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Research Article

The first case of familial non-syndromic gastric neuroendocrine-adenocarcinoma in Iraq

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Abstract

Background: Gastric adenocarcinoma is the most important type of stomach cancers, and it is generally sporadic. However, about 10% of gastric adenocarcinoma occurs in familial pattern. The most important genetic causative factor in gastric adenocarcinoma is CDH1 germline mutations which cause the diffuse stomach cancer syndrome. Chen was probably the first to suggest the existence of neuroendocrine carcinoma of the stomach as a separate entity in 1988.

Patients and methods: The case of the first Iraqi patient with familial mixed gastric neuroendocrine-adenocarcinoma in Iraq is described.

Results: At the age of 46 years, a male patient who had strong history of gastric malignancy was diagnosed as havening stomach cancer during screening studies. His father who was himself a surgeon died at about the age of 62 years after he was operated, and found to have disseminated stomach cancer, and no surgical resection was made. The patient had two healthy younger brothers and two younger healthy sisters. A screening gastroscopy were performed also on one of his brothers and one of his sisters, and showed normal findings. The paternal grandfather died from disseminated stomach cancer, and his brother died from stomach cancer also.

An initial microscopic examination of resected giant polyp on the body of the stomach showed moderately differentiated adenocarcinoma. However, further tests including serum chromogranin on resected area suggested a neuroendocrine tumor.

Conclusion: Ikue Nonogaki and his research group were probably the first to report the occurrence of non-syndromic familial adenocarcinoma-neuroendocrine gastric cancer. This paper reported the occurrence of the first case of disease in Iraq which may be the fourth reported case in the world.

Key words: familial adenocarcinoma-neuroendocrine gastric cancer, Iraq

Introduction

Gastric adenocarcinoma is the most important type of stomach cancers, and it is generally sporadic. However, about 10% of gastric adenocarcinoma occurs in familial pattern. The most important genetic causative factor in gastric adenocarcinoma is CDH1 germline mutations which cause the diffuse stomach cancer syndrome [1].

Chen was probably the fist to suggest the existence of neuroendocrine carcinoma of the stomach as a separate entity in 1988. Chen studied 100 patients with carcinoma of the stomach and found that the cancer cells in 19 patients were positive for gastrin, somatostatin, serotonin, and argyrophil particles. In four of these nineteen patients, endocrine tumor cells were more than half of the total cancer cells. These four patients were considered by Chen as having neuro-endocrine type of stomach cancer.

The tumor in 16 of 50 patients with undifferentiated carcinomas showed neuroendocrine cells. The remaining patients had well-differentiated adenocarcinomas, the tumor in three of them showed neuro-endocrine cells [2]. Hereditary neuroendocrine stomach cancer is very rare [5].

Patients and methods

The case of the first Iraqi patient with familial mixed gastric neuroendocrine-adenocarcinoma in Iraq is described.

Results

At the age of 46 years, a male patient who had strong history of gastric malignancy was diagnosed as havening stomach cancer during screening studies. His father who was himself a surgeon died at about the age of 62 years after he was operated, and found to have disseminated stomach cancer, and no surgical resection was made. The patient had two healthy younger brothers and two younger healthy sisters. A screening gastroscopy were performed also on one of his brothers and one of his sisters, and showed normal findings. The paternal grandfather died from disseminated stomach cancer, and his brother died from stomach cancer also.

On the 23rd of June 2022, gastroscopy showed a large polypoidal, well demarcated gastric mass with congested overlying mucosa with a 4 cm ulcer located at the fundus (Figure-1). Multiple biopsies were taken and showed moderate nodular gastropathy.

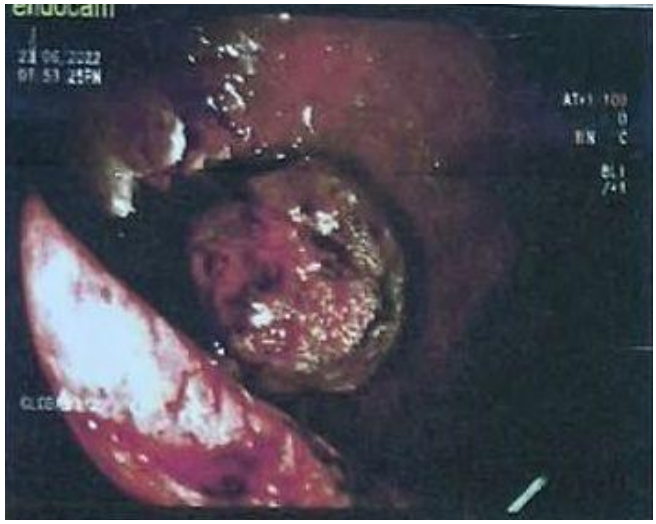

Figure-1A: On the 23rd of June 2022, gastroscopy showed a large polypoidal mass

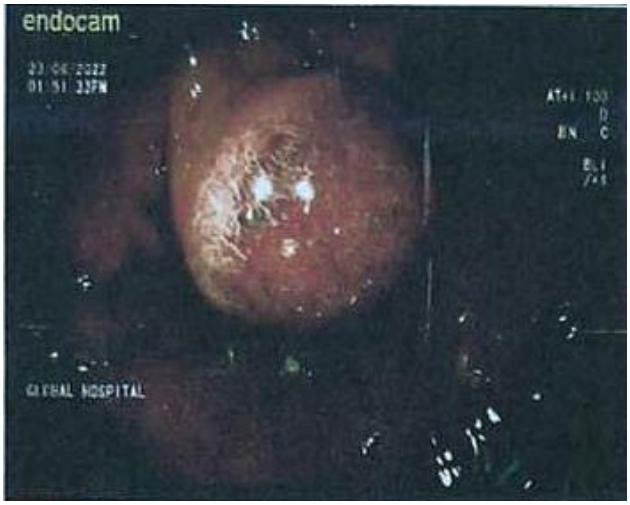

Figure-1B: On the 23rd of June 2022, gastroscopy showed a large polypoidal mass

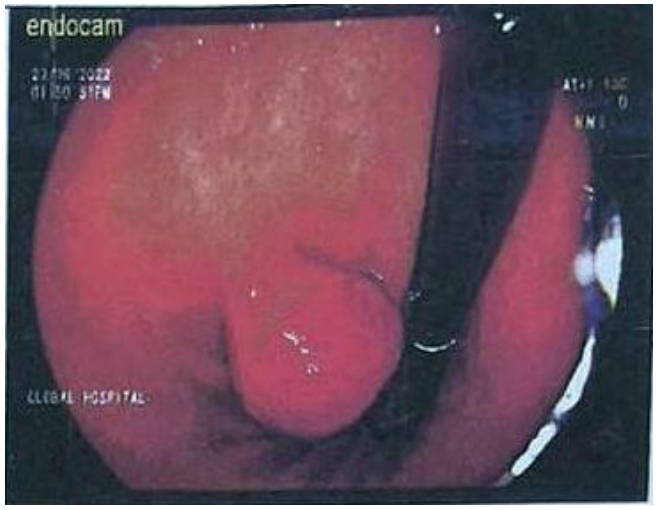

Figure-1C: On the 23rd of June 2022, gastroscopy showed a large polypoidal mass

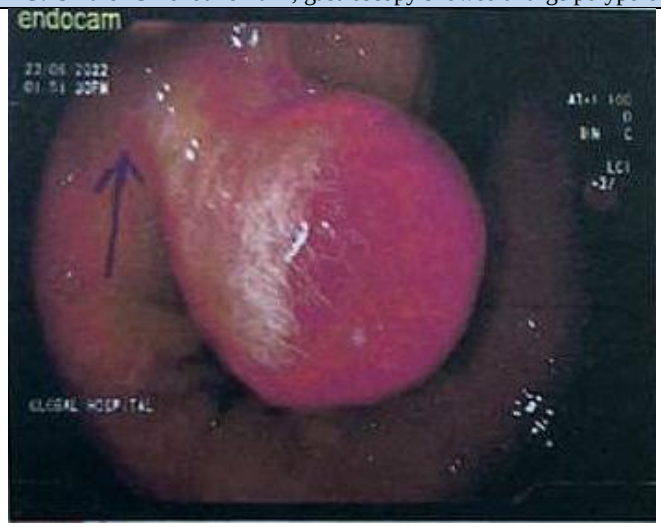

Figure-1D: On the 23rd of June 2022, gastroscopy showed a large polypoidal mass

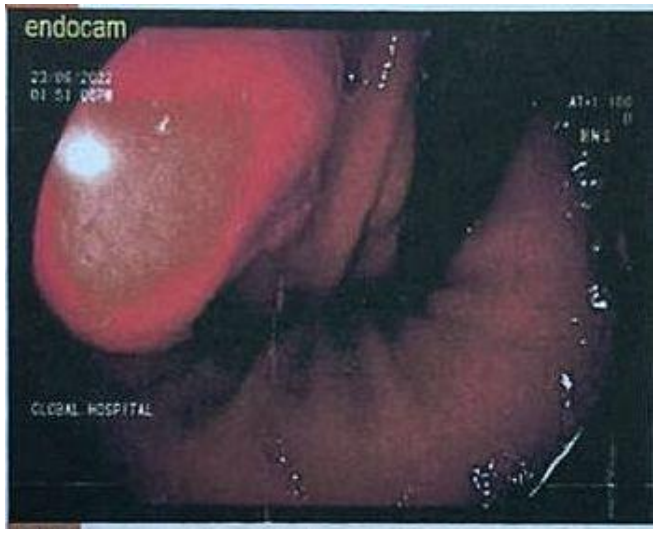

Figure-1E: On the 23rd of June 2022, gastroscopy showed a large polypoidal mass

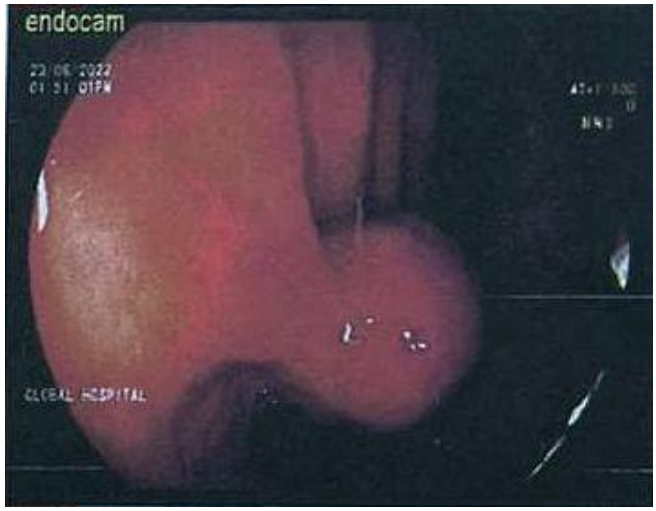

Figure-1F: On the 23rd of June 2022, gastroscopy showed a large polypoidal mass

Gastric polpectomy was performed on the 20th of August, 2022. On the 30th of June, 2022, gastric mass biopsy (pieces of tissues measured in aggregate 0.8 cm all were taken) showed chronic gastritis with prominent intestinal metaplasia. No malignancy was seen in the examined material despite serial and deeper sectioning.

On 20th of October, 2022, resection of giant polyp on the body of the stomach was performed. Microscopic examination showed irregular sheets, nests, and strands composed of atypical glandular epithelial cells with high epithelial cells with high nuclear-cytoplasmic (N: C) ratio, hyperchromatic nuclei with clumped chromatin pattern with desmoplastic tissue reaction. Single lymph node was detected and showed reactive lymphadenitis. The excision margins were free from malignancy. The histopathological diagnosis was moderately differentiated adenocarcinoma (pT2).

Further tests on resected area were also perfumed in India. Microscopic examination showed a tumor nodule in the submucosa and infiltrating the muscularis with histomorphological features of neuroendocrine tumor.
Mitosis is occasional.
Lympho-vascular emboli are seen.

Immunohistochemistry tests:
Tumor cells are Pan CK dot positive.
Chromogranin: Positive.
CDX2: Negative
Ki67: 8%.
Neuroendocrine tumor WHO grades 2.
Serum chromogranin was performed on the 10th of November, 2022 was 145.5 µg/ml (0-100) Post-surgery gastrodudenoscopy was performed on 27th of October, 2022 in India (Figure-2). The stomach showed friable and thickened folds with superficial ulcerations extending about 5 cm along the greater curvature in corpus. Evidence of gastric surgery with suture material seen in the same area. No thickening or ulcer in the fundus or pylorus.
Rapid urease test for H pylori was negative. Endoscopic diagnosis: Gastric mass possibly neoplastic.

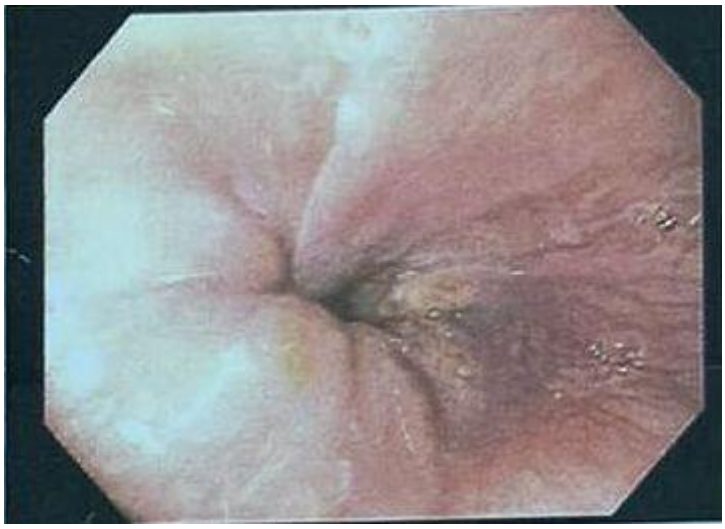

Figure-2A: post-surgery gastrodudenoscopy was performed on 27th of October, 2022

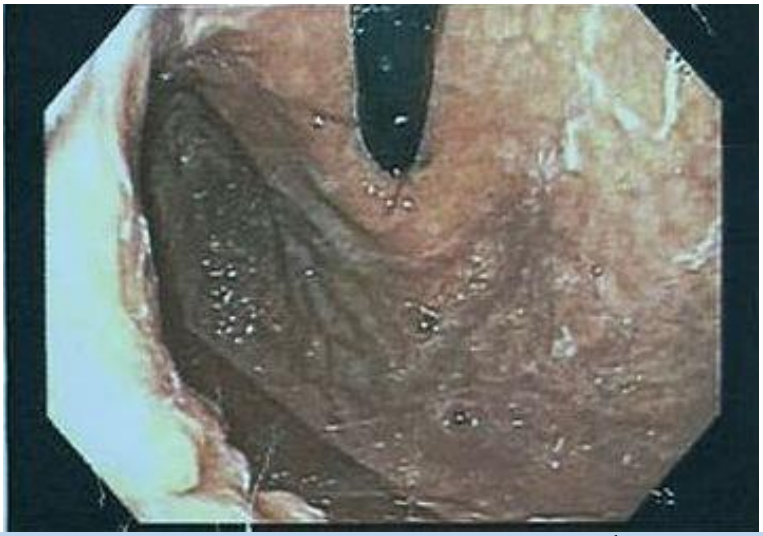

Figure-2B: post-surgery gastrodudenoscopy was performed on 27th of October, 2022

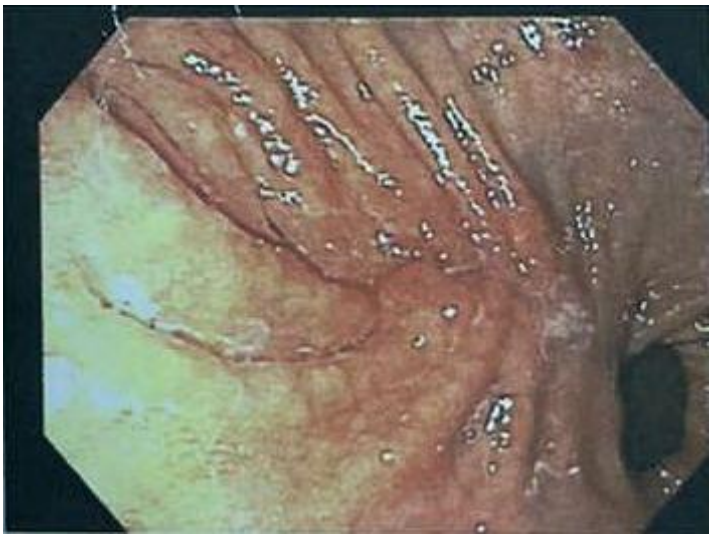

Figure-2C: post-surgery gastrodudenoscopy was performed on 27th of October, 2022

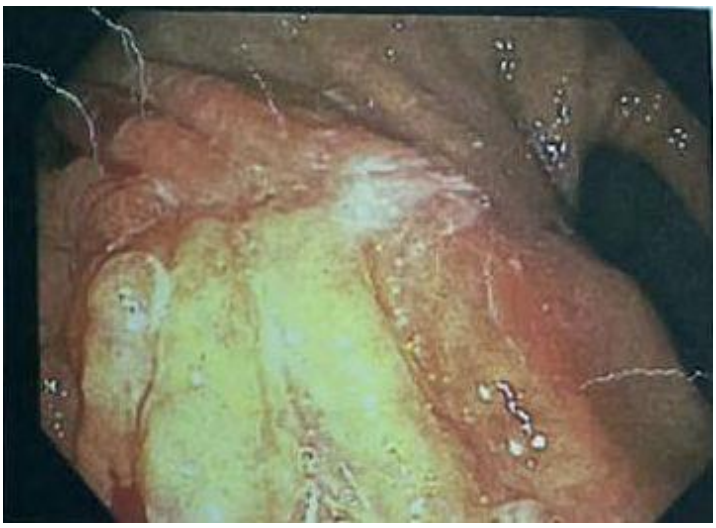

Figure-2D: post-surgery gastrodudenoscopy was performed on 27th of October, 2022

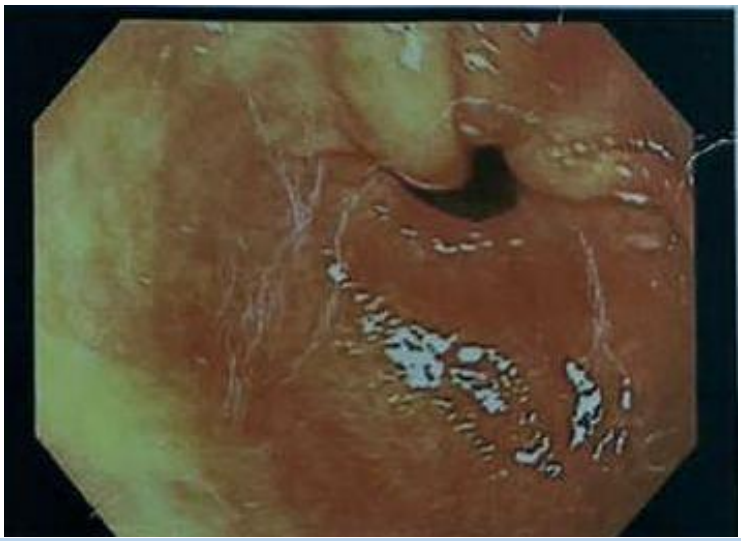

Figure-2E: post-surgery gastrodudenoscopy was performed on 27th of October, 2022

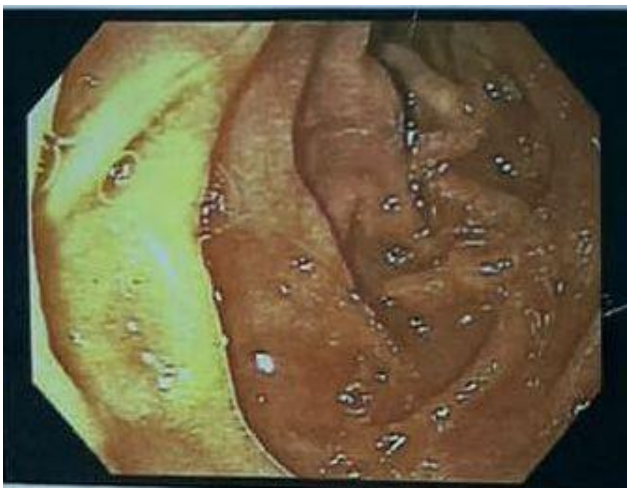

Figure-2F: post-surgery gastrodudenoscopy was performed on 27th of October, 2022

Body low dose PET (Positron Emission Tomography) CT-scan performed on 31st of October, 2022 showed no evidence of residual disease after surgery (Figure-3).

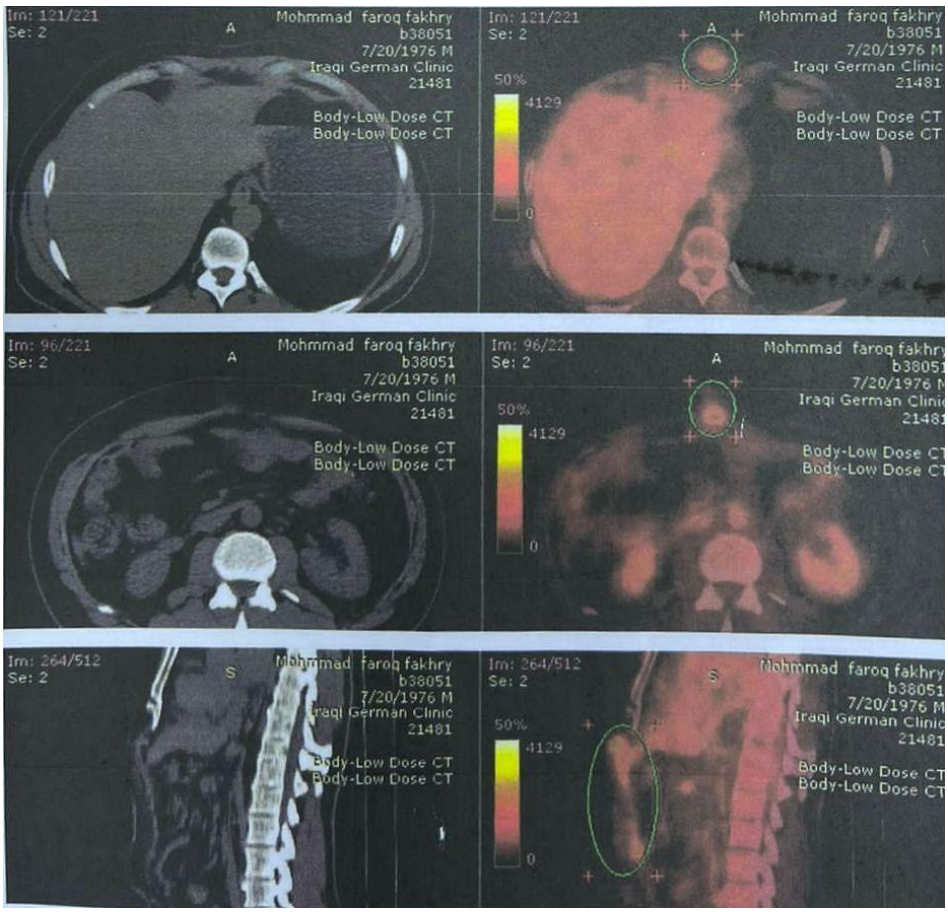

Figure-3A: post-excision of gastric tumor, body low dose CT-scan performed on 31st of October, 2022 showing liner F-fluorodeoxyglucose (FDG) uptake in the midline anterior abdominal wall along the incision site suggesting inflammatory changes

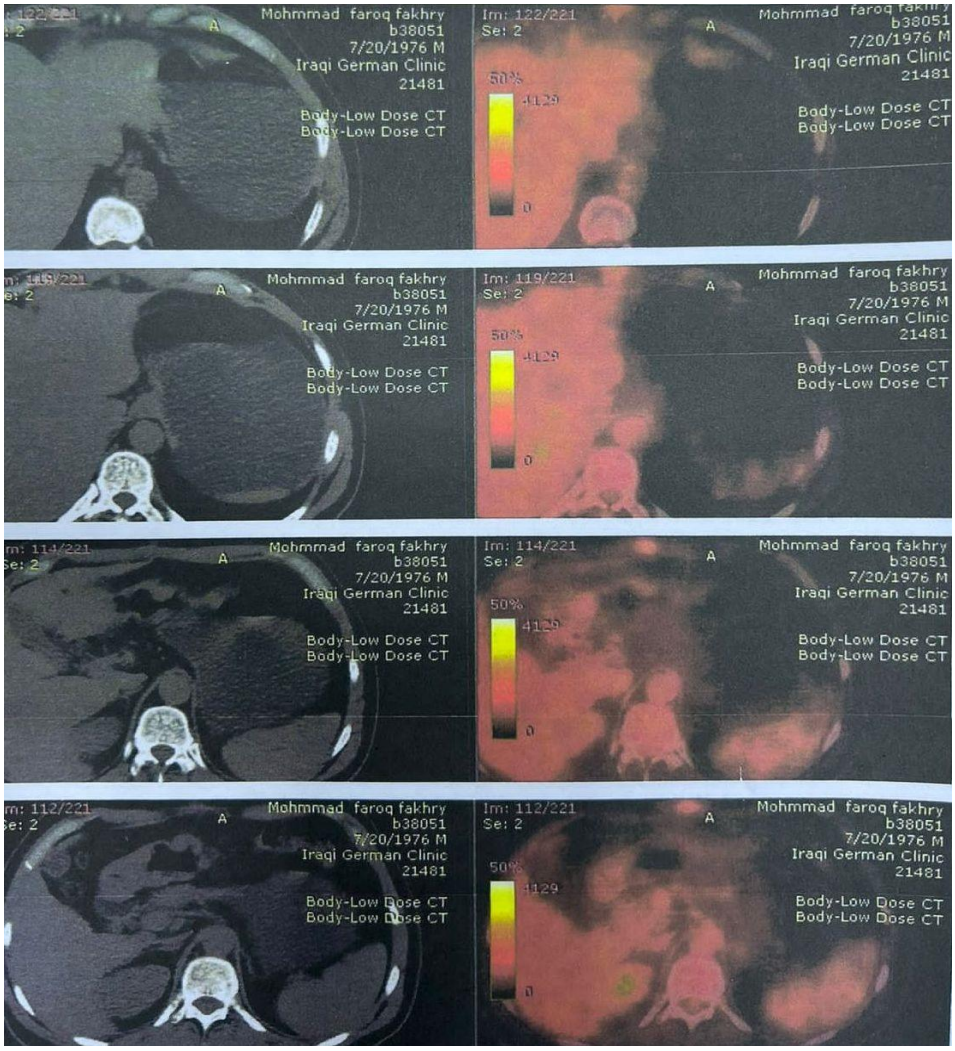

Figure-3B: post-excision of gastric tumor, body low dose CT-scan performed on 31st of October, 2022 showed no evidence of FDG avid abnormal wall thickening or mass lesion in the stomach

DOTA-NOC PET (Positron Emission Tomography) CT scan was performed during the year 2023 showed the absence of somatostatin receptor expressing lesion related to the stomach or elsewhere in the body to suggest residual or recurrent disease (Figure-4).

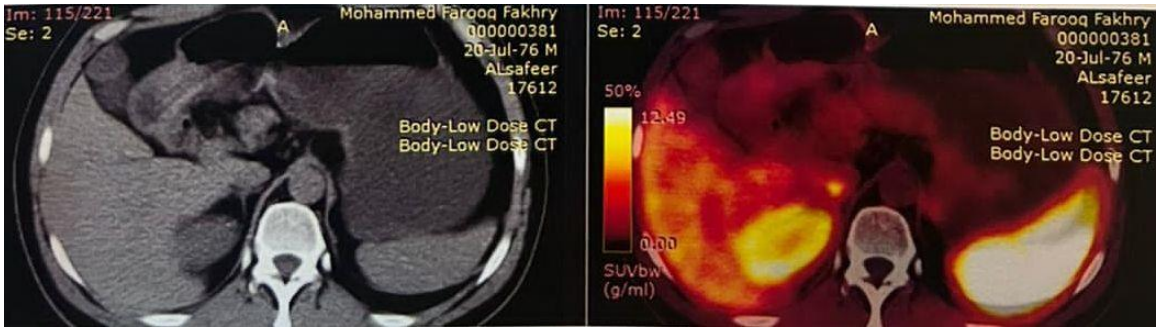

Figure-4: DOTA-NOC PET (Positron Emission Tomography) CT scan was performed during the year 2023 showing well distended stomach with no evidence of radiotracer avid lesion

Mutation analysis of 33 genes associated with hereditary cancers (APC, APM, AXIN2, BARD1, BLM, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, EPCAM, GAL NT12, GREM1, HOXB13, MLH1, MSH2, MSH3, MSH6, MUTYH, NBN, NF1, NTHL1,PALB2,PMS2,POLD1,POLE, PTEN, RAD51C, RAD51D, SMAD4, STK11, TP53) was performed during November, 2022 in India and revealed no pathogenic/likely pathogenic variant. Serum chromogranin A performed on May 23, 2023 was 105 ng/ml,

and performed on April 25, 2023 was 169.3 ng/ml (Normal range: 19.4-98.1 ng/ml).

The patient received one cycle of oral capecitabine.

On the first of August, 2023, the patient was asymptomatic, gastroscopy showed normal
gastric mucosa with good peristaltic activity. However, there was moderate area of congestion and thickening at the proximal part of the stomach with obvious suture line of previous surgery (Figure-5).

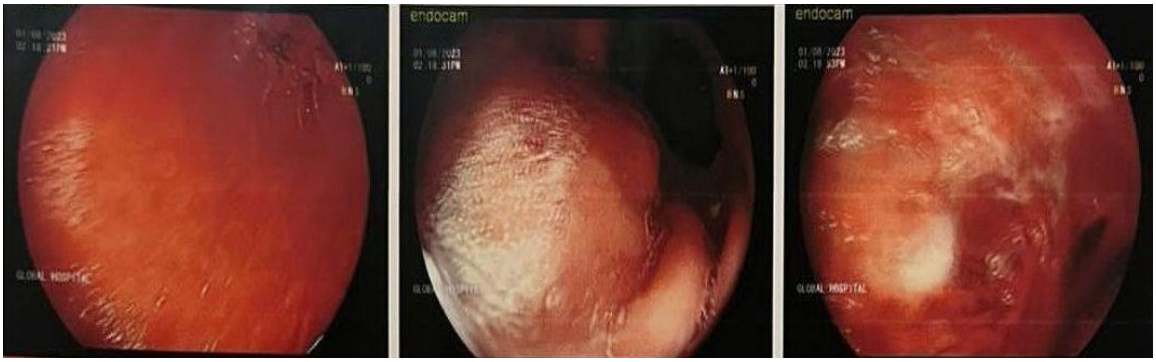

Figure-5 A: Gastroscopy performed on the first of August, 2023 showed moderate area of congestion and thickening at the proximal part of the stomach with obvious suture line of previous surgery

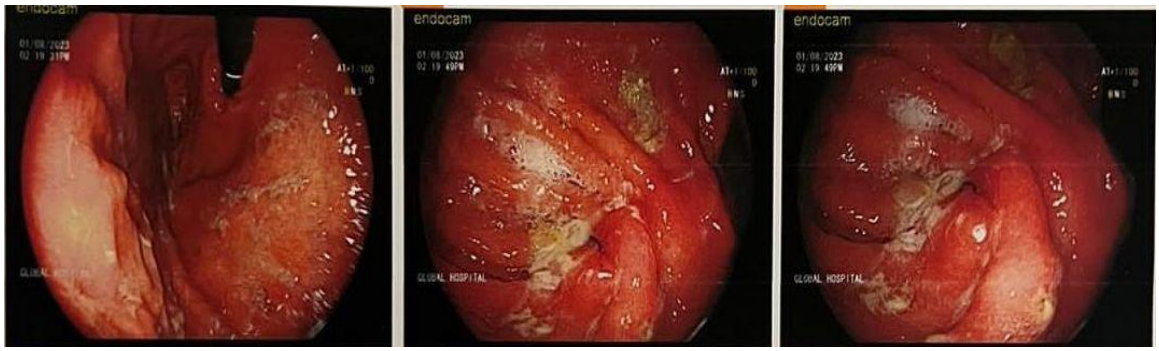

Figure-5B: Gastroscopy performed on the first of August, 2023 showed moderate area of congestion and thickening at the proximal part of the stomach with obvious suture line of previous surgery

On the seventh of August, 2023, multiple pieces of tissues measured in aggregate 1 cm all were taken. Gastric thickening biopsy showed chronic gastritis with prominent intestinal metaplasia. Serial deeper sections were performed and showed no malignancy in the examined materials.

Discussion

Gastric adenocarcinoma is the most important type of stomach cancers, and it is generally a sporadic. However, about 10% of gastric adenocarcinoma occurs in familial pattern. The most important genetic causative factor in gastric adenocarcinoma is CDH1 germline mutations which cause the diffuse stomach cancer syndrome [1].

In this Iraqi patient with familial adenocarcinoma-neuroendocrine gastric cancer, mutation analysis excluded CDH1 germline mutations as a cause of the cancer.

Hereditary neuroendocrine stomach cancer is rare. In 2019, Ikue Nonogaki and his research group reported six patients (Mean age: mean age of the patients: 73.3 years) with endocrine stomach cancer. Three patients had associated traditional adenocarcinoma (Mixed). Four patients were treated with total gastrectomy, and three of them were found to have liver metastases after gastrectomy. Therefore, prognosis of endocrine stomach cancer was considered poor because it rapidly metastasizes to the liver and lymph nodes.

Therefore, Ikue Nonogaki (Figure-6) and his research group were probably the first to report the occurrence of non-syndromic familial adenocarcinoma-neuroendocrine gastric cancer.

Figure-6: Ikue Nonogaki

Conclusion

Ikue Nonogaki and his research group were probably the first to report the occurrence of non-syndromic familial adenocarcinoma-neuroendocrine gastric cancer. This paper reported the occurrence of the first case of disease in Iraq which may be the fourth reported case in the world.

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