases. The presentation of SB NETs is characterized by variable gastrointestinal symptoms, which is frequently one of the causes of the delay in between symptom onset until diagnosis. In addition, the suspicion of a SB NET must be confirmed with a combination of biochemical tests, anatomical and functional images and finally with the anatomopathological study of tissue, the latter preferably carried out by a pathologist familiar with NETs. Each of them will facilitate clinical decision making. Finally, treatment depends on the extent of the disease; patients with localized disease are treated with surgery and those with metastatic disease will be treated with SSAs, everolimus or PRRT together with the consideration for resection of the primary tumour and cytoreductive surgery. It is necessary to know and understand the behavior, forms of presentation and therapeutic possibilities of NETs of the small intestine in order to improve the current management of this type of patient.

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