A RARE CASE REPORT OF MIXED GOBLET CELL CARCINOID - ADENOCARCINOMA

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Abstract: The concurrence of mixed carcinoid-adenocarcinoma in the gastrointestinal tract is a well known but an unusual phenomenon that has been reported in the esophagus, stomach, small intestine, appendix, liver, colon, rectum, and anal canal. It is an aggressive tumour metastasing to lymph nodes, peritoneal surfaces, omentum and solid organs like liver, lung and bone. Morphological features and immunohistochemistry distinguish the two components of this composite tumour. The neoplasm appears to be derived from a multipotential stem cell capable of bidirectional differentiation and has a worse prognosis than ordinary carcinoma.

Keyword: Goblet cell carcinoid, poorly differentiated adenocarcinoma, composite tumour, chromogranin, cytokeratin.

INTRODUCTION: Mixed adenoendocrine patterns characterise rare tumours of gastrointestinal tract. The first description dates back as far as 1924. A greater number of cases are reported in the appendix, which is also the most common location of carcinoid tumours, but they also develop in the small intestine and colon. It usually occurs in adults, with a mean age of 50 years. There is a female preponderance with a male to female ratio of about 1:2. Compared to typical goblet cell carcinoid, goblet cell carcinoid—adenocarcinoma is a more aggressive neoplasm. They generally have transmural extension and have propensity for transcocelomic spread. They may also metastasize to lymph nodes and liver.

CASE REPORT 68 year old man presented with history of abdominal pain and constipation of two months duration. On examination, a palpable mass was identified in the right iliac fossa. His laboratory investigations revealed anemia. Ultrasound abdomen showed multiple dilated bowel loops. There was narrowing at the ileocecal junction and wall thickening in the cecum and appendix. Colonoscopy revealed ulceration in the ileocecal region; ileum could not be entered. The patient underwent right hemicolecetomy. The intraoperative findings include mass of size 6cm, which was hard in consistency occupying terminal ileum, cecum, ascending colon. Liver was free; no omental deposits were noted.

GROSS FINDINGS: Gross pathological examination revealed an ulceroinfiltrative growth in the ileocecal region partly extending into the cecum measuring 4.5 x 4cm. The cut section of the tumour was grey white, firm with a depth of 2cm and involved the serosa grossly. Mucosa adjacent to the tumour was edematous. Appendix could not be made out grossly. Cut section of the attached pericolic fat revealed eight lymph nodes, ranging in size from 0.2 to 1.5cm.

MICROSCOPIC FINDINGS: Multiple sections studied from growth terminal ileum and ileocecal junction showed features of mixed adenocarcinoma-carcinoid. Microscopically, admixture of two tumour components were noted. The Goblet cell carcinoid component was characterised by well formed cohesive oval or round goblet cell clusters. The tumour cells exhibited minimal cytologic atypia. As the tumour cells infiltrated through the musculature, the clusters exhibited a compressed linear configuration oriented along the axis of muscle fibres (fig-1). The glandular component showed malignant epithelial cells of poorly differentiated type arranged in confluent sheets. The tumour cells showed significant cytologic atypia (fig-2). There was transition between the two tumour components (fig-3). The malignant cells of both the components were seen invading all the layers of wall including full thickness of muscle coat, extending into serosal fibrofatty tissue. There was focal desmoplastic response in the stroma. Neural and vascular invasion were also noted. Multiple sections studied from eight lymph nodes showed metastatic tumour deposits in five nodes (5/8). (fig-4)
IMMUNOHISTOCHEMISTRY: Immunoreactivity with chromogranin - a neuroendocrine marker, showed focal cytoplasmic granular positivity in carcinoid component (fig-5). The adenocarcinoma component showed diffuse positivity with cytokeratin (fig-6).

DISCUSSION: Mixed Goblet cell carcinoid-adenocarcinomas have a mixed phenotype exhibiting neuroendocrine and glandular differentiation features. Microscopic examination showed the tumour was a poorly differentiated adenocarcinoma with a distinct carcinoid component. According to WHO, the arbitrary limit of at least 30% of either component should be identified for this definition. Identification of scattered neuroendocrine cells by immunohistochemistry in adenocarcinoma does not qualify for this definition. The classification scheme proposed by Tang and his colleagues, divided the Goblet cell carcinoid tumors at the primary site into 3 groups based on the morphology of the tumor. This classification shows distinct morphologic and prognostic characteristics.

Group A – Typical Goblet cell carcinoid
Group B – Adenocarcinoma ex goblet cell carcinoid, signet ring type
Group C – Adenocarcinoma ex goblet cell carcinoid, poorly differentiated carcinoma type

The present case met the criteria of WHO and comes under Group C classification scheme proposed by Tang et al.
Histogenesis: This distinctive neoplasm is of considerable interest histogenetically. The presence of both cell lines in the same neoplasm supports the more recent review that both mucinous and endocrine cells arise from common endodermal crypt base stem cells. The stem cells have the potential to differentiate along multiple cell lines depending upon the expression of relevant genes governing specific cellular characteristics.

The aggressiveness of the tumour is recognised by the following:

1. presence of lymphovascular invasion
2. 2.00 or more mitoses /10 hpf
3. a carcinomatous growth pattern in >50% of the tumour (i.e., presence of fused or cribiform glands, single file pattern, densely infiltrating signet ring cells and solid sheets of malignant epithelial cells)
4. spread beyond the primary organ

The present case showed neural and vascular invasion with metastatic tumour deposits in lymphnodes. The tumour deposits in the lymphnodes demonstrated both the mucinous and endocrine elements confirming the malignant nature of each component. The neoplastic cells showed focal positivity for endocrine component with chromogranin, as Goblet cell carcinoids usually show focal positivity of 5 % to 25% only. The neoplastic glandular component showed diffuse positivity with cytokeratin. The usual treatment protocol of surgical resection is combined with debulking and chemotherapy if the disease is advanced. The 5 year survival rate for mixed goblet cell carcinoid – adenocarcinoma (poorly differentiated type) is 0% as compared to 100% for typical goblet cell carcinoid.

CONCLUSION: Gastrointestinal tumours which contain both mucinous and endocrine elements are uncommon but have been reported with increasing frequency recently. The composite nature of the tumour is confirmed by the morphological features as well as immunohistochemical markers specific for the two components. The neoplasm appears to represent a distinct clinicopathological entity associated with poor prognosis.

BIBLIOGRAPHY: