Novel treatment (new drug/intervention; established drug/procedure in new situation)

Rare case of ER positive colorectal stricture demonstrating improvement with letrozole

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Summary

The authors present a rare case of a patient with an estrogen receptor (ER) positive malignant colorectal stricture, with no identifiable primary breast carcinoma. There was demonstrated endoscopic and symptomatic improvement after treatment with letrozole. Gastrointestinal metastases from breast cancer usually present with a previous history of breast cancer, however our patient had no prior or current proven history of breast cancer. Biopsy and immunohistochemical staining of the malignant colonic lesion showed an adenocarcinoma with positive ER staining. Mammogram, breast ultrasound and MRI of the breasts were all negative. She was successfully treated with letrozole for 3 years that resulted in endoscopic and symptomatic improvement in her colorectal stricture.

BACKGROUND

A novel method of treatment was used in an estrogen receptor (ER) positive colorectal stricture that resulted in symptomatic and endoscopic improvement. This case report has highlighted that further research is needed to identify the role of letrozole in all ER positive malignancies.

CASE PRESENTATION

A 65-year-old female was referred to the colorectal surgeons for investigation of anaemia and a positive faecal occult test. Her haemoglobin was 10.2. At presentation, the patient had no gastrointestinal (GI) symptoms. Her medical history included hypertension and a history of unknown duration use of hormone replacement therapy. She had no medical history of breast cancer and there was no family history of bowel cancer. Abdominal examination was normal.

INVESTIGATIONS

A rigid sigmoidoscopy showed a firm narrowing in the rectum 9 cm from the anal verge, which was not obviously malignant. Biopsies showed an extrinsic invading poorly differentiated adenocarcinoma. Histopathological features were consistent with a non-colonic upper GI primary tumour (figure 1). However ER staining was strongly positive.

Table 1 below shows the receptors expressed from the rectosigmoid biopsy. Tumour markers were elevated. CA15-3 was significantly elevated at 225. CA125 was 64. Carcinoembryonic antigen was 25. CA19-9 was normal.

The rectosigmoid stricture was also confirmed on barium enema and no other lesion was found in the rest of the large bowel. An MRI rectum and pelvis confirmed the rectal tumour. Imaging also confirmed mesorectal lymph nodes, multiple sclerotic lesions in the pelvic bones and upper femur. However, as part of staging the cancer the CT abdomen did not clearly identify the colorectal stricture. The patient was discussed at the colorectal multi-disciplinary

Figure 1 (A, B) Histopathology of rectosigmoid biopsies showing infiltrating differentiated adenocarcinoma through whole bowel wall. Rectosigmoid colon. Estrogen receptor staining positive, progesterone receptor and HER-2 negative. There is infiltration of the lymph nodes and tumour extends to the tumour margin.

Table 1 Immunohistochemical markers

Immunohistochemical marker	Positive	Negative
ER	✓	-
PR	-	✓
CEA	✓	-
CK7	✓	-
CK20	-	✓
TTF1	-	✓
WT1	-	✓
CISH	-	✓

CEA, carcinoembryonic antigen; CISH, Chromogenic in situ hybridisation; CK, cytokeratin; ER, estrogen receptor; PR, progesterone receptor; TTF1, thyroid transcription factor-1; WT1, Wilms tumour gene.

meeting where further investigations to identify a primary upper GI or breast malignancy were suggested. Upper GI endoscopy was macroscopically normal however random biopsies showed a diffuse poorly differentiated tumour in the body of the stomach. ER and PR staining was negative on the gastric biopsies (figure 2). The patient was referred to the breast surgeons to identify a primary breast cancer.

Clinical evaluation revealed no abnormality. A mammogram, breast ultrasound and MRI breast also showed no malignant features.

TREATMENT

The patient was seen by oncologists regarding the multiple site tumours. Due to the presence of multiple site tumours in the rectum, stomach and sclerotic bony lesions

Figure 2 (A, B) Histopathology of gastric biopsies showing diffuse poorly differentiated gastric tumour. Immunohistochemistry staining is negative. Estrogen receptor, progesterone receptor, Her-2 negative.

the patient was treated with hormonal therapy rather than surgery. The opinion was that the patient had an ER positive colorectal stricture that may show response to hormonal treatment. Therefore the patient was started on letrozole to treat the colorectal stricture.

OUTCOME AND FOLLOW-UP

Between investigations and starting treatment, the patient developed increased bowel frequency.

Within 1 month of starting letrozole there was a significant improvement in the size of the stricture and the patient's bowel function. At 4 months, flexible sigmoidoscopy showed an almost normal lumen and the patient's bowel function had returned to normal. The tumour markers also returned to normal. Nine months after starting letrozole, rigid sigmoidoscopy was reported as normal. Therefore letrozole improved the patient's malignant colorectal stricture.

The patient was maintained for 3 years on letrozole with regular outpatient monitoring in the colorectal and oncology clinic. The CT abdomen and tumour markers showed no evidence of colorectal recurrence therefore chemotherapy was not required. In addition, the patient did not develop symptoms from the gastric cancer. Letrozole was used to reduce the patient's colorectal stricture, demonstrating symptomatic and objective clinical improvement.

DISCUSSION

Literature searches could not identify case reports of patients demonstrating symptomatic and endoscopic improvement after being treated with letrozole for an ER positive colorectal cancer, with an unproven primary breast cancer.¹ GI metastases as a first presentation of breast cancer are rare² and tend to present much later.³ Axillary lymphadenopathy is the usual presentation of occult metastatic breast cancer. From literature searches, only two cases without involvement of the axilla were identified.^{4 5} However, this rare case demonstrates that letrozole improved the colorectal stricture and the gastric cancer did not progress. The follow-up period has been 3 years.

Immunohistochemical markers are increasingly being used to differentiate between primary and secondary cancers.⁶ The use of these markers can help identify patients who should be considered for hormonal treatment. This can improve patients quality of life and minimise the use of other treatments, thus avoiding potential side effects. The benefit of systemic chemotherapy and tamoxifen can have a positive effect on survival for metastatic breast cancer whereas surgery may not.⁷

Learning points

- Immunohistochemical staining can add value to the diagnostic process by differentiating between ER positive and negative malignancies. If staining is positive, letrozole can be used to improve patients' symptoms. This case report highlights the value of immunohistochemical staining in ER positive GI malignancies and the value of hormonal therapies.

Competing interests None.

Patient consent Obtained.

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