Is clear cell carcinoma of abdominal wall surgery scar associated with endometriosis a poor prognosis? A case report and literature review

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Case report

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Abstract

Background

Clear cell carcinoma of abdominal wall surgery scar is a rare condition that can have many potential causes, and its early diagnosis is difficult after undergoing obstetrical and gynecological surgery unless performing tumor biopsy. So far, about 45 cases have been reported in the literature. This paper provides a case report and literature review of clear cell carcinoma on abdominal wall surgical scar.

Case presentation

We described the case of a 47-year-old woman reporting two lumps in the scar of abdomen. Her medical history was marked by a previous Caesarean section and two excisions of benign endometriosis nodules at the scar. Physical examination found a mass of about 6×5×5 cm on the left side of the scar with mucoid on the surface and a fixed abdominal wall mass of about 10×10×8 cm in the 2 transverse fingers under the umbilicus. Histological examination proved a clear cell carcinoma result. The patient received tumor excision and first-line chemotherapy with complete remission. A review of the literature showed that 91.3% of the cases had had a Caesarean section. Besides, approximately 34.2% of women died 5–48 months after diagnosis. The average age of women was 46.5 years and the average tumor size was 10 cm.

Conclusion

The abdominal wall mass of middle-aged women is closely related to the scar left by the previous Cesarean section and must be investigated in time and properly. Preoperative diagnosis is difficult and often incorrect, and there is no specific marker for malignant transformation. Treatment usually includes surgery, chemotherapy, and radiotherapy, but the prognosis is poor.

Background

The incidence of scar endometriosis in abdominal surgery is between 0.03% and 1.08% in women undergoing pelvic surgery [1, 2]. Abdominal wall endometriosis caused by incisions is an often neglected disease [3]. Scar endometriosis is usually caused by the implantation of endometrial tissue into the soft tissue of the abdominal wall during surgery. Symptoms of endometriosis in abdominal surgical scars in obstetrics and gynecology include slowly developing lumps in or near the scar, as well as pain and abdominal swelling during menstruation. However, malignant transformation of abdominal wall endometriosis is very rare, including sarcomatoid degeneration [4], serous papillary carcinoma [5, 6], rhabdomyosarcoma [7] as well as clear cell carcinoma (CCC). The most common histological type is CCC [8]. CCC caused by endometriosis is an invasive disease with a poor prognosis, with a 5-year survival rate of about 40% [8]. Diagnosis is challenging because the disease develops slowly and has no specific markers of malignant transformation.

Here we report a patient with CCC of the abdominal wall at the scar site of a previous Cesarean section (CS). Besides, we reviewed the existing English literature on transparent clear cell carcinoma caused by endometriosis in the abdominal wall and compared the clinical features of abdominal wall masses of different sizes.

Case Presentation

A 47-year-old woman, grava 4, para 3, abortion 1, presented with two big abdominal masses, which were gradually enlarging after 2 previous excisions of an endometriotic nodule in a CS scar. This patient underwent a CS in 2001 due to fetal distress and transverse position. The CS procedure was successful, with no postoperative discomfort such as abdominal pain, abdominal distension, and the menstruation is regular. Early in 2017, she noticed a small mass of about 1 cm in right lower abdominal scar without menstrual period pain and itching. She underwent abdominal endometriosis mass resection in May 2017. During the operation, the boundary between the mass and abdominal wall tissue was not clear, and a mesh was placed to repair the abdominal wall. The mass containing chocolate-like fluid with a hard texture. The pathology of the nodule was reported as endometriosis with decidual degeneration. The mass in the abdominal wall is consistent with the adenomatoid tumor. Microscopically, a large amount of dilated cystic cavity was seen in the fibrous tissue, which was lined with a single layer of epithelium, which was flat or cuboidal cells, and interstitial mucus degeneration. Immunohistochemical stains included CKp (+), CK7 (+), ER (+), PR (-), CK (5/6), CR (+/-), D2-40 (+/-), CD34 (-), Ki-67-LI (10%).

At the beginning of 2018, the patient again realized that she could touch the mass in the right lower abdominal scar, which was about 3 cm in size. During exercise, the lower abdomen occasionally felt slight pain, relieved with rest, and had nothing to do with the menstrual cycle. The abdominal mass gradually increased. In November 2019, she underwent excision of abdominal wall endometriosis and mesh repair because of abdominal wall mass. Postoperative pathology showed that endometriosis with deciduous degeneration. She was then given a subcutaneous injection of Leuprorelin for the purpose of preventing recurrence. However, the size of the right lower abdominal mass remained enlarged, and a similar painless mass, about 2×1×1 cm, was also found in the scar of the left lower abdominal CS in April 2020. She didn't experience any pain at the scar during menstruation. She did not visit a doctor until the mass gradually enlarged and protruded the abdominal epidermis with broken ulcer and mucous bloody secretions in September 2020. She was then referred to our hospital for further management. At this time, physical examination revealed a 12 cm transverse shape of the CS scar of the lower abdomen. A purplish-black mass of about 6×5×5 cm can be seen on the left side of the scar with mucoid on the surface. A hard mass of about 10×10×8 cm can be palpated in the 2 transverse fingers under the umbilicus. Pelvic examination showed a normal-sized uterus

and lateral adnexa. A biopsy from the mass in combination of immunohistochemical examination confirmed a pathology of endometriosis-associated CCC.

The preoperative pelvic magnetic resonance imaging (MRI) showed that the parenchyma of the tumor showed equal T1 and long T2 signal intensity, with a clear boundary, and the larger one was 6.2x3.6x4.2 cm (Fig. 1A-C). No obvious enhancement was found on contrast-enhanced scan after injection of contrast agent. There was no abnormality in the uterus, bilateral adnexa, and no enlarged lymph nodes in the pelvis. Ultrasound scan showed normal liver, spleen, pancreas, kidneys, and no mass in the abdominal cavity. Hence, a multidisciplinary team including dermatology, gynecologic oncology, gastrointestinal glandular surgery, and plastic surgery department made a treatment plan for the patient preoperatively. During operation, gross complete excision with a surgical margin of 1 cm beyond the lesion of the abdominal wall including the rectus abdominis muscle, together with an abdominal wall reconstruction was performed (Fig. 2A-C, Fig. 3A, Fig. 4A and B). It can be seen that the tumor infiltrated part of the fascia and rectus abdominal tissue, the bottom of the tumor reached the peritoneum and protruded to the abdominal cavity, and part of the omentum majus, intestine adhered to the peritoneum. No abnormality was found in the uterus and bilateral adnex, omentum and intestine. The pelvic lymph nodes were not enlarged. After separating the abdominal wall mass, the defect of fascia, rectus abdominis, and peritoneum on the right side of the wound could be seen, with an area of 15X13cm. Considering the large defect of rectus abdominis and peritoneum, mesh repair was performed (Fig. 3B.C). Hysterectomy and bilateral salpingo-oophorectomy were not performed. The operation time was 300 minutes, of which 160 minutes were resected and 140 min was reconstructed. There were no intraoperative complications. The blood loss was estimated to be 200 mL. Pathologic examination of resected abdominal wall lesion showed CCC under the background of endometriosis with clear resection margins (Fig. 5). The patient was referred to plastic surgery for further care due to the huge surgical wound for 18 days. Chemotherapy with paclitaxel liposome and carboplatin regimen was conducted on day 19 and she was discharged on postoperative day 20. A month later, she returned to the hospital on time for chemotherapy, with no signs of recurrence. She is still closely followed up during the preparation of the manuscript.

Discussion

The diagnosis of malignant transformation of abdominal endometriosis is still a challenge for gynecologists. There are no characteristic symptoms and markers in the process of carcinogenesis. The best treatment for malignant transformation of abdominal endometriosis is not clear. We searched the articles published from September 1986 to December 2020 by Medline and EMBASE, and the search words were combined into medical subject entries. The keywords used for the search are as follows: "abdominal wall endometriosis" and "clear cell carcinoma". All relevant articles were retrieved and the list of relevant references was systematically reviewed to determine further reports that could be included in this analysis. Besides, reviews of cancer and endometriosis published over the same period were reviewed and their reference lists were searched for potential additional studies. We used SPSS 23.0 statistical software for statistical analysis. The unpaired t-test of continuous variables and the chi-square test of classified variables were used in the comparison between groups. GraphPad's Kaplan-Meier estimation was used for survival analysis.

Finally, we included 45 patients in our systematic retrospective analysis, including 44 from the literature review and 1 from our organization. All of them reported that endometriosis was associated with malignant transformation of the surgical scar. The characteristics of the patients are shown in Table 1. As shown in Fig. 6, it is more common than previously reported, especially if we consider the increasing rate of CS in western countries [9]. The average age of the patients at the time of diagnosis was 46.5 years (range from 37 to 60), which was consistent with the retrospective analysis of Endometriosis-associated malignant transformation in an abdominal surgical scar by Mihailovici et al. [8]. Fifteen cases (33.3%) had a history of endometriosis and 28 cases (62.2%) had never been diagnosed with endometriosis before admission (2 cases were not clear). The average delay from the first operation to diagnosis was 17.9 years (standard deviation 6.6). CCC is related to uterine surgery, mainly the CS. Forty-two cases (91.1%) had at least one CS, of which 15 cases had 2 CS s, 6 cases had 3 CSs, and 4 cases (8.9%) had undergone other gynecological operations, usually CS (Table 2). At least one excision of scar endometriosis was performed in 9 cases, including our case.

Table 1
Summary of studies included in the review.

Author	Year	Age	Delay from first gynecological surgery(yr)	Onset of symptoms(m)	Lump size(cm)	Surgery	Pathology	Patient outcome			
								Follow-up time (m)	Relapse	Follow-up time (m)	Death
Giannella [15]	2020	45	15	3	20	no	CCC	NA	yes	7	yes
Behbehani[20]	2019	48	NA	5	7	yes	CCC	NA	NA	NA	NA
Tsuruga [12]	2019	49	15	3	5	yes	CCC + EC	4.5	no	NA	NA
Rivera [19]	2019	48	NA	NA	7	yes	CCC	2	no	NA	NA
Lopes [10]	2019	48	12	84	12	yes	CCC	3	no	NA	NA
Lai [23]	2019	56	NA	396	6.5	yes	CCC	3	yes, Inguinal LN	11	yes
Lai [23]	2019	56	NA	252	12	yes	CCC	NA	NA	5	yes
Lai [23]	2019	45	NA	240	4.8	no	CCC	7	yes, Abd. wall, inguinal LN	7	yes
Gentile[26]	2018	42	7	8	10.6	yes	CCC	2	no	NA	NA
Mihailovici [8]	2017	47	22	264	11	yes	CCC	NA	NA	NA	NA
Wei [24]	2017	46	18	2	9.5	yes	CCC	3	no	NA	NA
Marques [27]	2017	47	24	3	8	yes	CCC	45	no	NA	NA
Kostrzeba [28]	2017	58	38	NA	25	yes	CCC	3	no	NA	NA
Graur[29]	2017	43	22	7	8.5	yes	CCC	11	no	NA	NA
Ferrandina [16]	2016	44	9	8	22	yes	CCC	5	yes, liver	6	yes
Sosa-Durán [30]	2015	45	NA	8	9	yes	CCC	16	no	NA	NA
Ruiz [11]	2015	41	20	NA	14.8	yes	CCC	6	yes, local	NA	NA
Ruiz [11]	2015	57	30	9	19.4	yes	CCC	NA	no	NA	NA
Aust [31]	2015	47	16	6	10	yes	CCC	10	no	NA	NA
Liu[32]	2014	39	10	60	6	yes	CCC	10	yes, local	12	yes
Heller [33]	2014	37	8	96	18	yes	CCC	5	yes,	NA	NA
Dobrosz [34]	2014	42	NA	16	NA	yes	CCC	NA	NA	NA	NA
Ijichi [35]	2014	60	37	48	4	yes	CCC	8	yes, local	23	no
Shalin [36]	2012	47	NA	10	3	yes	CCC	7	no	NA	NA
Sawazaki [17]	2012	41	18	NA	4.8	yes	CCC	4	no	NA	NA
Mert [37]	2012	42	NA	NA	17.8	yes	CCC	26	no	NA	NA
Mert [37]	2012	51	8	12	7	yes	CCC	49	no	NA	NA
Li [38]	2012	49	26	25	9	yes	CCC	8	no	NA	NA
Yan [21]	2011	41	5	4	6.3	yes	CCC	24	no	NA	NA
Bourdel [39]	2010	43	20	60	9	yes	CCC	6	yes	22	yes
Williams [40]	2009	53	24	4	4.7	yes	CCC	3	yes, local, InguinalLN, lung	11	yes
Matsuo [41]	2009	37	10	5	14	yes	CCC	24	yes, local	NA	NA

Author	Year	Age	Delay from first gynecological surgery(yr)	Onset of symptoms(m)	Lump size(cm)	Surgery	Pathology	Patient outcome			
								Follow-up time (m)	Relapse	Follow-up time (m)	Death
Rust [42]	2008	42	NA	24	4.9	yes	CCC	NA	NA	NA	NA
Barts [18]	2008	38	13	151	11	yes	CCC	8	yes	NA	NA
Achach [43]	2008	49	20	NA	8.5	yes	CCC	6	yes, bladder and pelvic bone	NA	NA
Razzouk [22]	2007	46	26	NA	17	yes	CCC + EC	3	yes, liver	6	yes
Harry [44]	2007	55	NA	15	4	yes	CCC	18	no	NA	NA
Sergent [45]	2006	45	25	17	20	yes	CCC	NA	yes	6	yes
Alberto [46]	2006	38	11	6	6	yes	CCC	NA	NA	NA	NA
Ishida [47]	2003	56	24	7	10	yes	CCC	NA	yes, lung, bone and brain	48	yes
Park [48]	1999	56	24	NA	5	yes	CCC	NA	NA	NA	NA
Miller [49]	1998	38	9	8	4	yes	CCC	60	no	NA	NA
Hitti [50]	1990	46	14	NA	6	yes	CCC	30	no	NA	NA
Schnieber Agner-Kolb [51]	1986	40	15	18	NA	yes	CCC	NA	yes	18	yes
our case	2020	49	19	204	6.3	yes	CCC	1	no	NA	NA

Table 2
Characteristics of patients.

		n	Percentage
Age(yr)	46.5 ± 4.9		
	31–40	7	15.22%
	41–50	28	60.87%
	51–60	10	21.74%
Previous gynecological surgery	1C	20	44.44%
	2C	15	33.33%
	3C	6	13.33%
	other surgeries	4	8.89%
Delay from fist gynecological surgery (yr)	17.9 ± 6.6		
	0–10	7	20.59%
	11–20	15	44.12%
	21–30	10	29.41%
	31–40	2	5.88%
Onset of symptoms(yr)	4.4 ± 5.2		
	0–1	19	52.78%
	1–2	6	16.67%
	2–10	6	16.67%
	10–33	5	13.89%
Follow-up time (m)	15.0 ± 11.5(1–60)		

Because some literature did not specify the time of the events, the results of the delay from fist gynecological surgery,onset of symptoms, and follow-up time only counted the cases with specific years.

As for tumor markers, CA 125 was detected in 24 cases before the operation. 14 cases were in the normal range (0-35U/mL), 10 cases were higher than the normal range, and the highest was 3157.9U/mL [10]. The preoperative detection of CEA,7 was in the normal range in 9 cases, above the normal range in 2 cases, up to 96.5 μg/L [11]. CA 199 was detected in 12 cases before treatment, and above the normal range in 4 cases, up to 222 μg/L [12]. (**Table S1**).

Previously, only 15 patients had a history of endometriosis (44 patients had available information) and 12 patients had no abdominal masses before diagnosis without any intermittent, periodic, or persistent pain. But all patients had palpable abdominal surgical scar masses with an average diameter of 10.0 cm (standard deviation 4.4 cm), up to 25 cm. The pathological results of the mass are shown in Table 3. The most common histological type is CCC, in 43 cases (95.6%), followed by CCC with endometrioid carcinoma in 2 cases (4.4%). Of these, only 22 cases (51.2%) found coexisting endometriosis implants (Table 3). In these cases, additional samples for a thorough search for residual lesions of endometrial glands were not all successful. In 1925, Sampson [13] put forward the criteria for the diagnosis of malignant transformation of endometriosis: (a) benign and neoplastic endometrial tissue were shown in the tumor at the same time; (b) histology was compatible with the origin of the endometrium; (c) no other primary tumor sites were found. Besides, Scott proposed the fourth criterion in 1953 [14], that was, (d) the morphological manifestation of benign endometriosis adjacent to malignant tissue is a prerequisite for judging malignant tumors originating from endometriosis. In the current situation, the first three criteria of the reported cases have been met, but the fourth criteria may not be met, which may be the result of the complete replacement of normal tissue due to the proliferation of a large number of tumors.

Table 3
Pathological characteristics of lumps.

Tumor size(cm)		Histology				Coexisting endometriosis			
Average	Range	CCC		CCC + EC		yes		no	
		Case(n)	Percentage	Case(n)	Percentage	Case(n)	Percentage	Case(n)	Percentage
10.0 ± 4.4	(3,25)	43	95.60%	2	4.40%	22	51%	23	49%
CCC: clear cell carcinoma, EC: endometrial cancer.									
Because some literature did not specify the pathological characteristics of lumps, the results of Pathological characteristics of lumps only counted the cases with specific results.									

Also, we classified the tumor into large masses and small masses by 10 cm in diameter. The correlation between mass size and clinical features was shown in Table 4. The results suggested that patients with abdominal masses larger than 10 cm had more symptoms of abdominal pain before admission than those with small masses, and complained more about the pain caused by palpable masses (P = 0.015). There was no significant difference in other characteristics (P > 0.05).

Table 4
The correlation between mass size and clinical features.

Clinical data	L-SE (8 cases)	S-SE (16 cases)	P
Mean age (yr) (range)	47.8 (38–57)	46.8(38–60)	NS
No. of gynecological sugeries (range)	1.3 (1–3)	1.5(1–3)	NS
Delay from first surgery(y)	14.8 ± 7.7	18.0 ± 8.3	NS
Onset of symptoms (m)	66.5 ± 74.9	34.6 ± 39.9	NS
pain	7	8	0.015
no pain	1	8	
L-SE: Large scar endometrioma(≥10cm); S-SE: Small scar endometrioma; NS: Not significant.			
NS: not significant.			

In terms of treatment, four patients received preoperative neoadjuvant chemotherapy (mainly platinum-based) [15–18], and one of them did not consider radical surgery because of the rapid progression of multiple metastases throughout the body [15]. Six patients were trying to treat vaginal estradiol medroxyprogesterone injection, leuprolide acetate, gestrinone, riptorelin, leiprim [10, 19–22], including our case, but the effect was not satisfactory. Surgery is the main treatment for the most of patients. The first-stage operation was performed based on extensive resection of the tumor and extensive abdominal tissue. Two cases were not treated surgically because of multiple metastases throughout the body and the rapid progression of the disease [15, 23]. Due to the extent of the fascia defect, 22 patients (47.8%) used mesh to reconstruct the abdominal wall (including our case]. Other regular operations include hysterectomy (27 cases, 60.0%) and/or salpingectomy (29 cases, 64.4%), and / or lymph node dissection (14 cases, 30.4%) and/or omental resection (15 cases, 33.3%). Although radical surgery is a major part of the treatment of all patients, our case did not performe hysterectomy and bilateral salpingo-oophorectomy plus pelvic lymphadenectomy, because no signs of the above organs were involved. Another reason is that we plan to perform postoperative radiotherapy for the patient after chemiotherapy. The follow-up adjuvant therapy is mainly chemotherapy, usually platinum and paclitaxel drugs. Twenty-nine cases (64.4%) received 1–9 cycles of adjuvant chemotherapy. However, due to the poor individual characteristics and compliance, adverse reactions, or partial reactions to the treatment, the treatment is interrupted and the efficacy of chemotherapy is difficult to evaluate. Only 16 patients (34.8%) received radiotherapy after surgery and chemotherapy (**Table S1**).

The above patients obtained the latest clinical follow-up information currently available, and eventually, 38 patients were able to know the outcome (**Table S1**). The follow-up time of the above patients ranged from 1 to 60 months, with an average of 15.0 months. 34.2% of women (13/38) died between 5 and 48 months after diagnosis. As shown in the Kaplan-Meier survival curve (Fig. 7), the median survival time is 48 months and the five-year survival rate is 35%. Seventeen patients were reported to relapse. The sites of recurrence were local (5 cases), lymphatic metastasis (3 cases, all inguinal lymph nodes) [15, 20, 24], distant metastasis (4 cases of liver, 2 cases of lung, 2 cases of brain, and 2 cases of bone). Univariate Cox regression model showed that the prognosis of patients with metastasis (17 cases, 17/37, Of the 38 cases with a specific follow-up period, one death was excluded because it was not known whether there was metastasis.) was worse than that without metastasis (20 cases, 20/37), as shown by Kaplan-Meier curve (Fig. 8), suggesting that metastasis invasion is a poor prognostic factor affecting patient survival. This is consistent with Taburiaux's study [25].

At present, there is no multicenter RCT in the study of abdominal CCC. However, we can put forward some general directions for future treatment and research, and emphasize several findings that seem to appear from our data: (a) abdominal wall scar CCC appears in relatively young women and is an invasive disease with a poor prognosis, with a 5-year survival rate of about 35%. (b) it is an iatrogenic disease of abdominal wall scar formation after

gynecological surgery, and CS is the most common. (c) the progression of the disease was slow, and the average time of diagnosis was 17.9 years after the first gynecology and obstetrics operation. In this case, it often relapses to benign nodules of endometriosis, and sometimes patients undergo repeated surgery. (d) the size of the tumor was large at the time of diagnosis, and most of them needed extensive surgical repair of abdominal wall defects. (e) the use of progesterone or gonadotropin-releasing hormone analogs (GnRH-a) before surgical treatment is limited to the number of cases, and the effects are not clear.

The limitation of the review lies in the rarity of the disease, resulting in data collection based only on case reports, with heterologous information from different specialties. This leads to a lack of useful data, which limits statistical analysis. Although we have carried out a lot of statistical analysis, no clear results have been obtained. However, the results of this analysis can guide us to better understand the CCC risk factors and optimal treatment of abdominal wall endometriosis.

Conclusion

The transformation of abdominal endometriosis to CCC is a rare and little-known complication, but invasive surgical resection with a safe margin in combination with lymph node dissection is still the most effective and survival treatment. The role of adjuvant therapy is still unclear, so further research is needed to assess the long-term benefits. Our case did not undergo radical hysterectomy and lymphadenectomy because there was no local, lymph node and distant metastasis, and planned follow-up radiotherapy and chemotherapy. Of course we need to long term and closely follow up to investigate if lymphatic metastasis and distant metastasis occurred, including liver, lung, brain and bone metastasis.

Abbreviations

CS: cesarean section; CCC: clear cell carcinoma; MRI: magnetic resonance imaging.

Declarations

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Author Contributions

Liang XZ and Zeng H wrote the first draft of the manuscript, Tang Z and Liao JJ participated in the patient's management; Liang XZ and Fan JT performed the literature review; Fan JT performed radiological diagnosis and supervised the patient's management, critically revised the paper and gave a scientific contribution.

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Ethics approval and consent to participate

Approval of the Ethics Committee of the First Affiliated Hospital of Guangxi Medical University was obtained for this study, and the patient signed informed consent form.

Consent for publication

The patient signed consent for publication.

Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated.

Competing interests

The authors declare that they have no competing interests

References

1. Kocakusak A, Arpinar E, Arikan S, Demirbag N, Tarlaci A, Kabaca C: **Abdominal wall endometriosis: a diagnostic dilemma for surgeons.***Med Princ Pract* 2005, **14:**434-437.
2. Van Gorp T, Amant F, Neven P, Vergote I, Moerman P: **Endometriosis and the development of malignant tumours of the pelvis. A review of literature.***Best Pract Res Clin Obstet Gynaecol* 2004, **18:**349-371.
3. Nirula R, Greaney GC: **Incisional endometriosis: an underappreciated diagnosis in general surgery.***J Am Coll Surg* 2000, **190:**404-407.

4. Leng J, Lang J, Guo L, Li H, Liu Z: **Carcinosarcoma arising from atypical endometriosis in a cesarean section scar.***Int J Gynecol Cancer* 2006, **16:**432-435.
5. Da Ines D, Bourdel N, Charpy C, Montoriol PF, Petitcolin V, Canis M, Garcier JM: **Mixed endometrioid and serous carcinoma developing in abdominal wall endometriosis following Cesarean section.***Acta Radiol* 2011, **52:**587-590.
6. Fargas Fabregas F, Cusido Guimferrer M, Tresserra Casas F, Baulies Caballero S, Fabregas Xaurado R: **Malignant transformation of abdominal wall endometriosis with lymph node metastasis: Case report and review of literature.***Gynecol Oncol Case Rep* 2014, **8:**10-13.
7. Nezhat C, Vu M, Vang N, Ganjoo K, Karam A, Folkins A, Nezhat A, Nezhat F: **Endometriosis Malignant Transformation Review: Rhabdomyosarcoma Arising From an Endometrioma.***JSLS* 2019, **23**.
8. Mihailovici A, Rottenstreich M, Kovel S, Wassermann I, Smorgick N, Vaknin Z: **Endometriosis-associated malignant transformation in abdominal surgical scar: A PRISMA-compliant systematic review.***Medicine (Baltimore)* 2017, **96:**e9136.
9. Francica G: **Reliable clinical and sonographic findings in the diagnosis of abdominal wall endometriosis near cesarean section scar.***World J Radiol* 2012, **4:**135-140.
10. Lopes A, Anton C, Slomovitz BM, Accardo de Mattos L, Marino Carvalho F: **Clear cell carcinoma arising from abdominal wall endometrioma after cesarean section.***Int J Gynecol Cancer* 2019, **29:**1332-1335.
11. Ruiz MP, Wallace DL, Connell MT: **Transformation of Abdominal Wall Endometriosis to Clear Cell Carcinoma.***Case Rep Obstet Gynecol* 2015, **2015:**123740.
12. Tsuruga T, Hirata T, Akiyama I, Matsumoto Y, Oda K, Fujii T, Osuga Y: **Mixed endometrioid and clear cell carcinoma arising from laparoscopic trocar site endometriosis.***J Obstet Gynaecol Res* 2019, **45:**1613-1618.
13. SAMPSON JA: **ENDOMETRIAL CARCINOMA OF THE OVARY, ARISING IN ENDOMETRIAL TISSUE IN THAT ORGAN.***Archives of Surgery* 1925, **10:**1-72.
14. Scott RB: **Malignant changes in endometriosis.***Obstet Gynecol* 1953, **2:**283-289.
15. Giannella L, Serri M, Maccaroni E, J DIG, Carpini GD, Berardi R, Sopracordevole F, Ciavattini A: **Endometriosis-associated Clear Cell Carcinoma of the Abdominal Wall After Caesarean Section: A Case Report and Review of the Literature.***In Vivo* 2020, **34:**2147-2152.
16. Ferrandina G, Palluzzi E, Fanfani F, Gentileschi S, Valentini AL, Mattoli MV, Pennacchia I, Scambia G, Zannoni G: **Endometriosis-associated clear cell carcinoma arising in caesarean section scar: a case report and review of the literature.***World J Surg Oncol* 2016, **14:**300.
17. Sawazaki H, Goto H, Takao N, Taki Y, Takeuchi H: **Clear cell adenocarcinoma arising from abdominal wall endometriosis mimicking urachal tumor.***Urology* 2012, **79:**e84-85.
18. Bats AS, Zafrani Y, Pautier P, Duvillard P, Morice P: **Malignant transformation of abdominal wall endometriosis to clear cell carcinoma: case report and review of the literature.***Fertil Steril* 2008, **90:**1197 e1113-1196.
19. Rivera Rolon MDM, Allen D, Richardson G, Clement C: **Abdominal Wall Clear Cell Carcinoma: Case Report of a Rare Event with Potential Diagnostic Difficulties.***Case Rep Pathol* 2019, **2019:**1695734.
20. Behbehani S, Magtibay P, Chen L, Wasson M: **Clear Cell Carcinoma of the Anterior Abdominal Wall Secondary to Iatrogenic Endometriosis.***J Minim Invasive Gynecol* 2020, **27:**1230-1231.
21. Yan Y, Li L, Guo J, Zheng Y, Liu Q: **Malignant transformation of an endometriotic lesion derived from an abdominal wall scar.***Int J Gynaecol Obstet* 2011, **115:**202-203.
22. Razzouk K, Roman H, Chanavaz-Lacheray I, Scotte M, Verspyck E, Marpeau L: **Mixed clear cell and endometrioid carcinoma arising in parietal endometriosis.***Gynecol Obstet Invest* 2007, **63:**140-142.
23. Lai YL, Hsu HC, Kuo KT, Chen YL, Chen CA, Cheng WF: **Clear Cell Carcinoma of the Abdominal Wall as a Rare Complication of General Obstetric and Gynecologic Surgeries: 15 Years of Experience at a Large Academic Institution.***Int J Environ Res Public Health* 2019, **16**.
24. Wei CJ, Huang SH: **Clear cell carcinoma arising from scar endometriosis: A case report and literature review.***Ci Ji Yi Xue Za Zhi* 2017, **29:**55-58.
25. Taburiaux L, Pluchino N, Petignat P, Wenger JM: **Endometriosis-Associated Abdominal Wall Cancer: A Poor Prognosis?***Int J Gynecol Cancer* 2015, **25:**1633-1638.
26. Gentile JKA, Migliore R, Kistenmacker FJN, Oliveira MM, Garcia RB, Bin FC, Souza P, Assef JC: **Malignant transformation of abdominal wall endometriosis to clear cell carcinoma: case report.***Sao Paulo Med J* 2018, **136:**586-590.
27. Marques C, Silva TS, Dias MF: **Clear cell carcinoma arising from abdominal wall endometriosis - Brief report and review of the literature.***Gynecol Oncol Rep* 2017, **20:**78-80.
28. Kostrzeba E, Barczyk M, Wichtowski M, Garstecki R, Murawa D: **Clear Cell Carcinoma of the abdominal wall.***Pol Przegl Chir* 2017, **89:**40-43.
29. Graur F, Mois E, Elisei R, Furcea L, Dragota M, Zaharie T, Al Hajjar N: **Malignant endometriosis of the abdominal wall.***Ann Ital Chir* 2017, **6**.
30. Sosa-Duran EE, Aboharp-Hasan Z, Mendoza-Morales RC, Garcia-Rodriguez FM, Jimenez-Villanueva X, Penavera-Hernandez JR: **[Clear cell adenocarcinoma arising from abdominal wall endometriosis].***Cir Cir* 2016, **84:**245-249.
31. Aust S, Tiringer D, Grimm C, Stani J, Langer M: **Therapy of a clear cell adenocarcinoma of unknown primary arising in the abdominal wall after cesarean section and after hysterectomy.***Wien Klin Wochenschr* 2015, **127:**62-64.

32. Liu H, Leng J, Lang J, Cui Q: **Clear cell carcinoma arising from abdominal wall endometriosis: a unique case with bladder and lymph node metastasis.** *World J Surg Oncol* 2014, **12:**51.
33. Heller DS, Houck K, Lee ES, Granick MS: **Clear cell adenocarcinoma of the abdominal wall: a case report.** *J Reprod Med* 2014, **59:**330-332.
34. Dobrosz Z, Palen P, Stojko R, Wlaszczuk P, Niesluchowska-Hoxha A, Piechuta-Kosmider I: **Clear cell carcinoma derived from an endometriosis focus in a scar after a caesarean section–a case report and literature review.** *Ginekol Pol* 2014, **85:**792-795.
35. Ijichi S, Mori T, Suganuma I, Yamamoto T, Matsushima H, Ito F, Akiyama M, Kusuki I, Kitawaki J: **Clear cell carcinoma arising from cesarean section scar endometriosis: case report and review of the literature.** *Case Rep Obstet Gynecol* 2014, **2014:**642483.
36. Shalin SC, Haws AL, Carter DG, Zarrin-Khameh N: **Clear cell adenocarcinoma arising from endometriosis in abdominal wall cesarean section scar: a case report and review of the literature.** *J Cutan Pathol* 2012, **39:**1035-1041.
37. Mert I, Semaan A, Kim S, Ali-Fehmi R, Morris RT: **Clear cell carcinoma arising in the abdominal wall: two case reports and literature review.** *Am J Obstet Gynecol* 2012, **207:**e7-9.
38. Li X, Yang J, Cao D, Lang J, Chen J, Shen K: **Clear-cell carcinoma of the abdominal wall after cesarean delivery.** *Obstet Gynecol* 2012, **120:**445-448.
39. Bourdel N, Durand M, Gimbergues P, Dauplat J, Canis M: **Exclusive nodal recurrence after treatment of degenerated parietal endometriosis.** *Fertil Steril* 2010, **93:**2074 e2071-2076.
40. Williams C, Petignat P, Belisle A, Drouin P: **Primary abdominal wall clear cell carcinoma: case report and review of literature.** *Anticancer Res* 2009, **29:**1591-1593.
41. Matsuo K, Alonsozana EL, Eno ML, Rosenshein NB, Im DD: **Primary peritoneal clear cell adenocarcinoma arising in previous abdominal scar for endometriosis surgery.** *Arch Gynecol Obstet* 2009, **280:**637-641.
42. Rust MM, Susa J, Naylor R, Cavuoti D: **Clear cell carcinoma in a background of endometriosis. Case report of a finding in a midline abdominal scar 5 years after a total abdominal hysterectomy.** *Acta Cytol* 2008, **52:**475-480.
43. Achach T, Rammeh S, Trabelsi A, Ltaief R, Ben Abdelkrim S, Mokni M, Korbi S: **Clear cell adenocarcinoma arising from abdominal wall endometriosis.** *J Oncol* 2008, **2008:**478325.
44. Harry VN, Shanbhag S, Lyall M, Narayansingh GV, Parkin DE: **Isolated clear cell adenocarcinoma in scar endometriosis mimicking an incisional hernia.** *Obstet Gynecol* 2007, **110:**469-471.
45. Sergent F, Baron M, Le Cornec JB, Scotte M, Mace P, Marpeau L: **[Malignant transformation of abdominal wall endometriosis: a new case report].** *J Gynecol Obstet Biol Reprod (Paris)* 2006, **35:**186-190.
46. Alberto VO, Lynch M, Labbei FN, Jeffers M: **Primary abdominal wall clear cell carcinoma arising in a Caesarean section scar endometriosis.** *Ir J Med Sci* 2006, **175:**69-71.
47. Ishida GM, Motoyama T, Watanabe T, Emura I: **Clear cell carcinoma arising in a cesarean section scar. Report of a case with fine needle aspiration cytology.** *Acta Cytol* 2003, **47:**1095-1098.
48. Park SW, Hong SM, Wu HG, Ha SW: **Clear cell carcinoma arising in a Cesarean section scar endometriosis: a case report.** *J Korean Med Sci* 1999, **14:**217-219.
49. Miller DM, Schouls JJ, Ehlen TG: **Clear cell carcinoma arising in extragonadal endometriosis in a caesarean section scar during pregnancy.** *Gynecol Oncol* 1998, **70:**127-130.
50. Hitti IF, Glasberg SS, Lubicz S: **Clear cell carcinoma arising in extraovarian endometriosis: report of three cases and review of the literature.** *Gynecol Oncol* 1990, **39:**314-320.
51. Schnieber D, Wagner-Kolb D: **[Malignant transformation of extragenital endometriosis].** *Geburtshilfe Frauenheilkd* 1986, **46:**658-659.

Figures

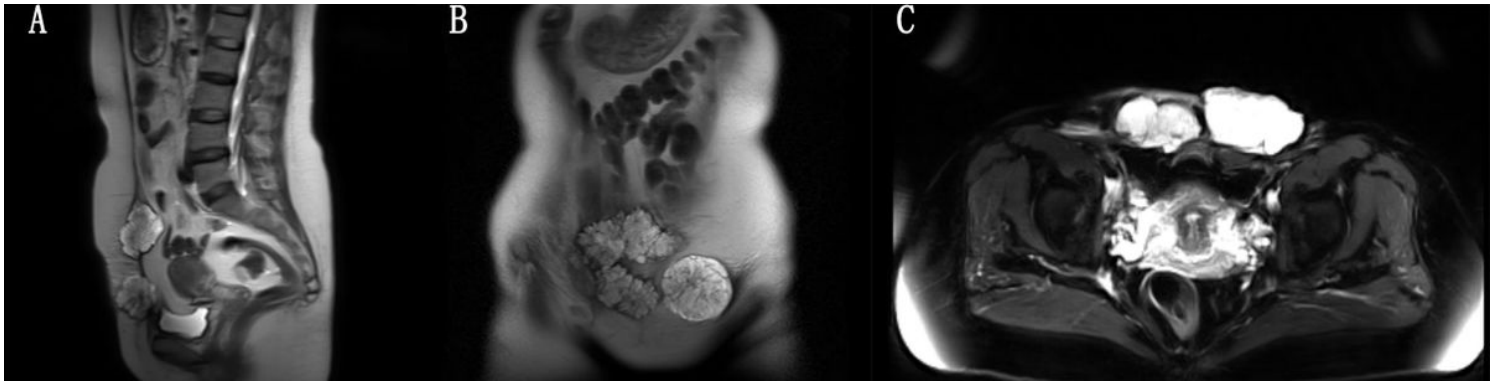

Figure 1

CT image of the abdominal mass shows two lower rectus muscle heterogeneous lumps: (A) Sagittal view. (B) Coronal view. (C) Transverse view.

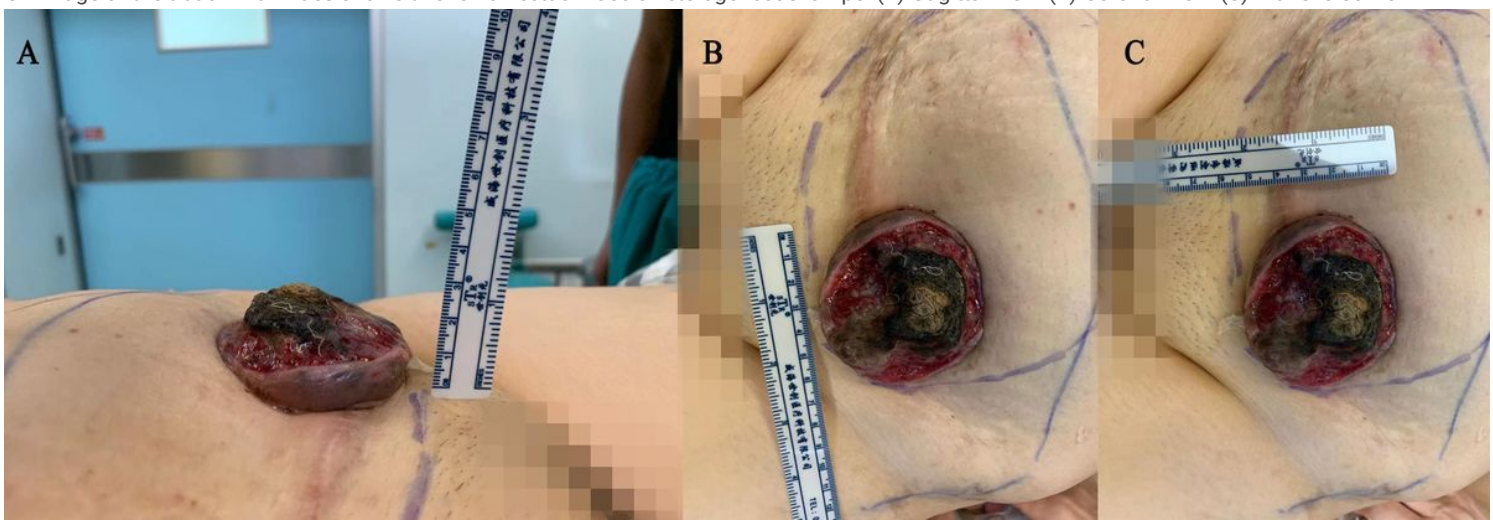

Figure 2

Photograph showing an ulcerated abdominal nodule associated with a cesarean section scar.

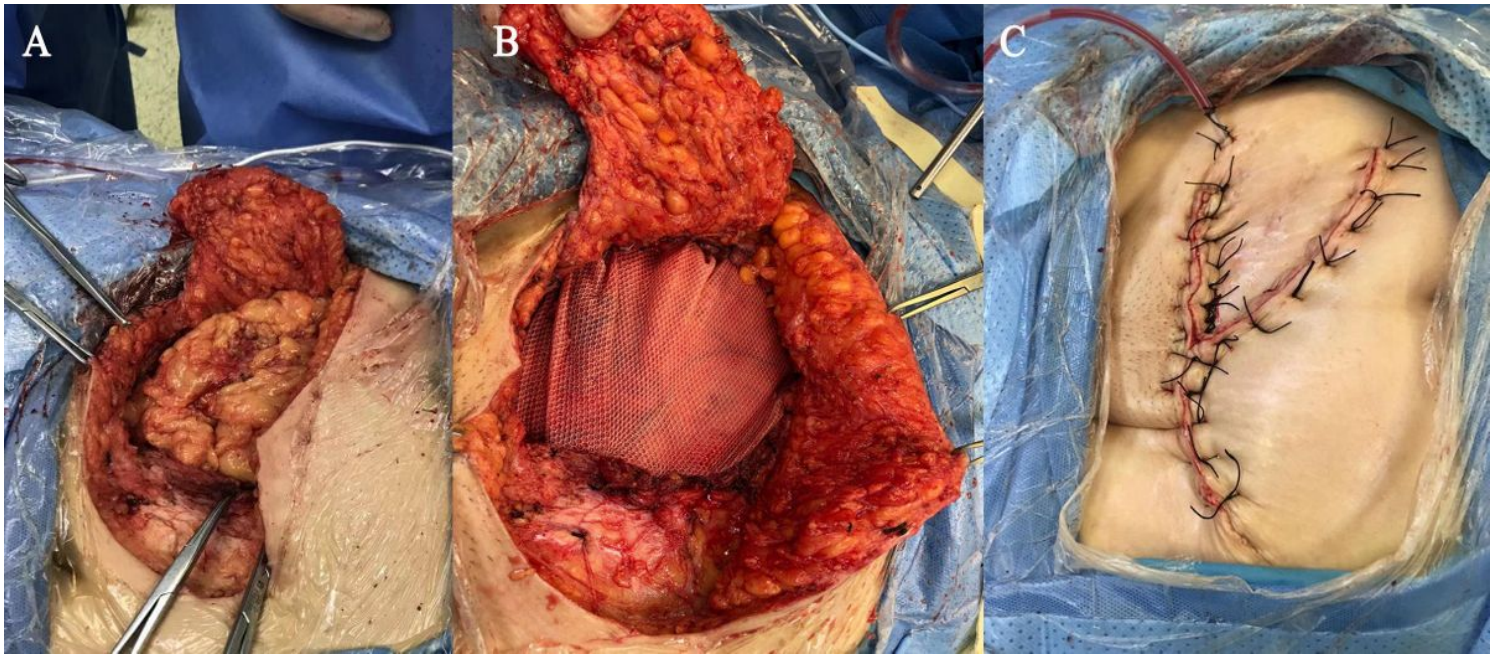

Figure 3

Photograph showing intraoperative tumor resection process. (A).Large defect of the abdominal wall after removal of the mass. (B).Placement of patch. (C).Surgical suture.

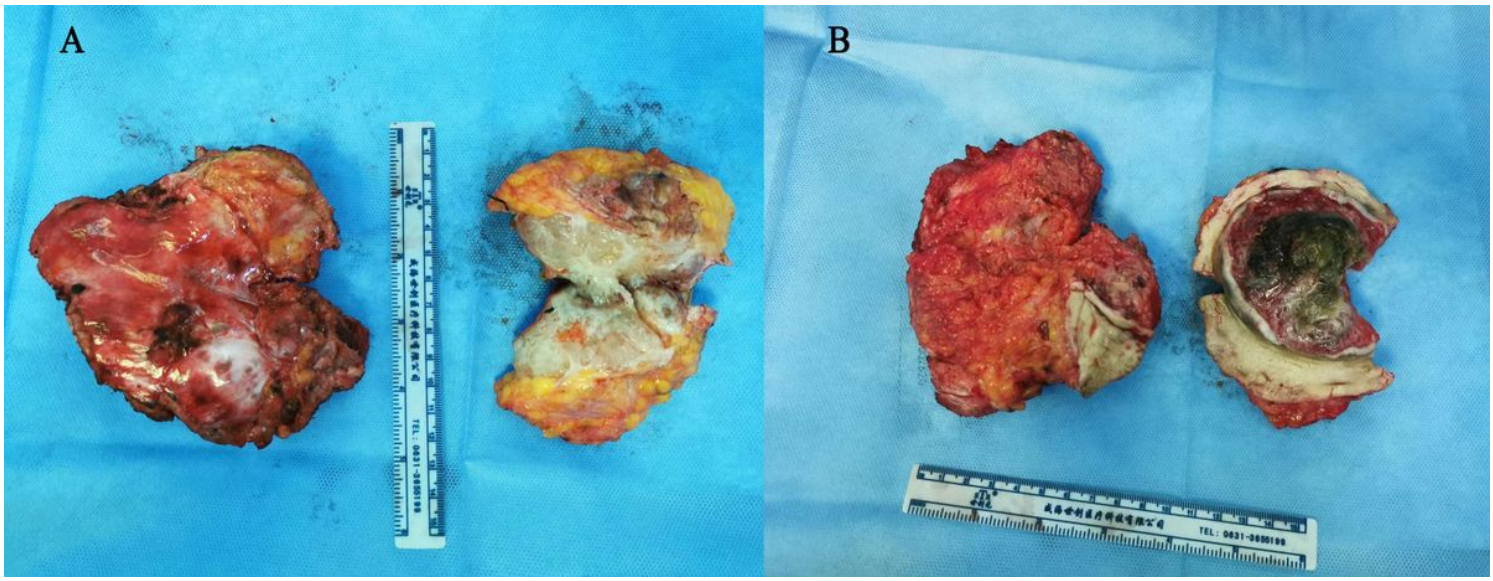

Figure 4

Macroscopic appearance demonstrating areas of cystic and solid components with brittle texture. (A).Gross appearance. (B). Internal components were shown after dissection.

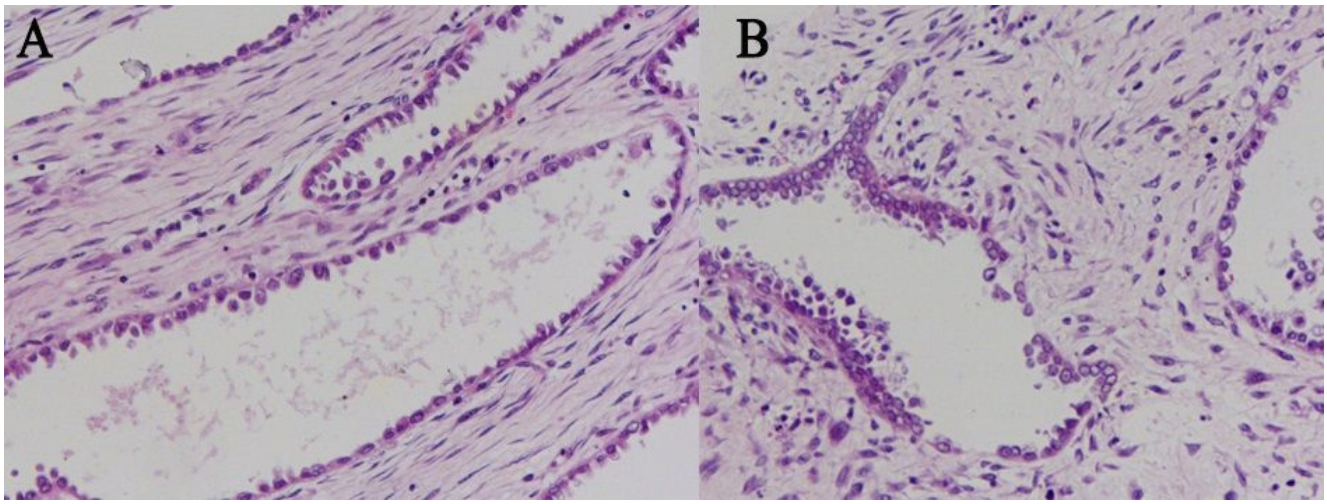

Figure 5

Histologic images of the tumor. (A). Higher magnification of cystic spaces lined by bland-appearing, flattened cells (H&E stain, X200). (B). In other areas, the tumor shows irregular infiltrating glands with fibrous stroma.

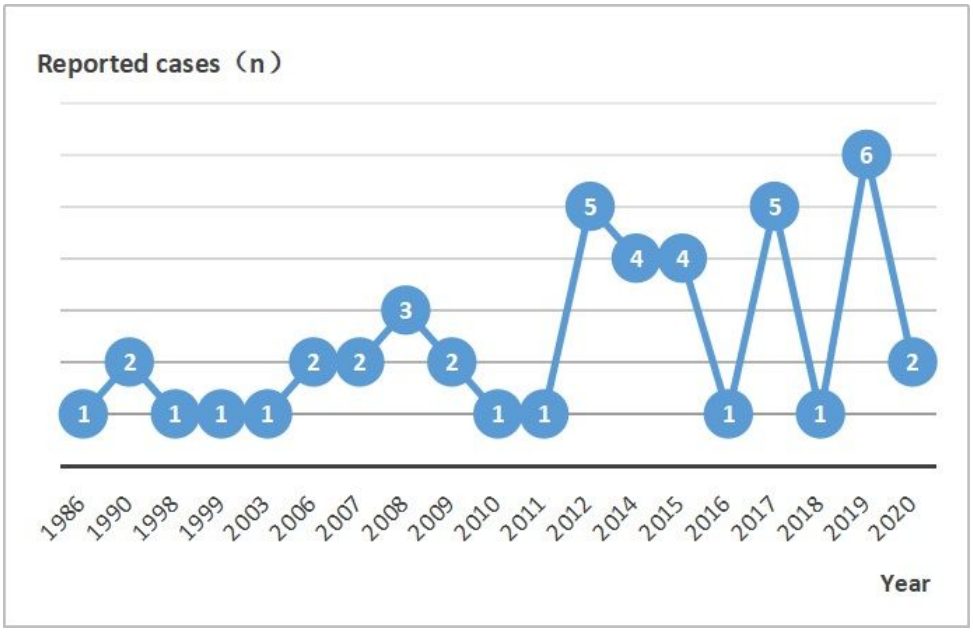

Figure 6

The year distribution of clear cell carcinoma caused by endometriosis in abdominal wall surgical wound has been reported.

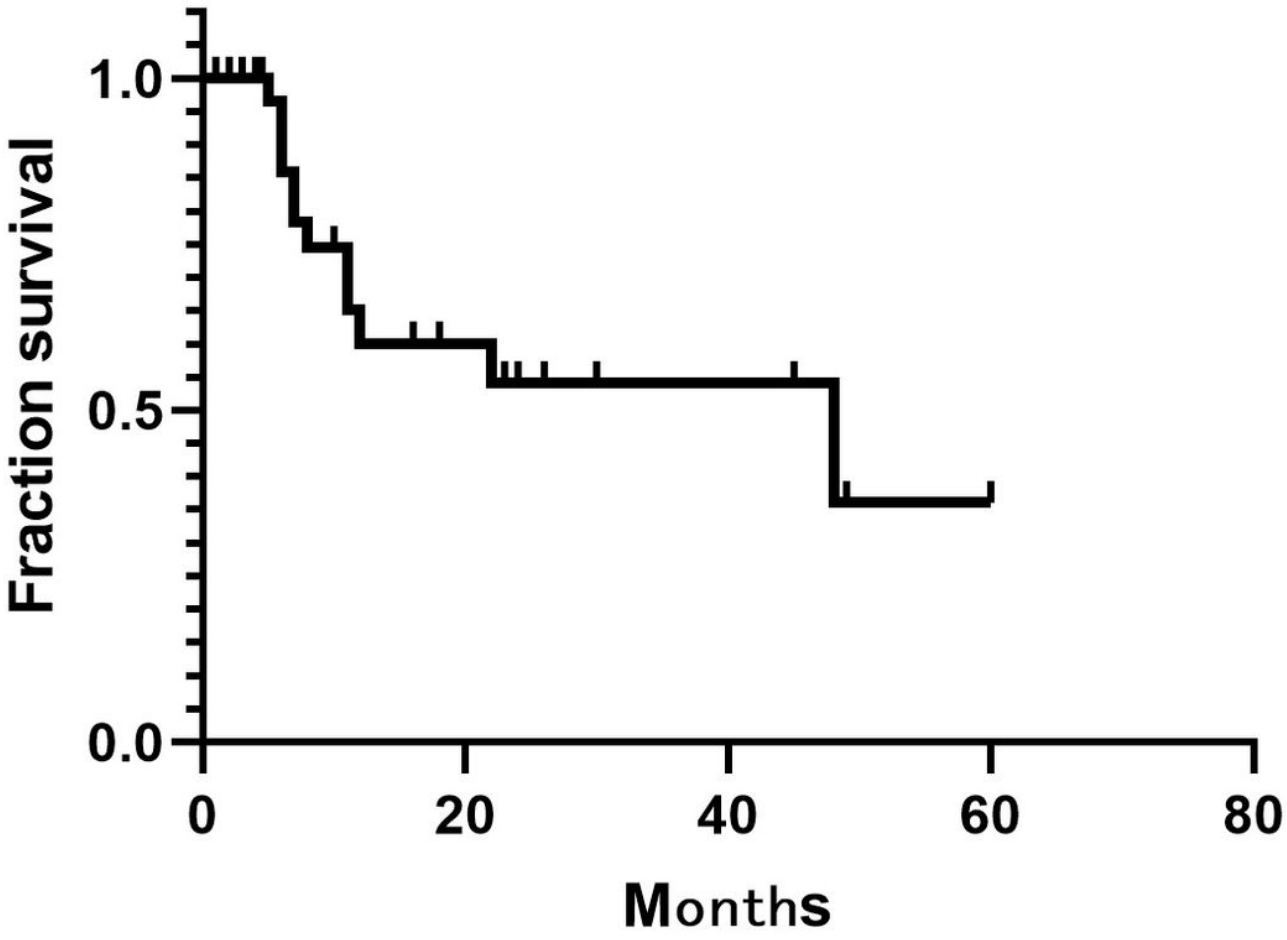

Figure 7

Kaplan–Meier curve for survival in patients with endometriosis-associated malignant transformation in abdominal surgical-scar showing high mortality up to 60 months following diagnosis. The median survival time is 48 months and the five-year survival rate is 35%

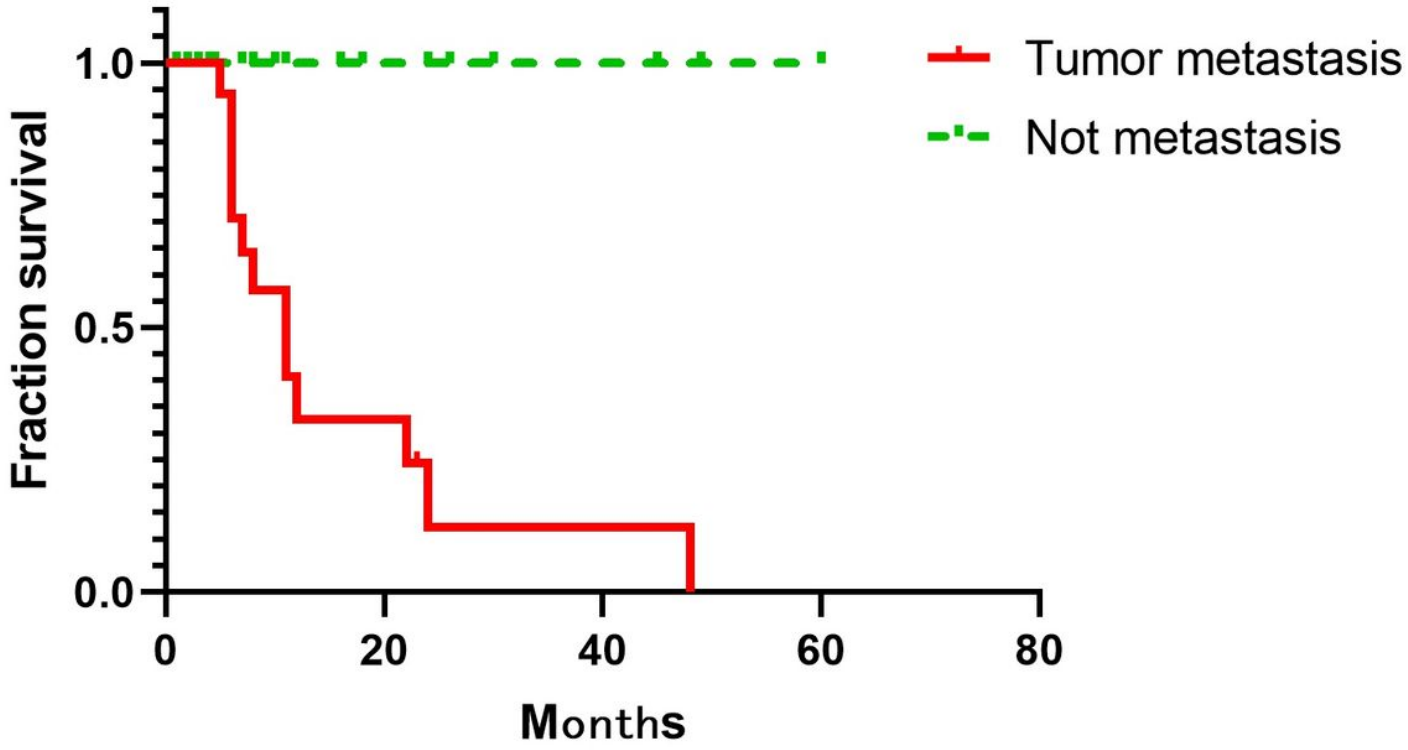

Figure 8

Kaplan–Meier curve for survival between patients with metastasis and without metastasis during the follow-up treatment.

Supplementary Files

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- TableS1.xlsx