CASE REPORT

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Appearance of ductal breast and colon carcinoma with gastrointestinal stromal tumor (GIST) in a female patient: an extremely rare case

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Abstract

Background: Gastrointestinal stromal tumor (GIST) is a mesenchymal tumor of the gastrointestinal tract. Very few cases of coexistence of GIST and adenocarcinoma in other organs have been described. *Case presentation*: We present the case of a 63-year-old female patient diagnosed with breast cancer. After five years of the diagnosis, the findings of colon adenocarcinoma and GIST in stage IA were discovered incidentally during surgical treatment of the colon carcinoma. This tumor display: mixed spindle–epithelioid cell cytological type, of moderate cellularity, mitotic index (1/10) with low anaplasia, low proliferative status (Ki-67 index 12%), without necrosis and immunophenotype profile: antiendomysial antibody (EMA)–, vimentin+++, CD117++, CD34+++, alpha-smooth muscle actin (α-SMA)+, desmin+/–, S-100–, CD68–. *Conclusions*: The present case is extremely rare since the patient has adenocarcinoma with GIST in a previously diagnosed breast carcinoma. Based on this, in clinical practice should always think about possibility occurrence of synchronous and metachronous tumors.

Keywords: gastrointestinal stromal tumors, adenocarcinoma, colon, synchronous tumors, breast adenocarcinoma.

Introduction

Gastrointestinal stromal tumor (GIST) is the most common mesenchymal tumor of the gastrointestinal (GI) tract with epithelioid cells that express the Kit-protein (CD117) or platelet-derived growth factor receptor alpha (*PDGFRA*) gene [1, 2]. In some cases, GIST represents incidental findings either during surgery, at autopsy or during other diagnostic procedures performed for unrelated diseases [3].

GIST occurrence is most frequently observed in people between the sixth and eighth decades of life and more frequently in men. These tumors are most frequently localized in the stomach (60–70%), small intestine (20–30%), large intestine and rectum (5–10%). Few cases involving a synchronous appearance of GIST and adenocarcinoma in other organs have been described [3, 4]. Due to the paucity of cases described in the literature, there is no information regarding the connection between the two different types of tumors affecting the prognosis of the patient.

Case presentation

In 2005, a 63-year-old patient was presented for the first time at the Department of Oncology for a lump palpated in her left breast. In her family history, there are data on common cardiovascular diseases, but there are no known relatives of those with malignancies. There was no professional exposure of the patient to chemical carcinogens. At that time, mammography revealed an ill-defined, soft-tissue opacity, measuring 25×20 mm, at the joining of the left breast. For an *ex tempore* analysis, a sample of tissue from surgery, 50×40 mm diameter, was crossed with a gray whitish change, more consistency, circumscribable border, 10 mm from the nearest surgical margin. Subsequently, the material obtained after the surgical resection of the breast and axillary fat tissue was examined. No invasive and *in situ* carcinoma has been found by macroscopic and microscopic examination of breast tissue. Of the 10 microscopically examined lymph nodes, the presence of metastatic deposits in one lymph node (1/10) was confirmed. The pathological stage of the disease was designated as pT2N1M0. Given the fact that *ex tempore* histopathology verified malignity, the surgical intervention, radical mastectomy, was performed immediately.

Definite histopathology confirmed a moderately differentiated invasive ductal breast carcinoma, positive for hormone receptors (estrogen and progesterone receptors 90% cells, strong intensity of expression – score 8), HER-2 negative with low expression of Ki-67 (12%). According to the molecular classification, the Luminal A type histology of tumor was defined (Figure 1). The treatment was continued with six cycles of adjuvant chemotherapy according to the CMF protocol (Cyclophosphamide 600 mg/m^2 i.v, Methotrexate 40 mg/m^2 i.v. and 5-Fluorouracil 600 mg/m^2 i.v.), coupled with hormonal therapy, Tamoxifen, which the patient was taking over the course of two years.

After five years, at the beginning of 2010, when the patient was 68 years old, without signs of breast tumor recurrence, but regarding gastric symptoms, performed colonoscopy revealed an infiltrative proliferative change at a distance of about 14 cm from the anal brim, narrowing the lumen by 10 cm in length. The biopsy and histopathology of the described change confirmed the colon adenocarcinoma histological grade I and nuclear grade II (Figure 2). Without previous staging of illness, the tumor was surgically removed. The macroscopic finding of the tissue of the removed sigmoid and rectal parts of the colon together with the tumor showed that the tumor infiltrates the entire thickness of the wall of the intestine by reaching the pericolic fatty tissue at a length of 5 cm, without presenting tumor elements on the radial, proximal and distal margins from surgical resection and without metastases in 15 analyzed regional lymph nodes. The definitive histopathology confirmed a low-grade colon adenocarcinoma and the pathological stage of the disease was T2N0M0L0V0R0. A distinctly defined tumor was incidental found in the gastric wall during the surgical procedure, measuring about 4 cm in size. The tumor was removed completely and immediately, with a minimum distance from the nearest resection margins of 8 mm. Immunophenotype of the tumor was: antiendomysial antibody (EMA)–, vimentin+++, CD117++, CD34+++, alpha-smooth muscle actin (α-SMA)+, desmin+/–, S-100–, CD68– and the immunohistochemical analysis indicated a GIST of the stomach (GIST ventriculi): gastrointestinal leiomyogenic tumor (GILT) type, stage IA (pTNM: G1 T2 NxMx), palisade-vacuolar + sclerosing syncytial mixed histological type, spindle + epithelioid cytological type, of moderate cellularity, mitotic index 1/10 high power field (HPF) with low anaplasia (Figure 3). Given the fact that this was a case of stage IA of the disease with low malignity potential GIST, it was decided that the patient should come for periodic follow-up examinations. After the surgery, the patient refused the chemotherapy prescribed for colon carcinoma.

In August 2013, due to abdominal pains and the presence of a palpable mass in the right iliac region, the patient returned to the hospital. Tumor marker levels were as follows: carcinoembryonic antigen (CEA) 783 ng/mL, carbohydrate antigen 19-9 (CA19-9) 1731 U/mL and carcinoma antigen 125 (CA125) 5.5 U/mL. Computed tomography (CT) of the abdomen and the pelvis minor was performed, which indicated the presence of a substantially expansive, predominantly cystic change in the right parametrium (Figure 4). In September 2013, extirpation of the right adnexa with reduction of the tumor mass was performed. The histopathology confirmed metastasis of the colon adenocarcinoma into the right ovary. The patient was presented to the Committee for Malignant Diseases, which suggested that the treatment should be continued with first-line systemic chemotherapy according to the FOLFOX4 protocol (Oxaliplatin 85 mg/m^2, Leucovorin 400 mg/m^2, 5-Fluorouracil 400 mg/m^2 i.v. bolus, 5-Fluorouracil 600 mg/m^2 by continuous infusion over 23 hours; repeat every 14 days), which was started in October 2013.

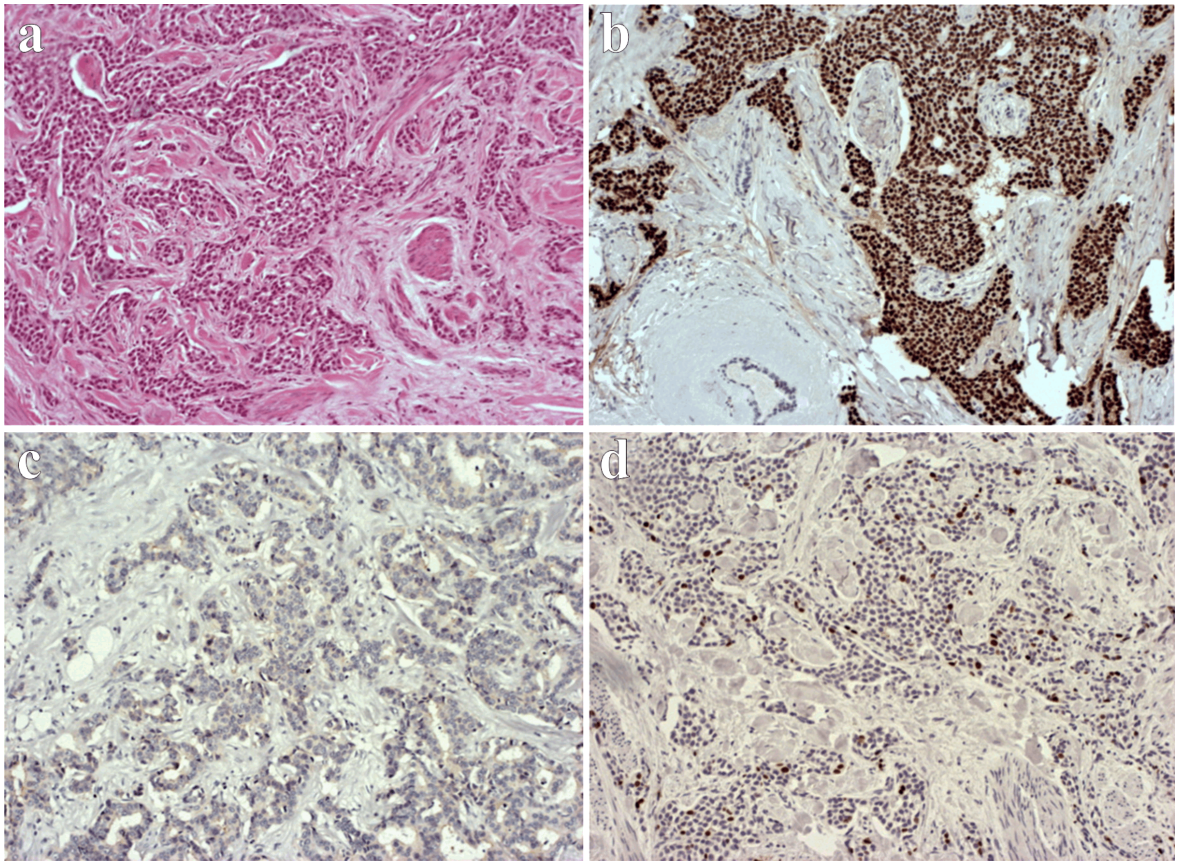

Figure 1 – ***(a) Invasive ductal breast carcinoma [Hematoxylin–Eosin (HE) staining, ×200]; (b) Tumor cells were strong positive (score 8) for estrogen receptor; (c) Complete HER-2 negative; (d) Low Ki-67 proliferation index (Immunomarking with Hematoxylin counterstaining, ×200).***

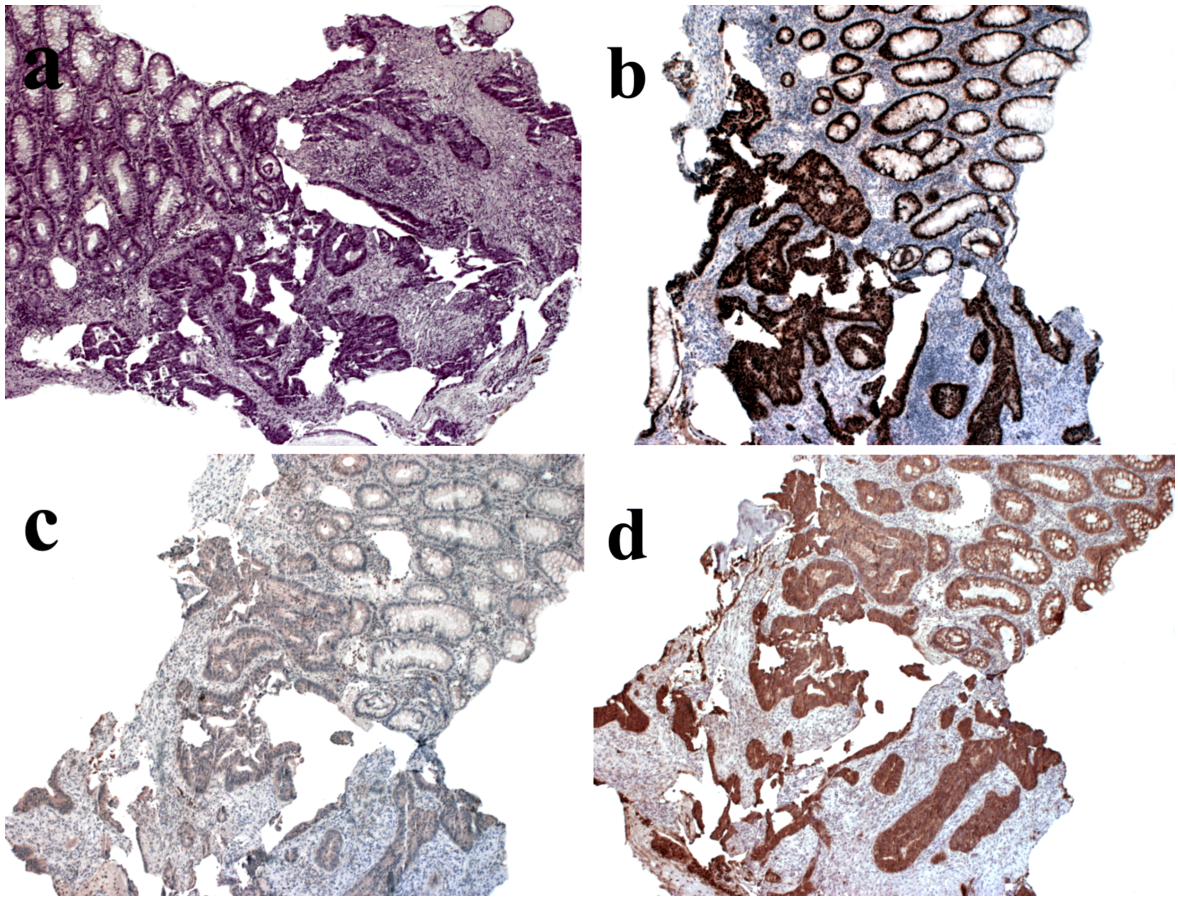

Figure 2 – *(a) Invasive colon adenocarcinoma (HE staining, ×100); (b) Tumor cells were strong nuclear positive for CDX-2; (c) Complete membrane cytokeratin (CK) 7 negative; (d) CK20 positive (Immunomarking with Hematoxylin counterstaining, ×100).*

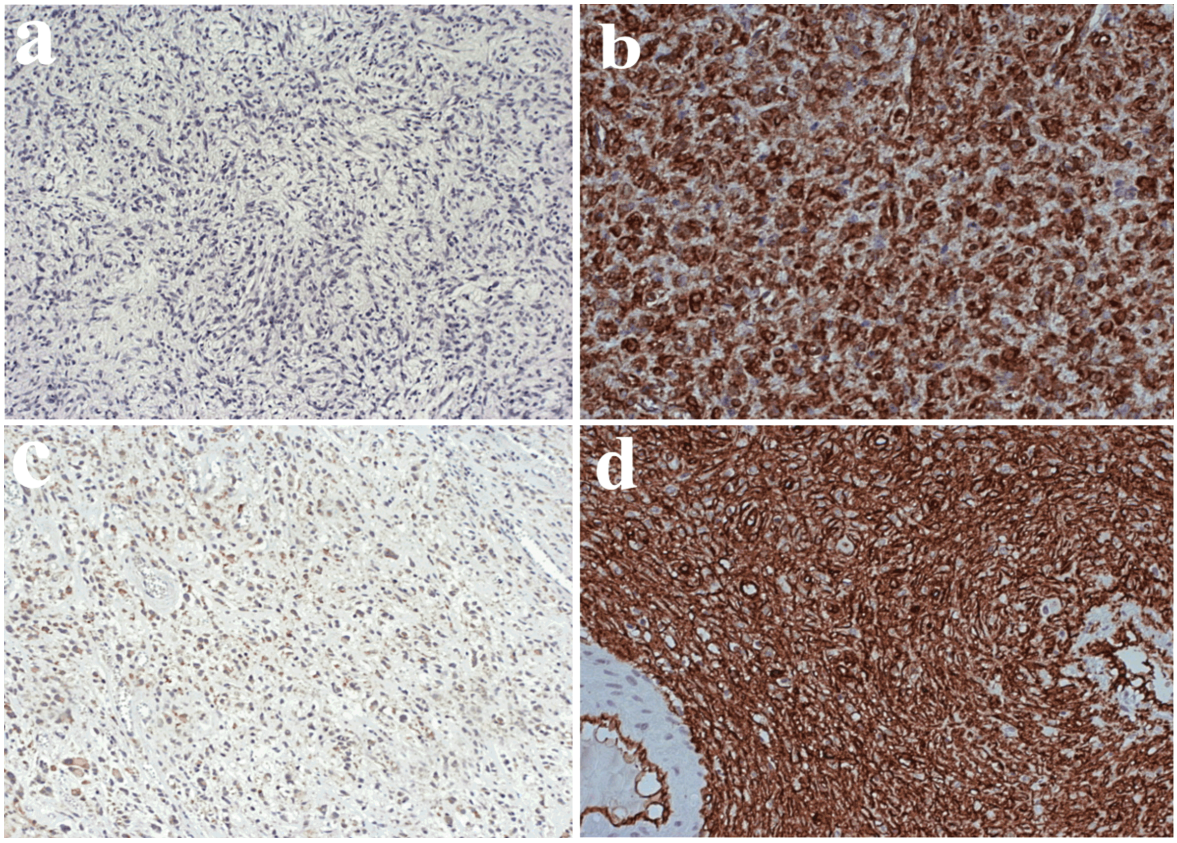

Figure 3 – *GIST diagnosis was confirmed on (a) routine HE-stained sections (×200) of the tumor tissue and (b–d) immunohistochemical analysis (×200). Tumor cells were diffuse positive for (b) vimentin, (c) CD117, (d) CD34.*

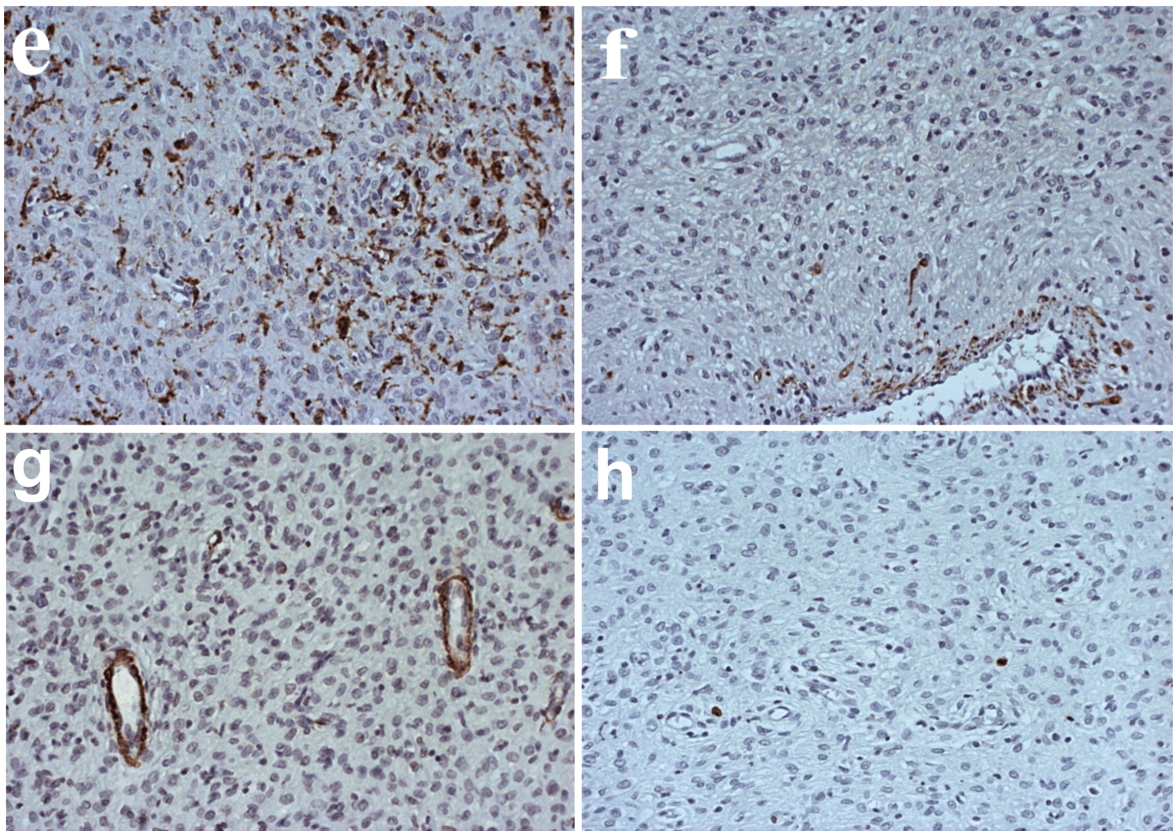

Figure 3 (continued) – ***GIST diagnosis was confirmed on (e–h) immunohistochemical analysis (×200). Tumor cells were focally positive for (f) desmin, (g) α-SMA, and negative for (e) S-100 protein and (h) Ki-67 proliferation index was very low.***

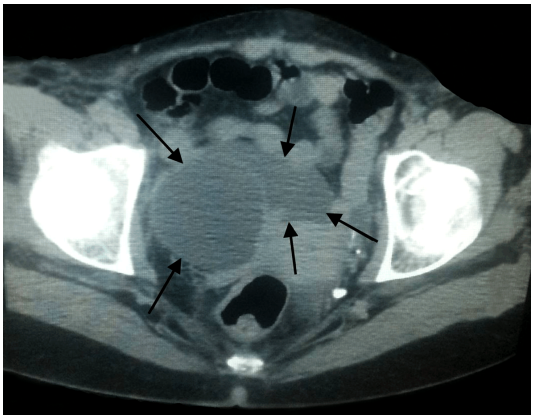

Figure 4 – ***CT of the abdomen and pelvis showing inhomogeneous tumor mass in the right parailiac region.***

In March 2014, a follow-up CT of the abdomen and the pelvis indicated that the disease was stable, and the treatment was continued according to the same chemotherapeutic regimen. However, the patient died due to metastatic colon cancer in 2015. Death occurred due to respiratory insufficiency caused by pneumonia proven by clinical, laboratory and radiographic findings.

Discussions

The present case is extremely rare since the patient has adenocarcinoma of colon with GIST in a previously diagnosed breast carcinoma. A concurrence of GISTs and adenocarcinoma was rarely described in the literature. Concurrence of breast carcinoma with GIST has also been described but sporadically [3–5]. Some authors consider the concurrence of adenocarcinoma with GIST to be based on mere coincidence, whereas others endorse a theory that unknown carcinogens provoke the proliferation and oncogenesis of both epithelial and stromal cells [5]. In 10–30% of cases, GISTs are detected as a coincidental finding during a surgical treatment conditioned by other disorders [3, 6]. The low rate of preoperative diagnostics can be ascribed to small dimensions and intramural localization of the tumors.

The concurrence of GISTs with other neoplasms was analyzed in a large study involving a total of 4777 patients with GIST [7, 8]. Patients with a diagnosed GIST concurring with two or more other primary tumors have a shorter survival compared to those patients who only have a diagnosis of GIST or GIST concurring with another tumor. However, no difference was detected in the total survival rates depending on whether the GIST was diagnosed before or after the other malignancy [9].

GIST typically demonstrates CD117 expression, usually present in 95% cases and CD34 in 40–50% cases [10]. Simultaneous expression of CD117/CD34 positivity can be in favor of appearance of concurring tumors, like the situation in this case, and such a finding can indicate a low-grade GIST [11–15]. Using more important markers for classification and according to their immunophenotype, S-100 negativity and α-SMA positivity, this case was classified as GILT type, much common type between GISTs.

Gastric GISTs can be found in all areas of the stomach, but they are most frequently located on the fundus and corpus of the stomach [16]. Tumors with this localization

are less aggressive than tumors with intestinal localization. Tumors measuring larger than 5 cm in size are associated with a greater risk of metastasis. A low mitotic rate, less than five mitoses/HPF, most frequently indicates benign clinical behavior, while GISTs with more than 50 mitoses/HPF have a high degree of malignity [17].

Tumors measuring less than 5 cm in size, with a low or very low malignity potential, were accidentally discovered during a surgical intervention or follow-up of other neoplasms, and among these patients, non-GIST was diagnosed in 13.8% of the cases analyzed in a study that include 101 GISTs [18]. The diameter of the tumor and invasion risk was lesser in patients with simultaneous GISTs and other tumors compared to the other group of patients who had only GISTs [19].

GISTs measuring 0.6–5 cm in size can be diagnosed also during staging, surgical intervention and follow-up of gastric adenocarcinoma, such in the present case.

Conclusions

Based on this case, we want to emphasize that within the clinical examination of patients with tumors, should always think about the possibility occurrence of synchronous and metachronous tumors, and not just the occurrence of metastatic diseases.

Conflict of interests

The authors declare no conflict of interest.

Patient consent

Written consent was obtained from the patient.

Acknowledgments

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