Indian Journal of Surgical Oncology
https://doi.org/10.1007/s13193-021-01352-2

CASE REPORT

Does Preoperative Diagnosis Will Change the Treatment Plan of Clear Cell Carcinoma of Endometrium Masquerading as Desmoid Tumor of Anterior Abdominal Wall?: a Case Report

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Received: 4 May 2020 / Accepted: 13 May 2021

Abstract

Clear cell carcinoma (CCC) of the female genital tract can arise in the ovary, endometrium, cervicovaginal region, in peritoneal and other extra pelvic sites. However, CCC involving anterior abdominal wall is a very rare entity. We are reporting a case of 55-year-old postmenopausal lady with ECOG PS-I with no comorbidity had history of cesarean section about 30 years back and presented with pain in abdomen at periumbilical region about 9 months back. She underwent evaluation at outside clinic with finding of an anterior abdominal wall swelling of size approximately 3 × 3 cm which was completely neglected by the patient. In the next period of 2 months, the swelling suddenly increased in size. CECT/PET CT showed a solid cystic mass involving anterior abdominal wall with possibility of desmoid tumor. We had decided to plan for surgical excision of the tumor. Intraoperatively we found that there was bicornuate uterus. The lesion was arising from one of the cornue of uterus and it was extended anteriorly to anterior abdominal wall with no ascites, no pelvic, or retroperitoneal lymphadenopathy. She underwent hysterectomy with bilateral salpingo-oophorectomy and defect was closed with bioabsorbable mesh. Final histopathology report was clear cell endometrial carcinoma mostly mullerian tract origin arising from endometriosis focus. Tumor cells were diffusely positive for PAX-8 and Napsin-A and negative for WT 1 with patchy positivity for P53 (wild type expression). She had received adjuvant chemotherapy and she is disease free after 2 years of completion of the treatment. Clear cell endometrial carcinoma arising from malignant transformation of an endometriosis focus to anterior abdominal wall is a very rare phenomenon and it is a difficult task to reach its final diagnosis.

Keywords Clear cell endometrial carcinoma · Desmoid tumor · Endometriosis · Abdominal wall · Case report

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Introduction

Clear cell carcinoma (CCC) of the female genital tract can arise in the ovary, endometrium, cervicovaginal region, in peritoneal and other extra pelvic sites. However, CCC arising in abdominal wall is a very rare event and if it is found, then there may be chances of underlying pathology of endometriosis. There are chances of endometriosis focus in the operative scar which may turn from benign to its malignant counterpart. Hense it is possible in females who had undergone surgeries like abdominal hysterectomy, cesarean section, or any surgery related to ovary, fallopian tube, uterus, and sometimes cervix or vagina [1]. This transformation is very rare and the available literature is limited. It is a very rare incidence of malignant transformation occurring in the abdominal scar and the evidences supports only 1% chances of malignant transformation from endometriosis foci [2]. We are presenting a case in

which clear cell carcinoma of endometrium is arising from scar of anterior abdominal wall post cesarean section. Clear cell endometrial cancer (CCEC) is a rare entity and accounts about less than 5% of all endometrial cancer (EC). Usually the patients who suffer are elderly and postmenopausal [3].

Case Report

A 55-year-old postmenopausal lady with Eastern Cooperative Oncology Group (ECOG) Performance Status I with no comorbidity presented to our clinic. She had history of pain in abdomen at periumbilical region about 9 months back. It was dull aching pain with no disturbance in routine activities of the patient. She had history of cesarean section twice in the past with no relevant family, past, medical and personal history. She underwent evaluation at local hospital with finding of an anterior abdominal wall swelling of size approximately 3 × 3 cm which was completely neglected by the patient. In the next period of 2 months, the swelling suddenly increased in size. Patient reported to us with this swelling (Fig. 1).

On clinical examination of abdomen, there was a large single anterior abdominal wall swelling of size 20 × 16 cm extending downwards below the pubic symphysis as lower end was not palpable and cranially about 8 cm above the umbilicus with involvement of all the quadrants of abdomen except right hypochondriac region. It was fixed and hard on palpation with some cystic component at infraumbilical region (Fig. 2). Skin was tense and shiny over cystic component and at rest of the places it was free. Systemic examination was unremarkable. Patient was already evaluated with contrast enhanced computed tomography (CECT) of abdomen and pelvis. We advised her to undergo PET CT. Both imagings were suggestive of large anterior abdominal wall lesion with possibility of getting blood supply from inferior epigastric artery with presence of bicornuate uterus and presence of bilateral normal ovaries. There was no ascites, no pelvic or retroperitoneal lymphadenopathy and no distant metastasis. Imagings were suggestive of soft tissue sarcoma or desmoid tumor of

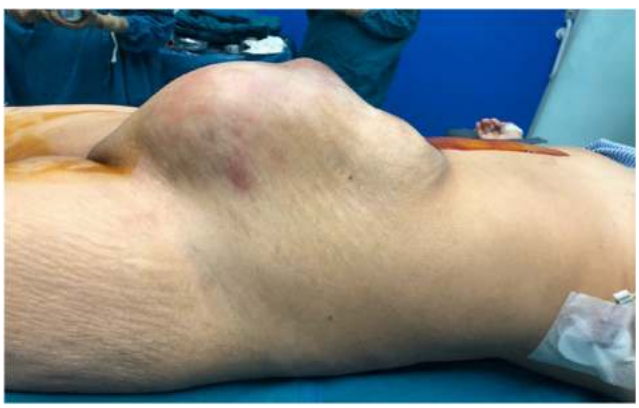

Fig. 1 Clinical presentation of abdominal wall tumor

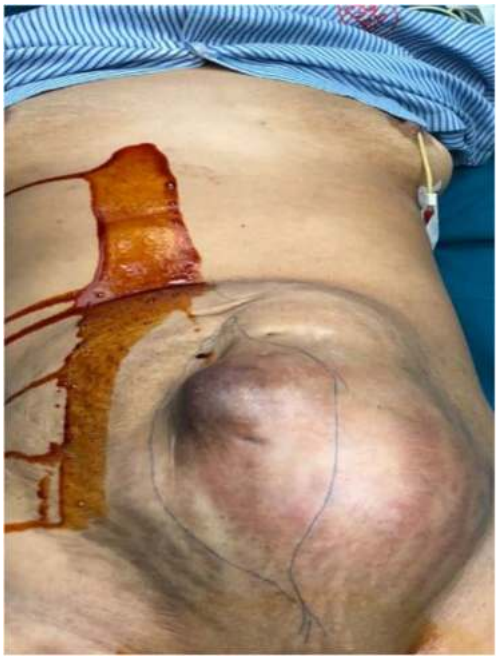

Fig. 2 Clinical presentation of abdominal wall tumor

anterior abdominal wall (Figs. 3, 4, and 5). As the radiology diagnosed it as soft tissue sarcoma or desmoid tumor, we did not go for histopathological confirmation. Therefore, we had planned and posted for surgery considering it as soft tissue lesion arising from anterior abdominal wall.

We had marked the incision as shown in the picture (Fig. 2) with determination of getting at least 2 cm circumferential tumor-free margin (Fig. 2). When we had defined the rectus sheath, we found that the lesion had intraabdominal extension. After exploring the peritoneum, the findings were presence of a bicornuate uterus and the lesion was arising from one of the cornue of uterus which was extended anteriorly to anterior abdominal wall (Fig. 6). Bilateral ovaries were normal. There was no ascites, no pelvic or retroperitoneal lymphadenopathy and no other metastatic foci. Hence, we had completed standard surgical staging with hysterectomy with B/L salpingo-oophorectomy with omentectomy with bilateral pelvic and retroperitoneal lymph node sampling as there was no lymphadenopathy. Defect was reconstructed with dual layer mesh by inlay technique. Liquid diet was started after 12 hours post surgery with gradual shift to solid food. Postoperative course was uneventful. She was discharged on 5th postoperative day.

During microscopic pathological examination of the specimen cystic areas were found adjacent to the tumor and they showed features of endometriosis. Uterus, cervix, bilateral ovaries and fallopian tubes were uninvolved by the tumor. There was no evidence of hyperplasia, atypia or malignancy in the endometrium and myometrium. Tumor cells were diffusely positive for PAX-8 and Napsin-A and negative for WT 1. There was a patchy positivity for P53 (wild type expression). Diagnosis was finalized as Clear Cell Carcinoma of

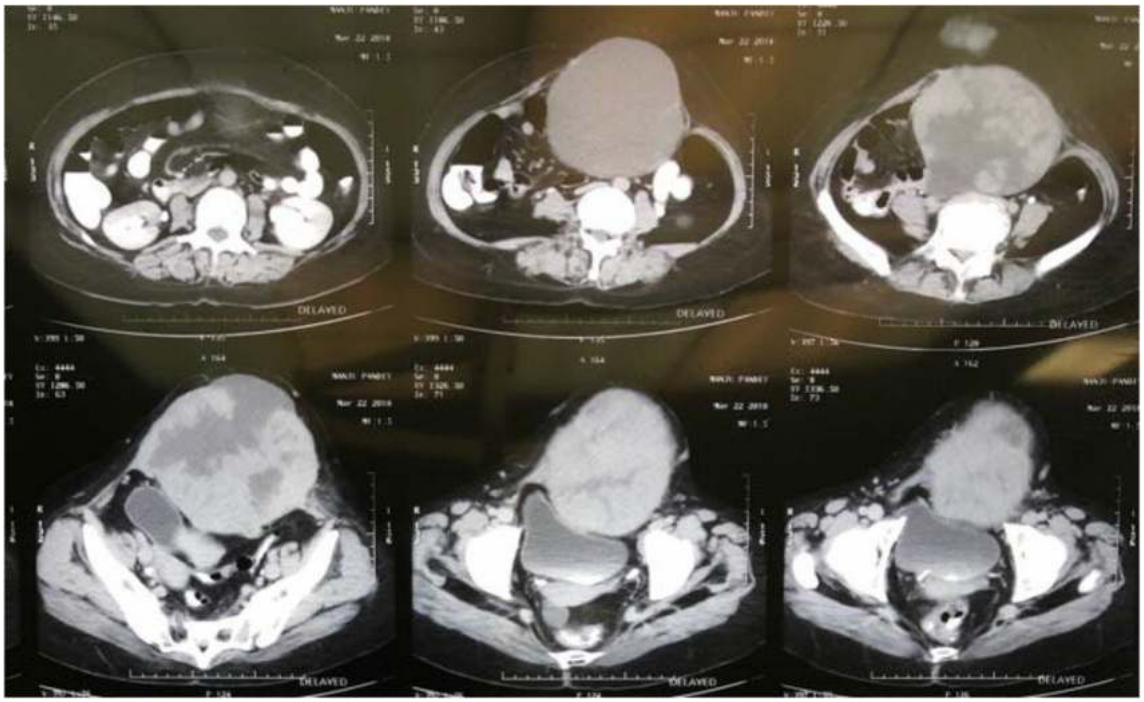

Fig. 3 CECT transverse section

Endometrium (CCEC) with Mullerian tract origin in view of presence of endometriotic cyst like foci in the vicinity of tumor possibility of its origin from endometriotic cyst (scar endometriosis) and IHC controls were found satisfactory. CCEC is a high-grade cancer and in the index case the tumor had already breached the rectus sheath with presentation as abdominal wall tumor. Considering it as stage IV CCEC, patient had been planned for adjuvant chemotherapy after discussing the case in our institutional multidisciplinary tumor board. She had been challenged with six cycles of carboplatin and paclitaxel. She had received and tolerated chemotherapy without any major adverse effects. She has been kept on periodic follow-up with us according to our institutional protocol. After 2 years of completion of treatment, she is disease free.

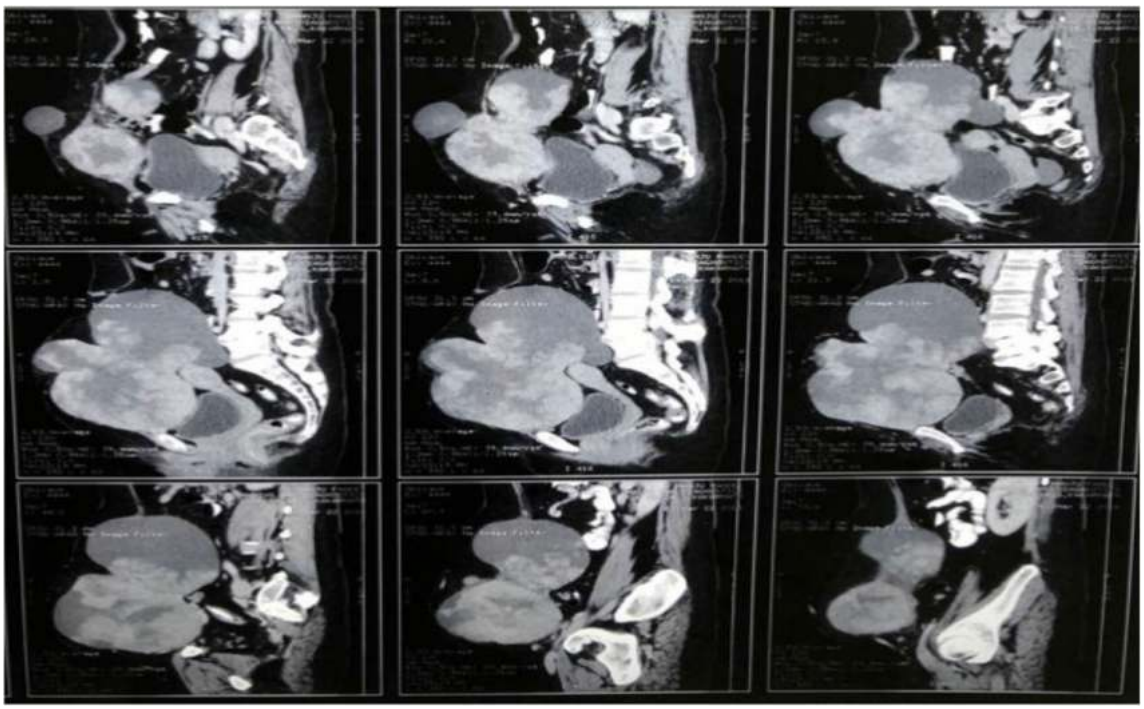

Fig. 4 CECT sagittal section

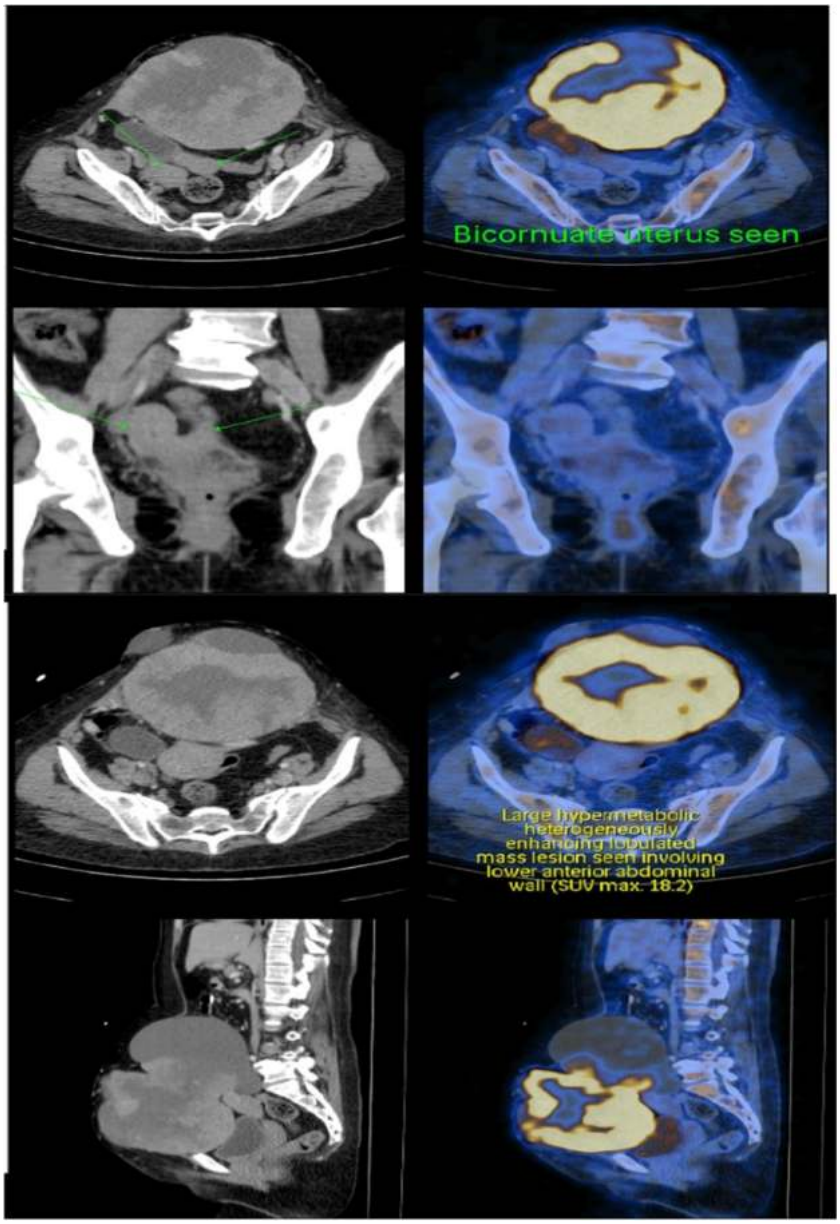

Fig. 5 PET CT images

Discussion

Already cases have been reported where endometriosis was found in the surgical scar [4]. The most common scars where these endometriosis implants were found are post hysterectomy and cesarean section. However, there are reported cases of endometriosis implants with hernia repair scar, post appendectomy, post laparoscopy trocar insertion site scar and also with episiotomy [5]. Surgical scars with endometriosis implants undergoing malignant transformation is a very rare phenomenon with the reported incidence is less than or near about 1% [6]. The most common entity found in these cases is CCC and the second entity which is found after CCC is endometrioid adenocarcinoma [7]. Some of the studies have mentioned association of malignant extraovarian endometriosis with carcinogen exposure, hyperestrogenism and some genetic alterations like loss of heterozygosity on chromosome 5q [8].

Any patient presented with malignant neoplasm with previous history of surgery in view of any obstetric or gynecological cause; the first impression should be the possibility of lesion arising from endometriosis or else other consideration should be cutaneous deposits arising from Mullerian gynecological pathology [9]. The definitive diagnosis of CCC can be achieved with the help of immunohistochemistry where a panel of markers are able to differentiate a malignancy from gynecological origin compared with other tumors with clear cells such as renal cell carcinoma (RCC) and adrenocortical carcinoma (ACC) [10]. Table 1 shows the comparative IHC panel. Therefore, clinical and radiological findings are not sufficient for diagnosing CCC. The key to final diagnosis is its

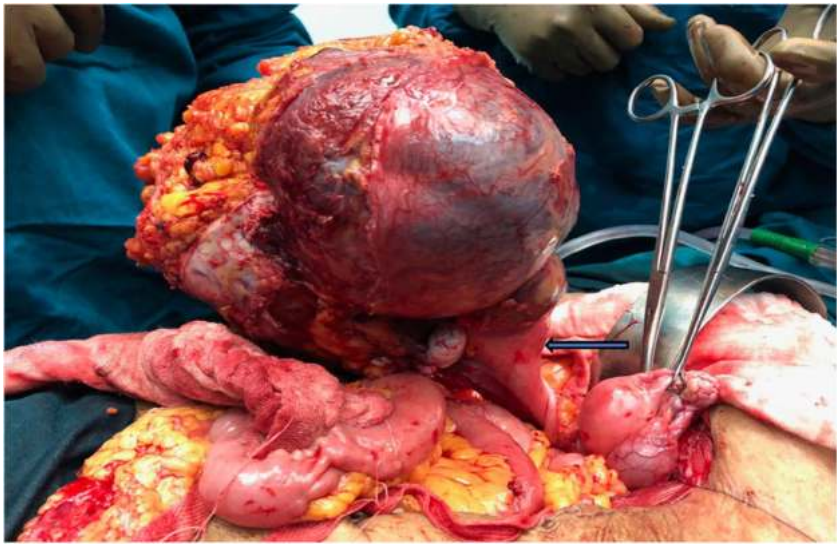

Fig. 6 Bicornuate uterus with lesion arising from one of the cornue (blue arrow)

pathological diagnosis with IHC panel under the care of expert pathologist. Clear cell ECs have other molecular subtypes. *POLE*mut clear cell ECs which has the most favorable prognosis, p53abn clear cell EC which is associated with aggressive behavior [11] and the mismatch repair (MMR) deficient EC which shows mixed morphology [12]. They are typically negative for estrogen receptor protein and positive for Napsin-A, which helps in distinguishing this form of high-grade carcinoma from Serous Endometrial Cancer. The index case tumor was also positive for Napsin-A. Histologically, Clear cell ECs present with papillary, glandular, tubulocystic and diffuse architectural patterns with psammoma bodies in up to 10% of cases [13]. In 80% of cases myometrial invasion occurs [14].

Some pathologist use the benchmark of ≥50% clear cell features to classify a tumor as a clear cell carcinoma while others use the benchmark of at least 25% clear cell component [15]. CCECs have a high tendency for lymphovascular invasion and intraperitoneal as well as extra-abdominal spread [16]. They are more commonly present at an advanced stage. One multi institutional review study found that about 50–70% of patients of CCEC present with stage III or IV disease [17]. The principle of surgical treatment is optimal cytoreduction and the strongest predictor of overall survival is the amount of residual disease following surgery [18]. Surveillance, Epidemiology and End Results (SEER) United States National Cancer Database between 1988 and 2001 had shown that the 5-year disease-specific survival rate for CCEC was 68% and it is 80% according to latest survival data from the International Federation of Gynecology and Obstetrics [19]. The rate of recurrence of CCEC (with distant spread) is more as compared to endometrioid cancers or uterine serous carcinomas [20]. As it was stage IV cancer, we addressed her with adjuvant chemotherapy and she had been challenged with carboplatin plus paclitaxel chemotherapy. The evidence for this regimen is based on the results of Gynecologic Oncology Group (GOG)-209, which were presented at the 2012 Society of Gynecologic Oncology Annual Meeting [21]. The trial demonstrated that carboplatin and paclitaxel results in an equivalent overall response rate, similar progression-free survival and is less toxic.

In the current situation, treating clinicians are still facing the challenge of diagnosing malignant transformation of abdominal wall endometriosis. We have reviewed the recent cases reported in the last 4 years (Table 2). Most of the cases had previous history of cesarean section with coexistent history of endometriosis. It proves that there are no specific signs and symptoms or availability of any markers for ruling out this malignant transformation and imaging may be misleading. In the index case also imaging was suggestive of abdominal wall desmoid tumor and no malignant transformation was suspected in the preoperative set up hence, we proceeded with surgery.

Table 1 Comparative immunohistochemical markers

Diagnosis	Immunohistochemical markers
Mullerian clear cell carcinoma	Napsin-A, racemase, hepatocyte nuclear factor (HNF-1b)
High-grade serous carcinoma	WT1, p53
Clear cell renal cell carcinoma	CA-IX, RCC antigen, EMA, CD10
Adrenocortical carcinoma	SF-1, Melan-A, calretinin, S100, inhibin

Table 2 Recently reported case studies

Author	Year	Age	Previous surgery	Coexistent endometriosis	Follow-up (months)	Outcome
Lie et al. [22]	2014	39	CS	Yes	10	DOD
Sosa-Duran et al. [23]	2015	45	CS	Yes	16	NED
Aust et al. [24]	2015	47	CS	No	10	NED
Wei and Huang [25]	2017	46	CS	Yes	3	NED
Ferrandina et al. [6]	2016	44	CS	Yes	6	DOD
Marques [26]	2017	47	CS	Yes	36	NED
current case	2018	55	CS	No	24	NED

CS, cesarean section; *NED*, no evidence of disease; *DOD*, died of disease)

When we presented this case in our monthly oncology meet, the issue of preoperative biopsy was raised and again the question was raised if the tissue diagnosis was done in the preoperative period what are the benefits, efficacy or response of neoadjuvant chemotherapy in case of CCEC presenting as abdominal wall desmoid tumor. We will be able to answer this question in near future with the availability of randomized control trial or prospective data base study.

Conclusion

Clear Cell Carcinoma of Endometrium (CCEC) is a high-grade malignancy and its diagnosis is difficult. The incidence of CCEC arising from abdominal wall is very rare. Whenever there is an increasing abdominal wall mass or increasing pain associated with history of previous surgical scar, the diagnosis of CCEC should be considered as one of the differential diagnosis.

Data Availability Not applicable.

Declarations

Ethics Approval and Consent to Participate Not applicable.

Conflict of Interest The authors declare no competing interests.

Human Subject Informed consent was obtained from the patient for being included in the study.

Financial Relationships All authors have declared that they have no financial relationships at present or within the previous 3 years with any organizations that might have an interest in the submitted work.

Other Relationships All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

Consent for Publication An informed consent to publish this case was obtained from the patient.

Clinical Trial Transparency Not applicable

Guarantor of submission The corresponding author is the guarantor of submission.

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