



# Ascending colon metastasis after breast cancer surgery: a case report and literature review

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**Background:** Breast cancer is the most common cancer in women. The tumor is prone to metastasize in the brain, lung, liver, bone, and other organs; however, generally, it is less likely to metastasize in the digestive tract. Thus, breast cancer metastasizes to colon is rarely happened and easily ignored by clinicians. Such misdiagnosis may lead to delay the further diagnosis and treatment of patients, or even cause the life danger of patients due to the progress of the disease. Therefore, we propose such case reports to arouse clinicians' attention to the rare case of digestive tract metastasis after treatment of breast cancer. We also conducted a retrospective analysis of the relevant case reports. We suggest that because breast cancer with gastrointestinal metastasis rarely occurs, and because of the lack of specificity of syndromes, it is easily misdiagnosed. Thus, the attention of the receiving doctor needs to be drawn to this tumor. We also summarized the specificity and sensitivity of the commonly used immunohistochemical detection indicators of digestive tract metastasis of breast cancer.

**Case Description:** We presented a 67-year-old female went to hospital because of "acute pain in the right lower abdomen", after computed tomography (CT) examination, the patient was diagnosed as "acute appendicitis" and underwent laparoscopic appendectomy (LA), the post-surgery pathology confirmed metastatic carcinoma to the appendix from the breast that was removed 10 years early. The patient first came to our hospital 10 years ago because of the right breast malignant tumor. After modified radical mastectomy for right breast cancer, the patient underwent chemotherapy for 6 cycles. Tamoxifen endocrine therapy was administered after chemotherapy. The patient had a regular follow-up, with no signs of distant metastasis and local recurrence.

**Conclusions:** Metastasis from breast cancer to the gastrointestinal tract is extremely rare. For patients with breast cancer, endoscopy should be adopted as a routine follow-up item. For suspicious lesions found under endoscopy, immunohistochemistry stain should be adopted to ensure the diagnosis. For lesions that are confirmed to be metastatic from breast cancer, proper treatment should be carried out based on patients' condition to improve the prognosis.

**Keywords:** Immunohistochemistry; colon metastasis of breast cancer; case report

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## Introduction

Breast cancer is the malignant tumor with the highest incidence rate in women, and it is increasing year by year (1,2). The most common organ for distant metastasis are the bones (59.9%), lung (47.8%), liver (40.9%), and brain (38.8%) (3). However, metastasis to the gastrointestinal tract (GIT) is uncommon in breast cancer (4,5), Mclemore's retrospective review of 12,001 cases of metastatic breast cancer between 1985 and 2000, the result confirmed 73 patients (0.6%) with a pathological affirmation of metastasis to GIT and/or peritoneum. Only 24 out of 12,001 patients (0.2%) had colonic metastasis (6). Montagna and colleagues' review of 2,588 patients with breast cancer revealed that 40 patients (1.55%) had GIT metastasis, with only 2 having colonic metastasis (0.07%) (7). Those studies show that GIT metastasis is extremely rare in breast cancer.

We report the case of a patient with "ascending colon metastasis", after breast cancer surgery ten years ago. We also conducted a retrospective analysis of relevant case reports and analyses. We found that because breast cancer with gastrointestinal metastasis rarely occurs, it is easily misdiagnosed, and because of the lack of specificity of its clinical manifestations, it is easily missed, both of which have a great effect on the survival and prognosis of patients.

Colon metastasis of breast cancer is relatively rare, and the prognosis of such patients is very poor, and most of them die within 2 years of their diagnosis, which may be related to other distant organ metastasis and/or delayed diagnosis.

At present, there is no definite consensus or guidelines to the treatment of digestive tract metastasis after breast

cancer surgery. Chemotherapy, targeted therapy, and endocrine therapy are the main treatment measures for patients with digestive tract metastasis of breast cancer, and surgical treatment cannot improve the overall survival and prognosis of patients. Only a few patients are eligible for palliative surgery if they have symptoms of digestive tract obstruction (8,9).

Thus, early detection and effective systemic treatment may help to avoid unnecessary surgery and improve prognosis. We present the following article in accordance with the CARE reporting checklist (available at <https://gs.amegroups.com/article/view/10.21037/gs-22-642/rc>).

## Case presentation

The 67-year-old patient first came to our hospital 10 years ago. She had an operation at the local hospital because of "progressive enlargement of a right breast tumor for 1 year", and underwent "resection of the right breast tumor". The postoperative pathological return was "invasive ductal carcinoma", and she was transferred to our hospital for "modified radical mastectomy for right breast cancer". The postoperative pathology was "(modified radical mastectomy specimen of the right breast) no tumor residue was found around the original surgical incision of the right breast, and no tumor was involved in the papillary skin, epidermis, and basal connective tissue. No cancer metastasis was found in 23 lymph nodes. The results were as follows: right armpit 0/18, subclavian 0/2, and tip group 0/3". The immunohistochemistry (IHC) results were as follows: estrogen receptor (ER) (+++), progesterone receptor (PR) (±), human epidermal growth factor receptor 2 (HER-2) (-). After the operation, a chemotherapy regimen of epirubicin + cyclophosphamide (EC) was administered for 6 cycles. Tamoxifen endocrine therapy was administered after chemotherapy.

The patient had a regular follow-up, with all surveillance scans being negative for distant metastasis and local recurrence. The patient went to outpatient department in 2020-08-21, and endoscopic examination found no suspicious lesion (*Figure 1A,1B*).

The patient visited our hospital on May 5, 2021 because of "acute pain in the right lower abdomen". A physical examination revealed pain in the right lower abdomen. After an abdominal plain scan CT examination (patients in emergency room usually only receive plain CT examination, unless suspected of vascular disease), the patient was diagnosed with acute appendicitis and

### Highlight box

#### Key findings

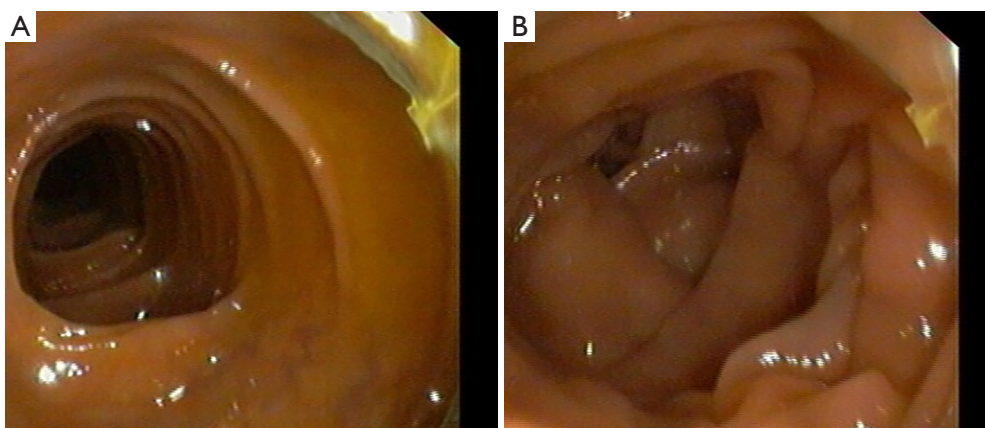
- Gastrointestinal metastasis of breast cancer is rare, but it still needs clinicians' attention.

#### What is known and what is new?

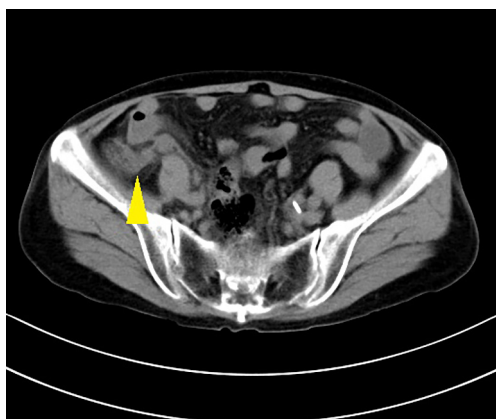
- Digestive tract metastasis from breast cancer is lack of specificity of clinical manifestations and endoscopic examination.
- Immunohistochemical staining is helpful to differentiate digestive tract metastasis of breast cancer.

#### What is the implication, and what should change now?

- In the follow-up after breast cancer surgery, if alimentary tract space occupying lesions are found, relevant immunohistochemical staining should be performed to exclude the possibility of breast cancer metastasis.



**Figure 1** Results of endoscopy. During the follow-up period, the patient underwent colonoscopy, and no obvious abnormal lesions were found.



**Figure 2** Plain scan CT before laparoscopic appendectomy. The yellow arrow points to the appendix, which is thickened, consistent with the manifestation of acute appendicitis. CT, computed tomography.

underwent laparoscopic appendectomy (LA). There was no abdominal and pelvic cavity contamination due to tumor rupture during operation. Simple inflammatory changes were observed in the appendix (*Figure 2*), and the ileocecal part and the visible part of the abdominal cavity had no obvious abnormalities. A LA was performed.

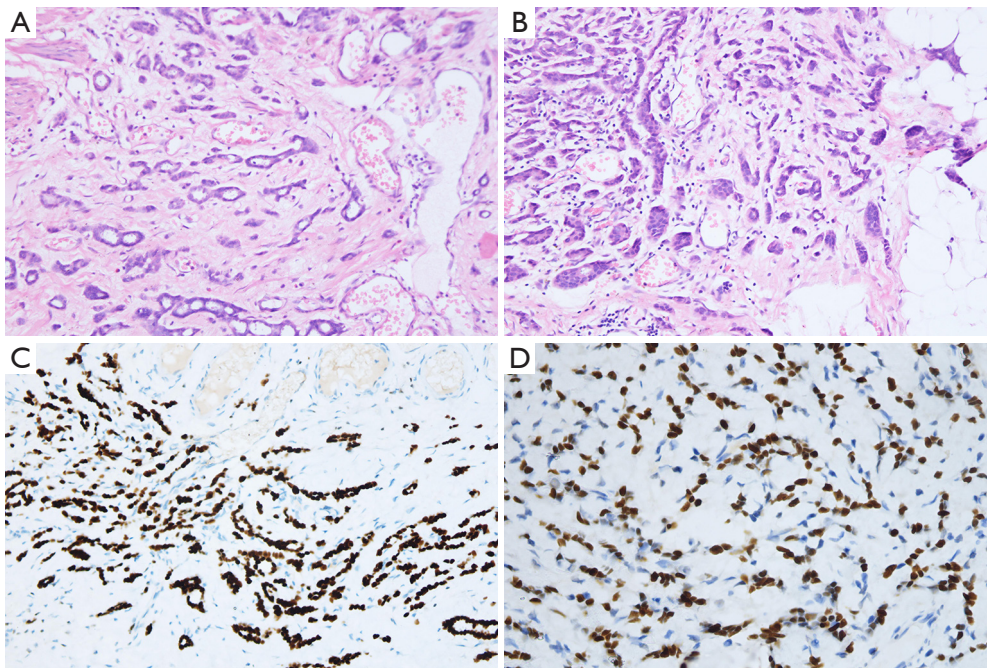
The patient's postoperative pathological report was as follows: a large number of heterotypic cells were observed in the wall of the appendix and mesangium, arranged in the form of cords and glandular tubes, and tumor thrombi were observed in the vessels. Combined with the immunohistochemistry results and the patient's history, the pathological results was consistent with non-

specific invasive cancer metastasis of the breast, and cancer involvement was observed at the cutting edge. The IHC results were as follows: ER (95% strongly positive), PR (15% strongly positive), HER-2 (+), E-cad (+), p120 (membrane +), GATA-3 (trans-acting T-cell-specific transcription factor) (+), gross cystic disease fluid protein-15 (GCDFP-15) (focus +), mammaglobin (focus +), cytokeratin-7 (CK7) (+), cytokeratin-20 (CK20) (-). The Ki-67 index was about 20% (*Figure 3A-3D*).

After LA, the patient underwent abdominal enhanced CT, and no abnormal signs, such as the thickening of the colon wall, were observed (*Figure 4A-4C*). The patient refused an endoscopy and positron emission tomography-CT (PET/CT), and then underwent laparoscopic radical right hemicolectomy.

The patient's postoperative pathological result of the right hemicolectomy specimen indicated a diagnosis of metastatic non-specific invasive breast cancer. The tumor showed multifocal metastatic invasion. The small foci showed the involvement of the muscularis propria of the intestinal wall. The tumor thrombi in the vessels were visible. The nerve invasion was not obvious. No cancer was found in the bilateral cutting ends of the specimen, and the "upper cutting end" and "lower cutting end". There were 37 lymph nodes without cancer metastasis. The IHC results were as follows: GATA-3 (+++), GCDFP-15 (focus +), ER (95%, strong +), PR (5%, medium), HER-2 (1+), E-cad (membrane ++), p120 (membrane ++), CK7 (+++), CK20 (-), satb-2 (-), villin (-), syn (-), chromophilic granulin A (CGA) (-), and CD56 (-). The Ki-67 index was about 5%.

The patient recovered well after the right hemicolectomy,



**Figure 3** Routine pathological examination and immunohistochemical examination after right semicolectomy. (A,B) Hematoxylin and eosin stain,  $\times 200$  showing fragments of post-surgery colon splices. (C) Immunohistochemical stains,  $\times 400$ , GATA-3 positive. (D) Immunohistochemical stains,  $\times 400$ , ER positive. ER, estrogen receptor.

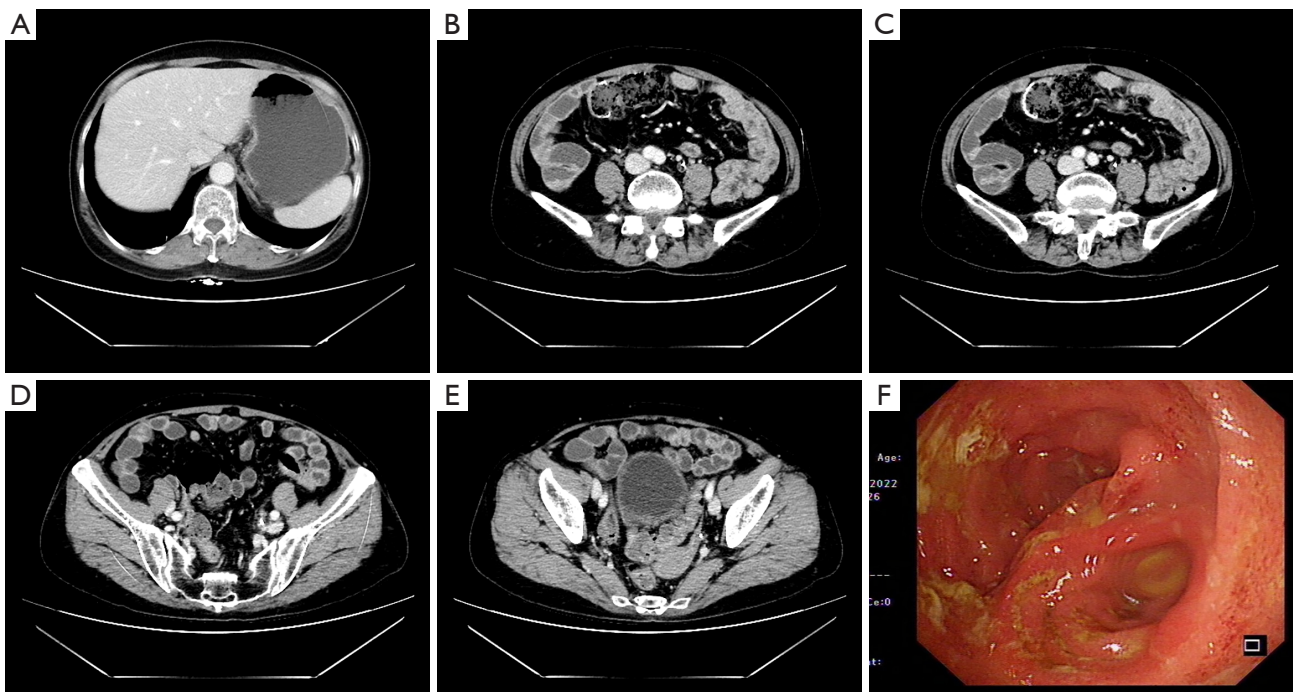


**Figure 4** Abdominal enhanced CT after LA: no abnormal signs, such as the thickening of the colon wall, were observed. CT, computed tomography; LA, laparoscopic appendectomy.

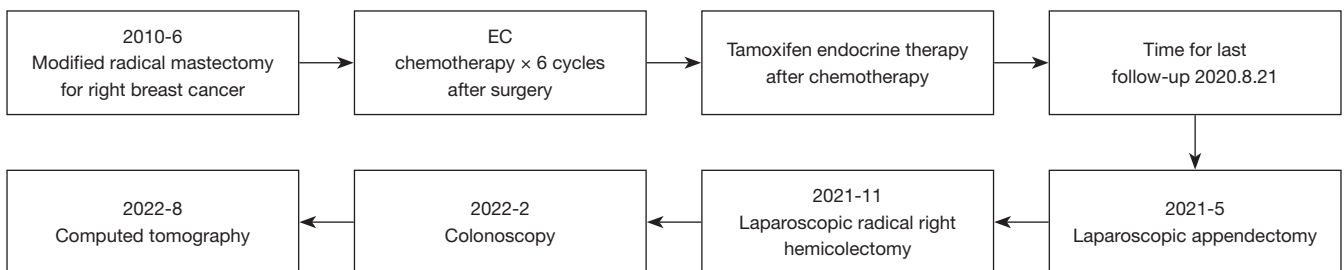
but she refused to any kind of further treatment, and regular follow-up. 1 year after operation in patients with reviewing a colonoscopy and CT examinations are not prompted to tumor recurrence (*Figure 5A-5F*). The patient's diagnosis and treatment timeline was summarized in *Figure 6*.

Colon metastasis of breast cancer is relatively rare, and the prognosis of such patients is very poor. The main reasons are the long interval between tumor recurrence,

the lack of specific clinical symptoms, and the lack of experience of the receiving doctor. The patients with digestive tract metastasis of breast cancer usually have no specific symptoms, as we summarized in *Table 1*, the most common symptoms include dyspepsia, nausea, changes of stool frequency (10), vomiting (11), abdominal pain (12), obstruction (13), loss of weight (14), and loss of appetite (20). Some were found during regular follow-up (15-19).



**Figure 5** Abdominal enhanced CT after laparoscopic radical right hemicolectomy (A-E): no abnormal signs, such as the thickening of the colon wall or metastasis to liver were observed. (F) Colonoscopy after laparoscopic radical right hemicolectomy: no obvious abnormal lesions were found. CT, computed tomography.



**Figure 6** Timeline of the diagnosis and treatment. EC, epirubicin + cyclophosphamide.

Endoscopic findings are non-specific (21-23). It is often difficult for patients to obtain an accurate diagnosis because of these non-specific symptoms.

Ambroggi *et al.* (20) conducted a retrospective analysis of more than 200 cases of breast cancer patients with gastrointestinal metastasis, and found that the most common sites of breast cancer metastasis were the stomach (60%), esophagus (12%), colon (11%), rectum (8%), and oropharynx (1%). A retrospective analysis of 12,000 cases of metastatic breast cancer patients at the Mayo Clinic showed that only 73 of those patients suffered from gastrointestinal metastasis during the follow-up, of whom 8% had

esophageal metastasis, 28% had gastric metastasis, 19% had intestinal metastasis, and 45% had colorectal metastasis. Among the breast cancer patients with gastrointestinal metastasis, about 54% had the pathological type of invasive lobular carcinoma (24).

At present, there is no definite consensus or guiding opinions on the treatment of digestive tract metastasis after breast cancer surgery. Chemotherapy, targeted therapy, and endocrine therapy are the main treatment measures for patients with digestive tract metastasis of breast cancer, and surgical treatment cannot improve the overall survival and prognosis of patients. Only a few patients are eligible for

**Table 1** Case reports of breast invasive ductal carcinomas with colonic metastases

Case	Time from diagnosis (year)	Treatment	Survival
Higley <i>et al.</i> (10)	38	Chemotherapy	Alive
Noor <i>et al.</i> (11)	30	Surgical resection	Alive
Blachman-Braun <i>et al.</i> (12)	15	Surgical resection	Alive
Katz <i>et al.</i> (13)	15	Right hemicolectomy	Unclear
Algethami <i>et al.</i> (14)	1	Unclear	Unclear
Do <i>et al.</i> (15)	7	Palliative care	Alive
Schellenberg <i>et al.</i> (16)	2	Biopsy surgery	Dead
Falco <i>et al.</i> (17)	12	Right hemicolectomy	Alive
Jones <i>et al.</i> (18)	4	Laparoscopic appendectomy	Alive
Imai <i>et al.</i> (19)	2	Unclear	Unclear

palliative surgery if they have symptoms of digestive tract obstruction (8,9,25).

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

## Discussion

Colon metastasis of breast cancer is relatively rare, and the prognosis of such patients is very poor. The main reasons are the long interval between tumor recurrence, the lack of specific clinical symptoms, and the lack of experience of the receiving doctor. The patients with digestive tract metastasis of breast cancer usually have no specific symptoms. Endoscopic findings are non-specific (21-23). It is often difficult for patients to obtain an accurate diagnosis because of these non-specific symptoms.

For patients suspected that digestive tract lesions may be metastatic from breast cancer, it is important to improve the biopsy and IHC stain of the lesions. GCDFP-15, mammaglobin, and GATA3 are relatively specific antibodies in the breast, and their combined application is helpful to determine the source of tumor cells.

We also summarized and compared the immunohistochemical detection indicators of digestive tract metastasis of breast cancer, and selected the immunohistochemical detection

indicators with high sensitivity and specificity. GCDFP-15, mammaglobin, and GATA3 are relatively specific antibodies in the breast, and their combined application is helpful to determine the source of tumor cells. Due to the diversity of the tumor histological types, the different immunophenotypes, the differences in the expression of primary and metastatic lesions, the differences in detection methods, and the differences in statistical methods, reports on the sensitivity and specificity of the expression of the above-mentioned 3 antibodies in breast cancer vary greatly. Notably, GCDFP-15 has a sensitivity of 5–74% and a specificity of 9–100%, mammaglobin has a sensitivity of 7–84% and a specificity of 85–100%, and GATA3 has a sensitivity of 32–100% and a specificity of 71–93%. ER and PR can also be expressed in primary gastric tumors. However, it is not recommended that they be used alone as immunohistochemical markers to determine the origin of tumors (26). In this case, the negative postoperative pathology immunohistochemical results for CK-20 and Cdx-2 for this patient largely excluded the presence of primary gastrointestinal tumors, and the positive results of CK-7, GATA-3, mammaglobin, and ER largely supported the presence of metastatic breast cancer.

At present, there is no definite consensus or guiding opinions on the treatment of digestive tract metastasis after breast cancer surgery. Chemotherapy, targeted therapy, and endocrine therapy are the main treatment measures for patients with digestive tract metastasis of breast cancer, and surgical treatment cannot improve the overall survival and prognosis of patients. Only a few patients are eligible for palliative surgery if they have symptoms of digestive tract

obstruction (8,9,25).

The early detection and timely and effective systemic treatment may help to improve prognosis. Thus, doctors treating patients with a history of breast cancer should be alert to the possibility of metastasis when gastrointestinal symptoms are observed. Additionally, in the clinical follow-up of patients with breast cancer, regular endoscopic examination are essential, especially when patients have gastrointestinal symptoms, such as a loss of appetite, nausea, vomiting, abdominal pain and discomfort, and changes in bowel habits. For abnormal lesions detected under endoscopy, whether ulcer or polypoid hyperplasia, a pathological examination and immunohistochemical examination should be carried out to avoid delay in diagnosis and treatment.

## Conclusions

The combination of a long interval from initial diagnosis of breast cancer to the presentation and the rarity of isolated colonic metastases makes the diagnosis of colonic metastases difficult and easily missed.

There are no certain guideline on how to manage colonic metastasis from breast cancer; however, surgical resection was not guarantee to improve the survival of patients with GIT metastasis and/or carcinomatosis over chemotherapy and/or hormonal therapy. So surgical procedure should only be considered in the case of life-threatening complications (e.g., to treat bleeding, obstruction, and perforation) (6).

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## Footnote

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*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at <https://gs.amegroups.com/article/view/10.21037/gS-22-642/coif>). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are

appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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