Biomarkers and Applications

Bajaj A. Biomark Applic 05:144.

www.doi.org/10.29011/2576-9588.100044

www.gavinpublishers.com

OPEN ACCESS

GAVIN PUBLISHERS

Editorial

Gyre and Hoop-Neuroendocrine Tumour Small Intestine

Anubha Bajaj*

Independent Researcher, Histopathologist, New Delhi, India

***Corresponding author:** Anubha Bajaj, Independent Researcher, Histopathologist, New Delhi, India

Citation: Bajaj A (2022) Gyre and Hoop-Neuroendocrine Tumour Small Intestine. Biomark Applic 05:144. DOI: 10.29011/2576-9588.100044

Received Date: 15 September, 2022; **Accepted Date:** 20 September, 2022; **Published Date:** 26 September, 2022

Editorial

Neuroendocrine tumour is a well-differentiated epithelial neoplasm demonstrating neuroendocrine differentiation, wherein majority of neoplasms are nonfunctioning. Although neuroendocrine tumours of small intestine and ampulla are exceptional, tumefaction is confined to duodenum, jejunum or ileum.

Additionally designated as intestinal neuroendocrine tumour, carcinoid tumour or well differentiated neuroendocrine tumour, neoplasm exhibits distinctive grades from grade I to grade III, contingent to proportionate mitotic activity or Ki67 proliferative index [1,2]. Functional or hormone- secreting neuroendocrine tumours are infrequent and comprise of subtypes as gastrinoma-not otherwise specified, somatostinoma-not otherwise specified or enterochromaffin cell carcinoid may be discerned [1,2]. Majority (> 95%) of duodenal neuroendocrine tumours are situated within first part or second part of duodenum. Neoplasms emerging within second part of duodenum are predominantly confined to ampullary region [1,2].

Somatostatin secreting neuroendocrine tumour is discerned within the ampulla. Gastrin secreting neuroendocrine tumour is confined to duodenum. Majority of jejunoileal neuroendocrine tumours are situated within distal ileum. Only a few neoplasms arise from jejunum. Serotonin expressing enterochromaffin cell neuroendocrine tumour emerges within Meckel diverticulum.

Neuroendocrine tumour exhibits a female preponderance with female to male proportion of 2.5:1 [1,2]. Majority of neuroendocrine tumours emerging within small intestine or ampulla of Vater may be detected upon endoscopy [1,2]. Upon confirmatory histological assessment, monotonous tumour cells configure nests, trabeculae or tubuloglandular articulations. Neoplastic cells are imbued with finely stippled nuclear chromatin [1,2]. Of obscure aetiology and pathogenesis, chromosomal alterations within sporadic, duodenal or ampullary neuroendocrine tumour remain undefined. Small intestinal neuroendocrine tumour exhibits distinctive genomic concurrence [1,2].

Majority (~90%) of jejunoileal neuroendocrine neoplasms depict deletion of chromosome 18. Metastatic neoplasms or lesions of advanced grade display genomic gains of chromosome 14. Ileal neoplasms delineate chromosomal mutations within CDKN1B gene. Majority (>50%) of ileal neoplasms enunciate a CpG island methylator phenotype [1,2]. Epigenetic alterations are frequent and epigenetic dysregulation is significant [1,2].

Neuroendocrine tumour exhibits distinctive molecular subgroups with potential prognostic outcomes denominated as

- Superior prognosis is encountered with small intestinal neuroendocrine tumour demonstrating loss of chromosome 18, genomic mutation within CDKN1B or absence of CpG island methylator phenotype.
- Intermediate prognosis is observed with small intestinal neuroendocrine tumour with lack of whole arm copy number variation and concurrence with CpG island methylator phenotype.
- Inferior prognosis is delineated with small intestinal neuroendocrine tumour demonstrating multiple whole arm copy number variations [1,2].

Few neoplasms may occur as a component of hereditary cancer predisposition syndromes. Individuals with multiple endocrine neoplasia (MEN) type I enunciate multiple duodenal gastrinomas. Few ampullary somatostatinomas may concur with neurofibromatosis type I (NF1) [1,2]. Non-functioning neuroendocrine neoplasms may manifest symptoms of mass effect as small bowel obstruction or hyper-bilirubinaemia [1,2].

Functioning neuroendocrine tumour may engender symptoms pertaining to secreted hormone denominated as

- Gastrinoma induces Zollinger-Ellison syndrome comprised of hyper-gastrinemia, gastric hypersecretion, refractory peptic ulcer disease and diarrhoea. Tumours associated with Zollinger-Ellison syndrome demonstrate an inferior prognosis and enhanced proportion of distant metastasis.
- Somatostatinoma is exceptionally associated with somatostatinoma syndrome constituted of diabetes mellitus, diarrhoea, steatorrhoea, hypohydrea or achlorhydia, anaemia and cholelithiasis.
- Carcinoid syndrome is infrequent and exhibits diarrhoea, bronchospasm, flushing or tricuspid valve fibrosis. Tumefaction may demonstrate distant metastasis into hepatic parenchyma [1,2].

Upon gross examination, duodenal and periampullary neuroendocrine tumour manifests as miniature, polypoid, submucosal neoplasm with magnitude < 2 centimetres. Exceptionally, tumefaction can be enlarged and infiltrative [1,2].

Jejunoileal neuroendocrine tumour is multifocal and manifests deep seated infiltration of muscularis propria or sub-serosa [1,2]. Upon microscopy, neuroendocrine tumour is composed of uniform tumour cells imbued with spherical to elliptical nuclei and 'salt and pepper' nuclear chromatin [1,2].

Neuroendocrine tumour exhibits diverse architectural configurations as

- Gastrin expressing 'gastrin' cell neuroendocrine tumour represents with trabecular pattern of tumour evolution
- Somatostatin expressing 'delta' cell neuroendocrine tumour delineates tubuloglandular articulations. Psammoma bodies may be discerned.
- Serotonin expressing enterochromaffin cell neuroendocrine tumour enunciates nests of tumour cells with peripheral palisading. Pseudo-glandular component is minimal.

Ultrastructural examination exhibits well formed, membrane bound, dense core secretory granules incorporated within neoplastic cells [1,2].

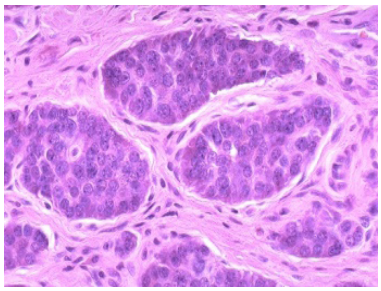

Figure 1: Neuroendocrine tumour depicting nests of small, round cells with uniform nuclei and surrounding fibrous tissue stroma [5].

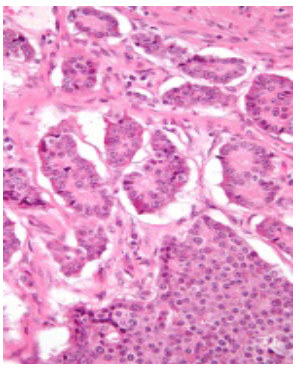

Figure 2: Neuroendocrine tumour delineating clusters of small round cells delineating uniform nuclei and scanty cytoplasm surrounded by a significantly vascular stroma [6].

TNM staging of neuroendocrine tumour of small intestine designated as

Primary tumour

- TX: Primary tumour cannot be assessed.
- T0: No evidence of primary tumour
- T1: Tumour ≤1 centimetre magnitude and invades lamina propria or submucosa.
- T2:Tumour > 1 centimetre magnitude, extends beyond lamina propria or submucosa or invades muscularis propria.
- T3: Tumour extends through muscularis propria into sub-serosal tissue and lacks penetration of subjacent serosa.

- T4: Tumefaction infiltrates visceral peritoneum or serosa and adjacent structures or organs [2,3].

Regional lymph nodes

- NX: regional lymph nodes cannot be assessed.
- N0: Regional lymph node metastasis absent.
- N1: Regional lymph node metastasis in < 12 lymph nodes.
- N2: Enlarged mesenteric tumefaction > 2 centimeter magnitude or extensive deposits within regional lymph nodes ≥ 12, especially upon nodes encasing superior mesenteric vessels.
- Regional lymph nodes are comprised of superior mesenteric and mesenteric nodes. Lesions confined to terminal ileum require evaluation of posterior caecal lymph nodes [2,3].

Distant Metastasis

- M0: Distant metastasis absent.
- M1: Distant metastasis present.
- M1a: Distant metastasis confined to hepatic parenchyma.
- M1b: Distant metastasis minimally into singular extrahepatic site as pulmonary parenchyma, ovary, non-regional lymph nodes, peritoneum or bone.
- M1c: Combined hepatic and extrahepatic metastasis [2,3].

Histological grading of neuroendocrine tumour of small intestine as per World Health Organization denominated as

- Grade 1 or low grade, well differentiated tumefaction: mitotic rate < 2 per 10 high power fields or Ki67 proliferative index at < 3%.
- Grade 2 or intermediate grade tumefaction: mitotic rate between 2 to 20 per 10 high power fields or Ki67 proliferative index between 3% to 20%.
- Grade 3 or high grade tumefaction: mitotic rate > 20 per 10 high power fields or Ki67 proliferative index > 20% [2,3].

Neuroendocrine tumour is immune reactive to cytokeratin AE1/AE3, CAM5.2, chromogranin A or synaptophysin [3,4]. Serotonin producing enterochromaffin cell neuroendocrine tumour is immune reactive to CDX2 or SSTR2A [3,4]. Neuroendocrine tumour is immune non reactive to mucin, CK7, CK20 or TTF1 [3,4]. Neuroendocrine tumour requires segregation from neoplasms such as neuroendocrine carcinoma, mixed neuroendocrine -non neuroendocrine neoplasm, adenocarcinoma, gangliocytic paraganglioma, Crohn's disease, ulcerative colitis, ileus, small intestinal diverticulosis, coeliac disease, intestinal motility disorders or irritable bowel syndrome [3,4]. Well differentiated neuroendocrine tumour demonstrates elevated serum chromogranin A delineating increasing levels upon enhancing tumour burden. Although minimally specific, chromogranin A may be employed to assess disease progression, response to therapy or tumour reoccurrence within definitive, advanced neuroendocrine neoplasms [3,4].

Evaluation of 24 hour urinary excretion of 5-HIAA is an optimal, preliminary investigative modality for appropriately discerning carcinoid syndrome. 5-HIAA represents as an end product of serotonin metabolism and is beneficially employed for discerning neuroendocrine tumours of jejunum, ileum, appendix or ascending colon, neoplasms which secrete enhanced quantities of serotonin [3,4]. Computerized tomography (CT) or magnetic resonance imaging (MRI) is mandatory for radiological staging of neuroendocrine tumour. Somatostatin receptor scintigraphy is optimally adopted to detect and scrutinize small intestinal neuroendocrine tumour [3,4]. Positron emission tomography (PET) with concomitant computerized tomography and assessment of 68Ga-DOTA somatostatin analogs (SSAs) is a contemporary technique for categorizing the neoplasm and discerning distant metastases [3,4].

Comprehensive surgical extermination of neoplasm along with regional lymph node dissection is an optimal, recommended strategy for treating neuroendocrine tumour [3,4].Small intestine neuroendocrine tumour frequently exhibits metastatic disease with occurrence of metastasis into hepatic parenchyma or localized, regional lymph nodes. Neoplasm is minimally proliferative and associated with extended survival [3,4].Ampullary tumours < 2 centimeter magnitude or neoplasms confined to ampulla exhibit a favorable prognosis [3,4]. Regional lymph node metastasis is frequently discerned although proportionate overall or disease free survival remains unaltered. Metastasis to hepatic parenchyma is commonly encountered. Factors such as regional lymph node metastasis, mesenteric tumour deposits, lympho-vascular invasion or perineural invasion enhance possible localized tumour reoccurrence [3,4].Localized disease enunciates a five year overall survival at ~ 100%. Neoplasms with distant metastasis exemplify a five year overall survival at ~ 60%. Delayed tumour reoccurrence occurs in ~50% neoplasms [3,4].

References

1. Aassouani F, Ettabyaoui A, Hinaje K, Bahri MO, El Bouardi N, et al. (2022)Small bowel carcinoid tumor causing intestinal ischemia: A case report with review of the literature. Radiol Case Rep 17: 3523-3526.
2. Khan MS, Pritchard MD (2022) Neuroendocrine tumours: what gastroenterologists need to know. Frontline Gastroenterol 13: 50-56.
3. Kartal I (2022) Childhood neuroendocrine tumours of the digestive system: A single centre experience. Medicine (Baltimore) 101 : e28795.
4. Klimstra DS, Yang Z, Goldberg RM (2019) Pathology, classification, and grading of neuroendocrine neoplasms arising in the digestive system. Uptodate Última actualització.
5. Image 1 Courtesy: Gastrointestinal pathology.
6. Image 2 Courtesy: Wikipedia.com