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Double Trouble: Rare Case of Metachronous Gastric Carcinoma in a Resected Case of Periampullary Carcinoma

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Abstract: ***Dual malignancies in an individual presenting at different times is of rare occurrence and management of such a case brings both, great amount of interest and challenge to the consulting surgeon. Survival of cancer patients is on improving trend globally and because of early detection techniques more and more cancers are brought to attention early to the surgeon. This is a case of 42 - year – old gentleman status post Whipple's Procedure done in view of periampullary carcinoma diagnosed in 2019, who presented to our surgery emergency with complaints of pain in central upper abdomen and multiple episodes of non - bilious vomiting (occurring 2 - 3 hours after meals) for last 2 months. On investigating further patient was diagnosed as having Grade 2 Adenocarcinoma of stomach. Feeding Jejunostomy was made for this patient and was planned for adjuvant chemotherapy. Our understanding of DNA and the mechanisms behind development of cancer is minuscule. The modalities that exist for management of malignancies can be both a boon as well as a bane for the patient as we saw in this case. Development of two primary malignancies in a patient who underwent surgical resection for first malignancy followed by chemoradiation is a rare incidence.***

Keywords: Metachronous dual malignancy, periampullary carcinoma, adenocarcinoma of stomach

1. Introduction

Mark Getty once said and I quote "Bad luck never lost a race. " Surviving one battle was just not enough for this patient. Maybe it was "The Fault in his stars" that he landed up in another misery whilst he just got recovered from his old battle scars.

Multiple primary cancers were first noticed by Billroth in 1869[1] and the likely contributing factors for development of same can be environmental, radiotherapy related, hormonal therapy related, or genetic predisposition.

It is very difficult to think how much we know about biological events on both macroscopic and microscopic level yet it is just the tip of the iceberg. Understanding the mechanism behind DNA mutations, development of faulty proteins and how they ultimately affect the phenotype, we have come a long way but nature has never failed to challenge our intellect.

Although there have been multiple explanations behind development of metachronous malignancies in a single patient but the exact mechanism is still unknown. That told, we hereby would like to acknowledge a rare case of an adult male who developed gastric adenocarcinoma after 3 years of diagnosis and treatment of periampullary adenocarcinoma.

2. Case Report

We present the case of a 42 - year - old chronic alcoholic male who complained of generalised itching and weight loss for 1 month back in September 2019 with no history of any fever, hematemesis, yellowish discoloration of eyes, passage of clay coloured stools or bleeding per rectum. On examination neither a lump was palpable in the abdomen nor any lymph node. Upon evaluating further his serum bilirubin was within normal limits but serum ALP was found to be raised (>400 IU/mL). Radiological investigations were performed and they showeda heterogeneously enhancing mass 30x11x28 mm in periampullary region causing abrupt cut off of common bile duct (diameter 17mm) and main pancreatic duct (diameter 12mm). The lesion was seen involving medial wall of duodenum with infiltration of adjacent pancreatic head. Hepatoduodenal and pancreatic oduodenal lymph nodes were found be enlarged with maximum diameter 11mm. An upper gastrointestinal endoscopy was performed which showed mass at ampullary region and biopsy was taken which showed high grade glandular dysplasia.

Patient was planned for surgery and Diagnostic Laparoscopy was performed followed by Whipple's Surgery and feeding jejunostomy. Biopsy of the resected surgical specimen showed grade 2 moderately differentiated adenocarcinoma in the periampullary region with negative margins and 2 involved lymph nodes were seen out of 23 resected lymph nodes with no lympho - vascular or perineural invasion. Post operatively patient was given radiotherapy for 1 month followed by chemotherapy with Gemcitabine and Cisplatin and showed good recovery.

Fast forward to April 2023 after 2019 this patient presented to us with complaints of pain central upper abdomen for last 2 months which was mild, dull aching, non - progressive and

was associated with non - bilious vomiting after 2 - 3 hours of intake of food. He lost around 10kgs of weight (documented) in these two months. He experienced early satiety, generalised weakness and burning sensation in chest with bloating. Again, there was no history of hematemesis, melena, or bleeding per rectum, nor that of yellowish discoloration of eyes, generalised itching, or passage of clay - coloured stools. On examination patient was observed to have a thin built with stable vitals and no cervical lymphadenopathy. On abdominal examination scar of previous surgery was visible on the abdomen with no palpable lump. Fluid resuscitation was done followed by insertion of nasogastric tube.

An abdominal CECT was obtained which showed circumferential heterogeneously enhancing thickening in body and antrum of stomach with 2.5 cm thickness extending over length of 8 - 9 cms causing significant luminal narrowing and proximal gastric dilatation along with large exophytic growth over greater curvature. Whole body PET CT scan was also done which showed metabolically active asymmetric circumferential wall thickening involving body and antrum of stomach with metabolically active mediastinal, left internal mammary and paracardiac lymph nodes. An upper gastrointestinal endoscopy was done which showed ulcerated friable structuring lesion and a biopsy was taken which showed Grade 2 moderately differentiated adenocarcinoma of stomach.

A Witzel feeding jejunostomy was made for this patient and then planned for further chemotherapy and radiotherapy.

3. Discussion

Metachronous malignancies are the ones which present more than 6 months apart and have a better prognosis than synchronous malignancies which occur within 6 months duration[2]. Individuals who suffer from malignancy exhibit a 14 - 20% higher risk of developing subsequent primary malignancies[3].

Periampullary carcinoma consists of four variants – carcinoma head of pancreas, duodenal carcinoma, ampullary variant and distal cholangiocarcinoma. In periampullary cancers recurrence occurs in 39 - 67% of patients with a mean delay of 13 months after resection[4]. The occurrence of new primary gastrointestinal cancer in a resected case of periampullary carcinoma is a rare entity and can easily be confused with locoregional recurrence.

In periampullary carcinomas margin resection status, lymph node involvement and grade of tumour differentiation affects the outcome. For periampullary carcinomas, resection of the tumour is the primary modality for treatment and for offering long term survival. Whipple's Procedure or Pancreaticoduodenectomy is the procedure of choice for these malignancies. Pylorus – preserving pancreaticoduodenectomy is preferred as it offers technical advantages, better quality of life and prevents the occurrence of post - gastrectomy syndromes. Whipple's procedure consists of en - block removal of the head of the pancreas, duodenum and regional lymph nodes with the distal part of the common bile duct[5].

Several studies have shown equivocal response regarding efficacy of adjuvant chemotherapy and radiotherapy following resection of periampullary carcinoma. Their result has been shown to be dependent on the histological subtype which can be – intestinal or pancreaticobiliary. The Intestinal - type originates from the intestinal epithelium overlying the ampulla, including duodenal carcinoma and some of the ampullary carcinomas. Whereas the Pancreaticobiliary - type originates from the epithelium of the distal common bile duct and the head of pancreatic duct, including pancreatic cancer, distal bile duct cancer, and some of the ampullary carcinomas. Hence the intestinal type responds better to 5 - Fluorouracil based regimen and pancreaticobiliary type to Gemcitabine based regimens[6]. Our patient received both radiotherapy (for 1 month) followed by Gemcitabine and Cisplatin based chemotherapy (for 3 months).

The early diagnosis and management of patients with various chemotherapeutic drugs and radiation has shown a predisposition to a second primary malignancy[7, 8]. Gastric adenocarcinoma is a radio - responsive tumor[9]and responds well to gemcitabine - cisplatin based chemotherapy[10] which our patient received. Despite of these two contradicting prepositions, the patient developed a second primary malignancy.

4. Conclusion

Dual malignancies can arise due to various factors including germline predisposition, exposure to carcinogens, environmental factors and the effect of previous cancer treatments. Common gene mutations associated with periampullary carcinomas include mutations of KRAS, BRAF, and HER2[10] and those of gastric adenocarcinoma include CDH1, BRCA2 and PALB2[12]. Having different genetic backgrounds, development of both periampullary carcinoma and gastric adenocarcinoma in the same patient becomes extremely rare even after receiving optimal doses of adjuvant chemoradiation.

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Declarations

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Conflict of interest: the authors report no conflict of any interests.

Ethical approval: As this is a case report with no mention of the patient's details anywhere in the report, hence ethical approval has not been sought.

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Figure 1: Showing findings of upper GI endoscopy performed in 2019

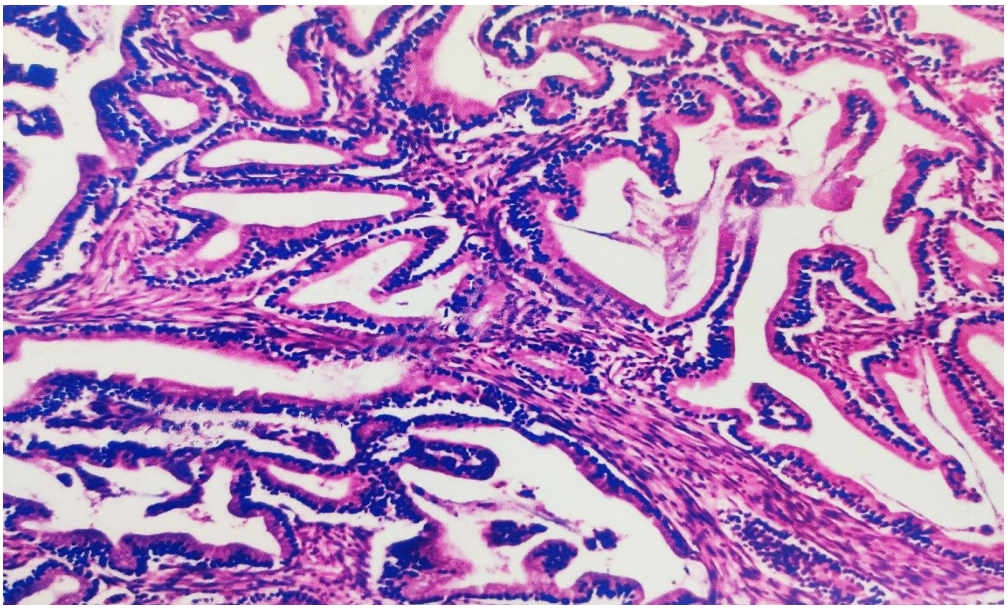

Figure 2: Showing microphotograph of periampullary adenocarcinoma from examined sections of resected specimen of Whipple's surgery

Figure 3: Sections from CECT Whole Abdomen showing growth in the wall of stomach

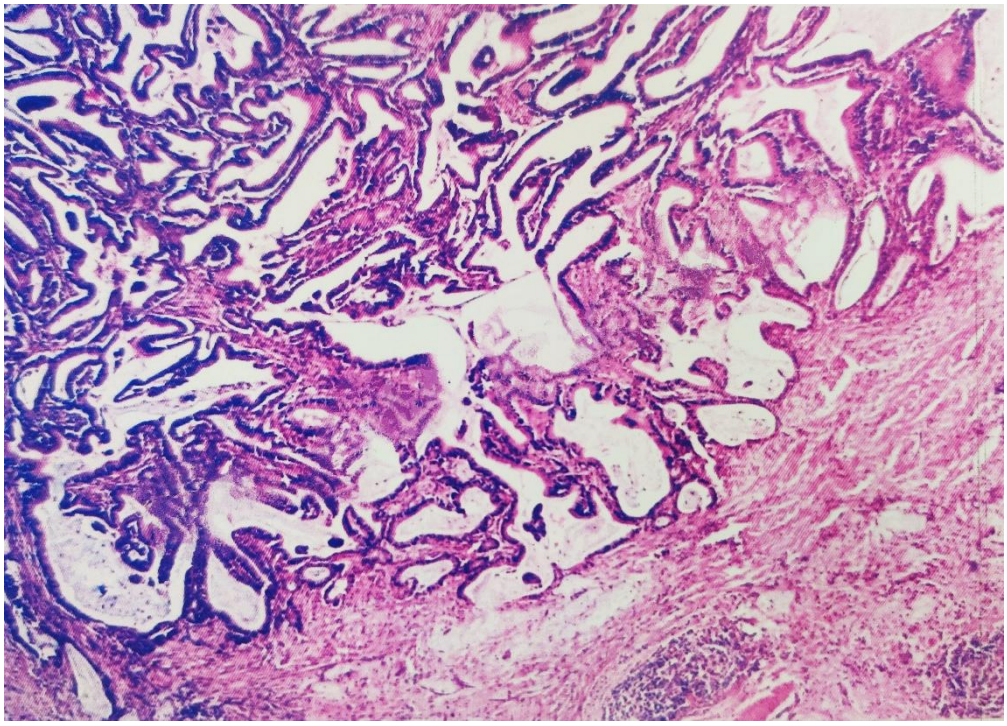

Figure 4: Shows microphotograph of biopsy specimen taken from upper GI endoscopy depicting adenocarcinoma of stomach