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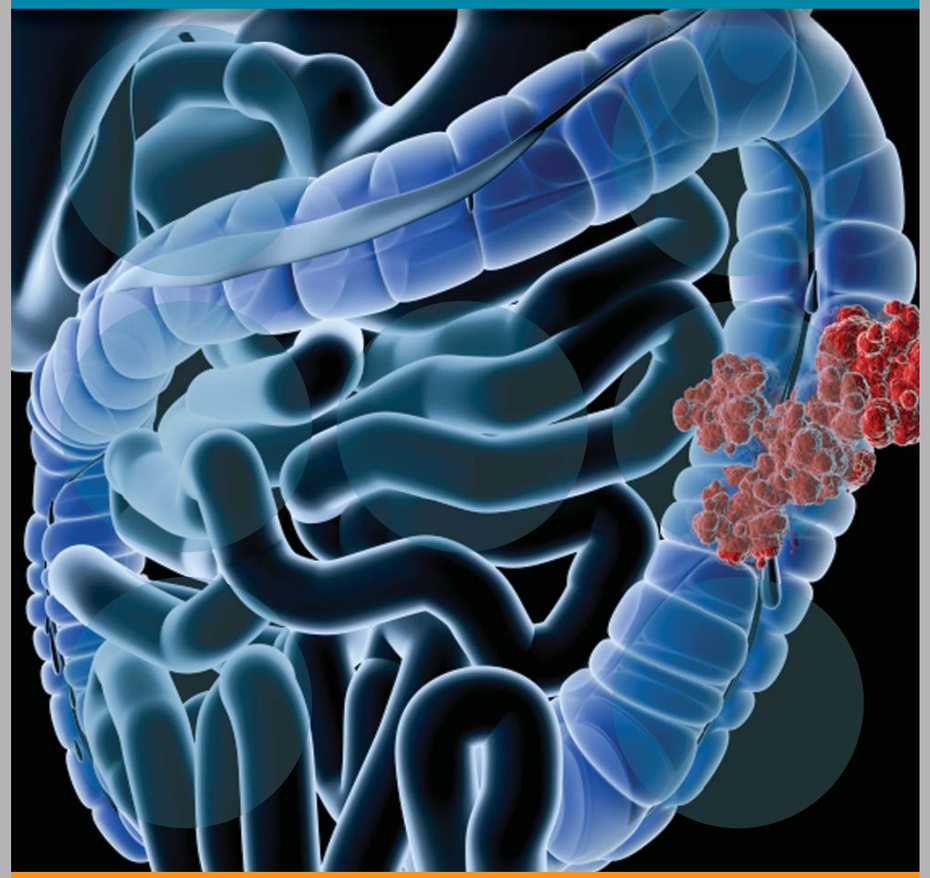
Multidisciplinary Team Management

Optimal Patient Management of Neuroendocrine Tumours



CONTENTS

AUTHOR BIOGRAPHIES 2

INTRODUCTION 3

NEUROENDOCRINE TUMOURS 4

- Epidemiology 5
- Sites of occurrence 6
- Aetiopathology 7
- Classification 8
- Clinical features 9
- Diagnosis 10
- Staging 11
- Treatment 12
- Algorithm for the management of NETs 13

ROLE OF THE MULTIDISCIPLINARY TEAM IN MANAGEMENT OF NEURO ENDOCRINE TUMOURS 19

- Multi-disciplinary approach in cancer care 20
- Advantages of multidisciplinary care 21
- NET as a candidate for the MDT approach 22
- The core MDT in NET 24
- Individual roles and communication 26
- Other key roles in the MDT 30
- Benefits of the MDT approach in NET 32

FUTURE PERSPECTIVES 36

KEY ISSUES 38

REFERENCES 40

GLOSSARY 42

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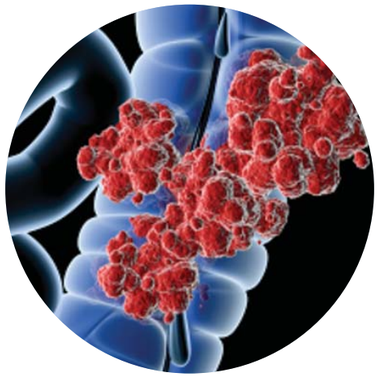
INTRODUCTION

More than 90% of all cancers of the gastrointestinal (GI) tract arise from the epithelial cells , in contrast, gastrointestinal stromal tumors affect connective tissue of the GI tract. Gastrointestinal stromal tumors (GISTs) are rare tumours of the gastrointestinal tract arising from the mesenchyme (mesoderm). The actual cell of origin of GISTs is a pluripotent mesenchymal stem cell.[1]

Gastrointestinal stromal tumors express tyrosine kinase receptor – CD117 (KIT) and are KIT signaling driven mesenchymal tumors. Many GIST tumors have an activating mutation in either KIT or platelet-derived growth factor receptor alpha (PDGFRα) [2]

The diagnosis and management of GISTS is challenging as most patients have non specific presentations and often present late in the disease. A variety of therapeutic options are available to manage GIST and the treatment has to be individualized to suit patient's needs. Hence amultidisciplinary team of physicians is essential to the successful treatment of GISTs. Evidence supports multi disciplinary team management with a gastroenterologist, surgeon, medical oncologist, pathologist and radiologist. The benefits of multidisciplinary disease management of patients include reducing recurrent disease, optimizing timing of surgery and organ preservation, prolonging survival for the patient and enhancing response to targeted therapies.



NEUROENDOCRINE TUMOURS

The various neuroendocrine tumours and are listed in **Table 1**.

TUMOURS	EXAMPLES
• Gastro-entero-pancreatic tumours o Carcinoid o Non-carcinoid	• Gastrinoma • VIP (vasoactive intestinal polypeptide) oma • Insulinoma • Glucaganoma • Somatastatinoma • GRFoma • ACTHoma
• Catecholamine-secreting tumours	• Phaeochromocytoma • Paraganglioma • Ganglioneuroma • Ganglioneuroblastoma • Sympathoblastoma • Neuroblastoma
• Thyroid	• Medullary carcinoma of the thyroid
• Pituitary	• Chromophobe pituitary tumour
• Lung	• Small cell lung cancer
• Skin	• Merkel cell tumour

Epidemiology

Neuroendocrine tumours account for about 0.5% of all malignancies. The incidence of NETs diagnosed during life is rising, with gastrointestinal carcinoids making up the majority; earlier estimates were of fewer than 2 per 100 000 per year but more recent studies have found rates approaching 3 per 100 000, with a continuing slight predominance in women. The risk of NET in an individual with one affected first degree relative has been estimated to be approximately four times that in the general population; with two affected first degree relatives, this risk has been estimated at over 12 times that in the general population. The main primary sites are the gastrointestinal tract (62-67%) and the lung (22-27%). Other sites include larynx, thymus, thyroid, adrenal, gonads and skin.

Presentation with metastatic disease accounts for 12-22%. Most neuroendocrine tumours are mainly sporadic, but association with the multiple endocrine neoplasia type 1 syndrome and clustering within families is known. An increased risk of secondary cancers has been reported, but numbers are small. The 5-year survival is mainly associated with stage: [2, 3

STAGE	5YSR
Local disease	93%
Regional disease	74%
Metastatic disease	9%

Sites of occurrence

NETs predominantly are seen in the gut wall but can be seen in other organs, including the lungs, mediastinum, thymus, liver, pancreas, bronchus, ovaries, prostate, and kidneys. In children, most tumours occur in the appendix.

The sites of occurrence of gut NETs and their frequencies is presented in **Fig.1 [102]**

NEUROENDOCRINE TUMOURS

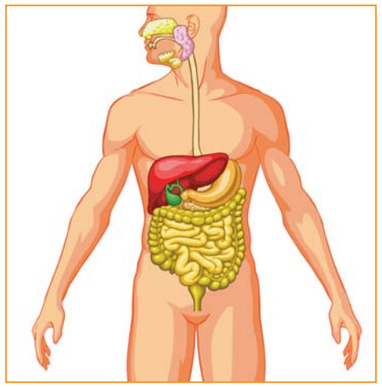


Fig.1: NETs in the gut [102]

Aetiopathology

Gastrointestinal and pancreatic neuroendocrine tumours originate from cells of the diffuse endocrine system. Most Gastrointestinal and pancreatic neuroendocrine tumours are sporadic, however, some of them, especially pancreatic endocrine tumours, may occur as part of familial syndromes.

In sporadic endocrine pancreatic tumours, losses of chromosome 1 and 11q as well as gain on 9q appear to be early invents in development of pancreatic tumours. Multiple genetic defects may accumulate with time and result in pancreatic neuroendocrine tumour progression and malignancy. Gastrointestinal endocrine tumours mostly show genetic alterations concentrated on chromosome 18. There are losses of the entire chromosome as well as smaller deletions. The most frequently reported mutated gene in gastrointestinal neuroendocrine tumours is b-catenin. Overexpression of cyclin D1 and cMyc has also been reported. A set of genes NAP1L1, MAGE-2D and MTA1 has been correlated with malignant behaviour of small intestinal carcinoids.

Pancreatic endocrine tumours, may occur as part of inherited syndromes such as multiple endocrine neoplasia type 1 (MEN1 syndrome), von Hippel-Lindau disease, neurofibromatosis type 1 and tuberous sclerosis [103]

NETs appear as small firm nodules. These tumours have a yellow, tan, or gray-brown appearance. The yellow colour is a result of cholesterol and lipid accumulation within the tumour. Tumours can have a polypoid appearance and occasionally become ulcerated. The tumours can expand and infiltrate locally. Metastases to the mesenteric lymph node and liver, ovaries, peritoneum, and spleen can occur.

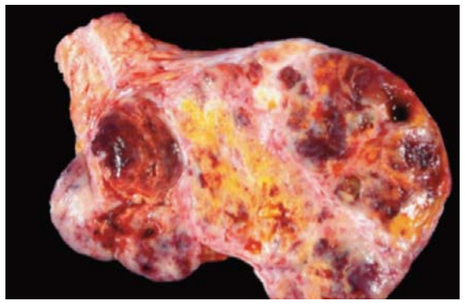


Fig.2: Gross appearance of Pancreatic NET [104]

Classification of NETs

1. Classification by site of origin: Most NETs are characterized as arising in the GI tract (stomach, appendix, duodenum, and small intestine), the bronchopulmonary system (lungs and thymus), the pancreas, and the colon and rectum

2. Functional vs. non functional tumours. Pancreatic neuroendocrine tumours can be either functional or non-functional. Functional pancreatic neuroendocrine tumours can secrete biologically active peptides like insulin, gastrin, glucagon, somatostatin, vasoactive intestinal polypeptide (VIP), whereas non-functional tumors also express and secrete peptides like neurotensin or chromogranin A,