CASE REPORT

The concurrent occurrence of neuroendocrine tumour and gastrointestinal stromal tumours

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Abstract

Gastrointestinal neuroendocrine tumours are hypothesised to arise from cells in the gastrointestinal tract's diffuse neuroendocrine system. The occurrence of Gastrointestinal Stromal Tumours (GIST) along with other primary gastrointestinal malignancies is not common. More than 60% of the GIST occurs in stomach and 37% in jejunum. GIST can coexist with single well-differentiated, occasional neuroendocrine tumours of small size. In terms of preventing metastatic illness, an adequate first curative approach combined with meticulous follow-up appears to have a substantial effect. Although a synchronous incidence of gastrointestinal tumours without any associated disorders is uncommon, any gastrointestinal tumour should be thoroughly investigated to rule it out. We report the case of coexistence of a high risk of neuroendocrine tumour along with gastrointestinal tumour in a 30-year-old male patient. Postoperative chemotherapy with imatinib 40 mg once a day for 6 months was given and followed-up. Patient had no recurrence for 6 months.

Keywords: Neuroendocrine Tumour, Gastrointestinal Stromal Tumour, Synchronous Multicentric Origin

Introduction

Gastrointestinal Neuroendocrine Tumours (NETs) are thought to derive from cells of the diffuse neuroendocrine system of the gastrointestinal tract [1]. The larger part of the carcinoid tumours occurs in adults in small intestine (29%) and many of them are present in ileum (20%), followed later by jejunum (3%) and duodenum (3%) [2]. Mazur and Clark first coined the term Gastrointestinal Stromal Tumours (GIST) in 1983, but in 1998 Japanese researchers found that the KIT protein and its genetic mutations were possibly present, that separates GIST from other tumours of the same type such as leiomyoblastoma, leiomyoma, and leiomyosarcoma [3]. Gastrointestinal tract malignancies are among the top ten leading sites for malignancies worldwide [4]. GIST can develop everywhere in the body, however the majority (50–70%) are found in the stomach (80% in gastric body, 15% in antrum, and 15% in cardia) and small intestine (30% in jejunum or ileum, 5% in duodenum) with colon, rectum and appendix, jointly accounting for 5% and oesophagus accounting for 2%–3%. They are seldom found at extra-GI sites like mesentery, omentum, retro-peritoneum and pancreas [5]. The expression of KIT protein in GIST has been a major focus of molecular biologic study since its discovery [3]. The estimated occurrence of GIST is approxi-mately 10-20 per million people, per year. The possibility of GIST turning malignant is 20 to 30%.Nearly 90% of the individuals with GIST are over the age of 40. Outside the gastrointestinal tract, the tumours are known as extra-GIST. Multicentric GIST are rare in elderly age group and

if found are dubbed as metastatic, though synchronously arising tumours have also been reported [6]. We analysed the pathological findings of neuroendocrine tumour synchronous with gastrointestinal tumour, and we assess the malignant potentiality of these synchronous tumours.

Case Report

A 30-year-old male patient presented to surgery outpatient department with complaints of lump in abdomen for 10 months, dyspepsia, dull aching epigastric pain, vomiting, and with weight loss for 6 months. There was no history of fever or rectum bleeding. Patient was a known hypertensive under treatment and had no other illness. The results of general physical examination were within normal limits. Clinically, abdominal examination showed rigidity/guarding, bowel sounds were present with irregular ill-defined hard lump palpable in lower abdominal quadrant and pelvic region. The results of cardiovascular, respiratory and central nervous system examination were within normal limits. There were no significant findings in laboratory investigations.

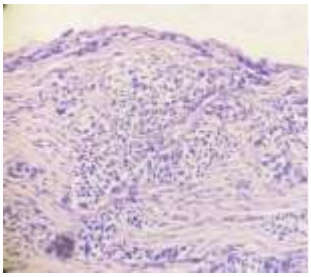
Computerized tomography scan of abdomen and pelvis revealed large well defined, lobulated heterogeneously enhancing extraluminal exophytic soft tissue density lesion in the abdominopelvic region with possible origin from small bowel (ileal loop) with extension, mass effect and abdominal lymphadenopathy, mesenteric and peritoneal soft tissue deposits, hepatosplenomegaly with multiple variable sized heterogeneously enhancing hypodense lesions. Intraoperative findings showed large whitish, vascular growth seen from recto-sigmoid colon. Multiple irregular deposits were seen in omentum, mesentery, liver and spleen. The bowel could not be resected, only omentum was resected. The omentectomy specimen was sent for histopathology.

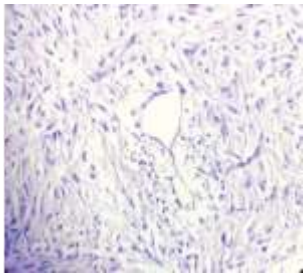
We present a rare case in which GIST was arising from loop of ileum, but exploratory laparotomy showed involvement of larger part of intestine with infiltration across omentum. Grossly, we received omentectomy specimen measuring 28 cm in length along with one detached nodular tissue. The specimen on one end contained whitish, multiple, nodules with the largest measuring 3.5×3×2 cm. Nodules were bony hard in consistency. On cut section, whitish homogenous areas were identified. Another nodule was measuring 2.5×2×1.5 cm. On another end, cystic tissue were identified showing vessels on external surface. On cut section, whitish solid cystic areas were seen measuring 2.5×2×1 cm. Along the omental tract, whitish nodules of variable sizes were identified (Fig. 1).

Figure 1: Gross appearance of omentectomy specimen with nodular and cystic areas

Microscopically, multiple sections showed that the tumour mass was composed of two areas showing different pattern of cell populations with predominance of spindle cells which were arranged in whorl-like pattern showing faintly eosinophilic

cytoplasm and elongated nuclei with inconspicuous nucleoli. At some places, round epithelioid cell predominance with vacuolated to clear cytoplasm and well-defined cell membranes arranged in a nest like pattern showing moderate nuclear pleomorphism were seen (Fig. 2). Another area of neuroendocrine tumour mass showing monomorphic population with round to oval nuclei with salt and pepper chromatin and moderate eosinophilic granular cytoplasm were seen. Tumour cells were arranged in nests with trabecular pattern showing nuclear pleomorphism (Fig. 3).





Figures 2 and 3: Microscopy H and E staining 40× magnification showing different pattern of cell populations with predominance of spindle cells which were arranged in whorl like pattern showing faintly eosinophilic cytoplasm and elongated nuclei with inconspicuous nucleoli. Neuroendocrine tumour mass showing monomorphic population with regular cells with round to oval nuclei with salt and pepper chromatin and moderate eosinophilic granular cytoplasm

On immunohistochemistry tumour cells demonstrated strong cytoplasmic staining for CD117 (Fig. 4).

Figure 4: Photomicrograph with immunohistochemistry-stained section (×10 view) from omental mass shows strong cytoplasmic staining signifying CD117 positive

Final histopathological diagnosis was suggestive of high risk of neuroendocrine tumour along with gastrointestinal tumour. Postoperative chemotherapy with imatinib 40 mg once a day for 6 months was given and advised regular follow up. Patient had no recurrence for 6 months. Postoperatively patient was stable.

Discussion

Gastrointestinal neuroendocrine tumours are hypothesised to develop from the cells in the gastrointestinal tract's diffuse neuroendocrine system. Most endocrine tumours in the stomach are present in the fundus or corpus, forming altogether a collection of non-functioning, enterochromaffin-like cell, well differentiated NETs (Carcinoids) [1]. The commonest mesenchymal tumours of gastrointestinal tract are GIST which mainly involve the stomach (50-62%), small intestine (20-30%), colon (11%) and the rectum (7%). There origin is from interstitial, pacemaker Cajal cells [1]. There are four forms of gastric NETs:

a) Type I is associated with Autoimmune Chronic Atrophic Gastritis (A-CAG);

b) Type II is associated with Multiple Endocrine Neoplasia type 1 (MEN-1) or the Zollinger-Ellison Syndrome (ZES);
c) Type III is sporadic and is unrelated to hypergastrinemia or A-CAG;
d) Type IV is representing a heterogeneous group of tumours that show affirmation of multidirectional differentiation, such as a mixture of neuroendocrine tumours and adenocarcinoma [1].

The occurrence of GIST and other primary gastrointestinal cancers at the same time is not common. GIST of the small intestine has a larger percentage of clinically malignant cases than GIST of the stomach [2]. The percentage of GIST in patients with additional neoplasms diagnosed ranges from 3 percent to 33 percent as per the report. It's unclear whether the presence of a GIST alongside other associated diseases or tumours is coincidental or the result of connected pathophysiological processes. Jejunum is the rarest site for GIST. The most prevalent symptoms of GIST are bleeding from mucosal ulceration and abdominal discomfort.

Janardhan *et al*. [2] reported a patient of GIST of jejunum along with neuroendocrine tumour of duodenum in a 73-year-old male patient and concluded that to rule out any gastrointestinal tumours, a complete workup should be done, although a synchronous occurrence of gastrointestinal tumors without any coexisting syndromes is rare.

Kaur *et al*. [7] reported a case of gastric GIST along with neoplasms of GI tract in a 62-year-old male. Synchronous GIST and duodenal neuroendocrine tumours are highly uncommon. In other literatures, only three patients of simultaneous gastric carcinoid and GIST have been recorded. GI carcinomas are the commonest secondary neoplasms. Other coexistent tumours include lymphoma/leukaemia, lung carcinoma, breast carcinoma, prostate carcinoma, kidney carcinoma, soft tissue carcinoma, seminomas, carcinoma of female genital tract, malignant melanoma and bone sarcomas [7]. GIST are not homogenous group of neoplasms; however, immunohistochemically some show differentiation towards nerve, histiocyte, smooth muscle, and few are undifferentiated. It also shows strong site-dependent genetic heterogeneity [2]. CD117 (c-kit protein) immunopositivity is a distinguishing immunohistochemical characteristic of these tumours, with tumour mitotic activity and size being the most important parameters in predicting clinical behaviour [1]. A mutation in the c-kit or platelet-derived growth factor receptor gene is seen in about 95% of GIST. Imatinib treatment of c-kit positive GIST cells resulted in the loss of growth factor support, resulting in tumour cell death [2].

If positive margin remains after initial resection or if there are poor prognostic indicators, surgical treatment should be considered. Although antrectomy has been utilised in the past as a surgical treatment option, single lesions are now treated with laparoscopic wedge resection, with more extensive surgery being explored in cases of more than 6 lesions or recurrence. However, whether surgery is the best therapy choice for NETs with poor prognostic characteristics is still debated [8].

In our case, imatinib 40 mg once a day for 6 months was given as postoperative chemotherapy and monitored. For six months, the patient had no recurrence. A coexisting tumour may not always be detectable preoperatively. Surgeons should be aware of the presence of a concomitant tumour

before or during surgery and be prepared to alter the surgical strategy as needed [7].

Conclusion

Synchronous GIST of the jejunum and duodenal neuroendocrine tumours are extremely uncommon. Both histopathologists and surgeons must be aware of the prevalence and pattern of GIST along with other neoplasms. In this study the related tumours may be both high-grade-like advanced colon carcinoma and low grade-like well differentiated neuroendocrine tumour. For a precise diagnosis, a thorough examination of the patient and appropriate investigations are required. This ensures that the patient receives therapy at an early stage, resulting in a better outcome and prognosis.

References

1. Samaras VD, Foukas PG, Triantafyllou K, Leontara V, Tsapralis D, Tsompanidi EM, *et al*. Synchronous well differentiated neuroendocrine tumour and gastrointestinal stromal tumour of the stomach: a case report. *BMC Gastroenterol* 2011; 11:27.
2. Janardhan K, Kumar VS, Kumar PL. Synchronous GIST of jejunum and neuroendocrine tumor of duodenum: A rare case report. *Arch Int Surg* 2014;4(1):57-59.
3. Tan CB, Zhi W, Shahzad G, Mustacchia P. Gastrointestinal stromal tumors: a review of case reports, diagnosis, treatment, and future directions. *ISRN Gastroenterol* 2012; 2012:595968.
4. Ekta, Bansal N, Roychoudhury AK, Shaffy. A histopathological spectrum of gastrointestinal tract lesions in a tertiary care centre in South Western part of India: An epidemiological study. *J Krishna Inst Med Sci* 2018;7(3):43-47.
5. Ahmed M. Recent advances in the management of gastrointestinal stromal tumor. *World J Clin Cases* 2020; 8(15):3142-3155.
6. Shukla S, Acharya S, Rajput DP, Vagha S. Synchronous gastrointestinal stromal tumors: a rare case report. *Indian J Clin Pract* 2013;24(2): 152-154.
7. Kaur R, Bhalla S, Nundy S, Jain S. Synchronous gastric gastrointestinal stromal tumor (GIST) and other primary neoplasms of gastrointestinal tract: report of two cases. *Ann Gastroenterol* 2013;26(4):356-359.
8. Lee J, Oh SJ. Gastric Neuroendocrine tumor mimicking gastrointestinal stromal tumor: A case report. *Case Rep Oncol* 2021; 14(3):1271-1276.

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