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CASE REPORT

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Extremely long survival in a patient with serous ovarian cancer. A case report and review of the literature

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Abstract

Background: Ovarian carcinoma is a malignant tumor with a poor prognosis. Due to the late onset of the first symptoms, most patients present with already advanced disease—at stage III or IV, which significantly reduces life expectancy. Despite advancements in surgical treatment, in particular, in chemotherapy, the mortality remains high, only slightly over 40% of female patients can expect a 5-year survival rate. **Case**: We report on an extremely rare case of a documented 45-year survival in serous ovarian cancer patient. The first diagnosis was confirmed in 1978, and she was treated surgically for histologically confirmed ovarian serous carcinoma. The first recurrence appeared in 2013 and was histologically confirmed in an open abdominal biopsy. The patient was successfully managed using carboplatin/paclitaxel chemotherapy and remained in remission. The second recurrence appeared in 2016 and was well managed with chemotherapy. In 2023, the histological examination of laparoscopic biopsy confirmed serous ovarian carcinoma relapse. The comparison of all biopsy samples proved the recurrence of the same tumor and excluded a secondary disease. **Conclusions**: This rare case of unusually long survival in serous ovarian cancer patient indicates that some patients may have a much better prognosis than typically observed. Advances in genetic determinations are needed to better understand the biology of this tumor to identify patients with the perspective of better survival.

Keywords

Serous ovarian cancer; Serous ovarian carcinoma; Recurrence; Overall survival

1. Introduction

Epithelial ovarian cancer (OC) is, after breast cancer, the second most common cause of gynecologic cancer death in the female population nowadays [1]. The incidence of ovarian tumors has fallen in recent years due to the use of oral contraceptive pills, with ovarian cancers being the seventh most common cancers, and the second most lethal gynecological malignancies in female patients worldwide [2, 3]. OC comes in fourth place in the structure of cancer mortality among women in Poland, right after breast, colorectum and lung cancers [4].

The main cause of the high death rate in this type of cancer is the significantly late onset of disease symptoms in affected women. When the tumor is detected, multiple metastases are often present in the abdomen [1]. Most cases are diagnosed at advanced stages of disease (III or IV) and are associated with a high mortality rate [5]. According to some Polish studies, the overall 5-year survival rate for OC is estimated at slightly over 40% [2]. Common symptoms of OC include palpable abdominal mass, abdominal pain, bloating, loss of appetite and loss of weight [6].

Ovarian tumors encompass three main histological groups: epithelial, stromal and germinal tumors [7]. Epithelial tumors can be benign (over 50% of cases), malignant (35%) and borderline (5%). In the group of epithelial cancers, serous and mucinous can be distinguished, with the serous type being the most common. Epithelial cancers account for approximately 90% of all ovarian cancer subtypes and are seen predominantly among adult women [8–10]. Serous tumors represent the predominant histological type among tumors in the female extrauterine genital tract [11]. Serous Ovarian Cancer (SOC) can be divided into Low-Grade Serous Ovarian Cancer (LGSOC) and High-Grade Serous Ovarian Cancer (HGSOC). LGSOC is relatively less common than HGSOC in clinical practice. About 3–9% of ovarian cancers are classified as LGSOC. Still, there is a lack of robust evidence for appropriate diagnosis and treatment strategies for LGSOC [12, 13].

Causes and risk factors of SOC can be divided into modifiable and nonmodifiable. The risk factors and protective factors are shown in Fig. 1 (Ref. [14–16]).

The most significant risk factor for ovarian cancer is a familial history of breast or ovarian cancer. Women with a first-degree relative who has a history of ovarian cancer face an approximately 50% higher risk of developing invasive epithelial ovarian cancer, and those with a first-degree relative diagnosed with breast cancer experience a 10% increase in risk.

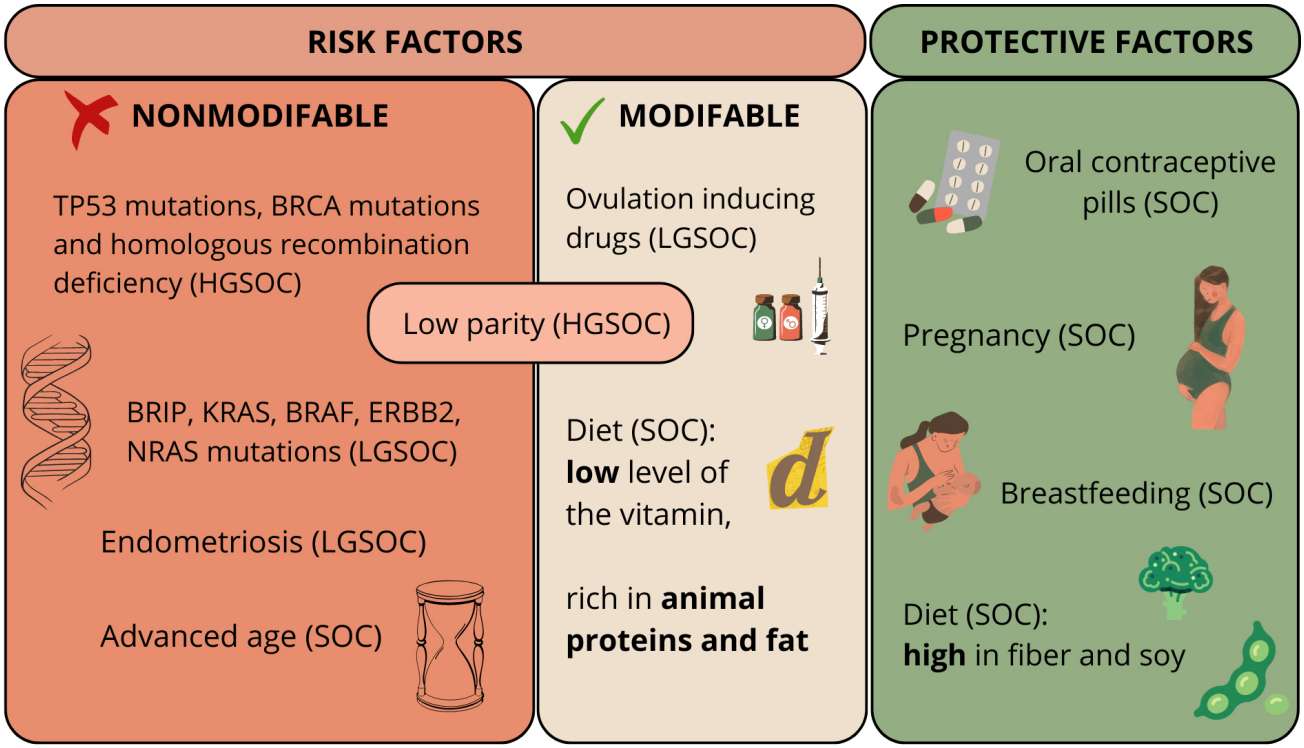

FIGURE 1. Risk and protective factors of serous ovarian cancer with a detailed specification of the causes of the given SOC subtype [14–16]. *BRAF*: v-raf murine sarcoma viral oncogene homolog B; BRCA: breast cancer; BRIP: *BRCA1*-interacting protein; ERBB2: receptor tyrosine-protein kinase erbB-2; HGSOC: high-grade serous ovarian carcinoma; *KRAS*: Kirsten rat sarcoma viral oncogene homolog; LGSOC: low-grade serous ovarian carcinoma; *NRAS*: neuroblastoma RAS viral oncogene homolog; SOC: serous ovarian carcinoma; TP53: Tumor protein 53.

In women carrying breast cancer type 1 (*BRCA1*) mutations, the likelihood of developing general ovarian cancer by the age of 80 is 44%, while for those with breast cancer type 2 (*BRCA2*) mutations, it is 17%, but carriers of *BRCA1* or *BRCA2* mutations do not have an elevated risk for LGSOC [13, 17].

Detection of a tumor is incidental, often during a routine ultrasound examination. The diagnosis is supported by a computed tomography (CT) or magnetic resonance imaging (MRI) scan of the chest, abdomen, and pelvis to fully evaluate the stage of the disease. Radiographic images of ovarian tumors may include a tumor mass in the abdominal cavity, ascites, disseminated carcinogenesis, and pleural effusions. Laboratory tests in ovarian cancer suspected patients include specific tumor markers such as cancer antigen 125 (CA125), cancer antigen 19-9 (CA19-9), carcinoembryonic antigen (CEA), human epididymis protein 4 (HE4), mucin-1 and prostasin. Their levels vary depending on the histological type of OC [18].

Our study aims to present the case of a woman surviving 45 years after the primary diagnosis of ovarian cancer and experiencing delayed relapses of the disease. Such long survival is very rare in ovarian cancer patients, especially in cases of serous OC, although this is significantly more common in patients with LGSOC than with HGSOC [17, 19].

2. Case report

The 76-year-old female patient was admitted to the oncological gynecology department due to the suspicion of the recurrence of serous OC. The patient had a 45-year-old long OC history, as her OC was first diagnosed in 1978 when she was 31 years of age. At present admission, the patient did not complain of any symptoms. The family history indicated the occurrence of colon cancer in the patient's father.

To date, the patient has undergone three surgeries: in 1978, 2013, and 2023. In 1978, the patient received radical operative treatment for a low-grade International Federation of Gynecology and Obstetrics (FIGO) IIA stage OC: she underwent a hysterectomy with bilateral salpingo-oophorectomy, followed by adjuvant radiotherapy (1979), according to the contemporary protocol. At final histology the following immunohistochemical profile was described: estrogen receptors (ER) (+) ~90%; progesterone receptors (PR) (−); cytokeratin 7 (CK7) (+); Wilms' Tumor 1 (WT1) (+); paired-box gene (PAX8) (+); antigen Kiel 67 (Ki67) (+) ~30%; p53 (−).

The first recurrence of the OC appeared in 2013. At that time the patient reported recurrent abdominal pain. The exploratory re-laparotomy with biopsy was performed, with samples demonstrating low-grade serous OC (FIGO IIIB stage). The patient received 6 cycles of the first-line cisplatin/paclitaxel chemotherapy, each in three-week intervals.

Over the years, the patient remained asymptomatic under the control of an oncological surgery outpatient clinic. Regular laboratory tests, including CA125 level and computed tomography of the abdomen and pelvis were scheduled. CA125 levels alterations from 2013 to 2024 are presented in Fig. 2.

In October 2016 patient was referred for positron emis-

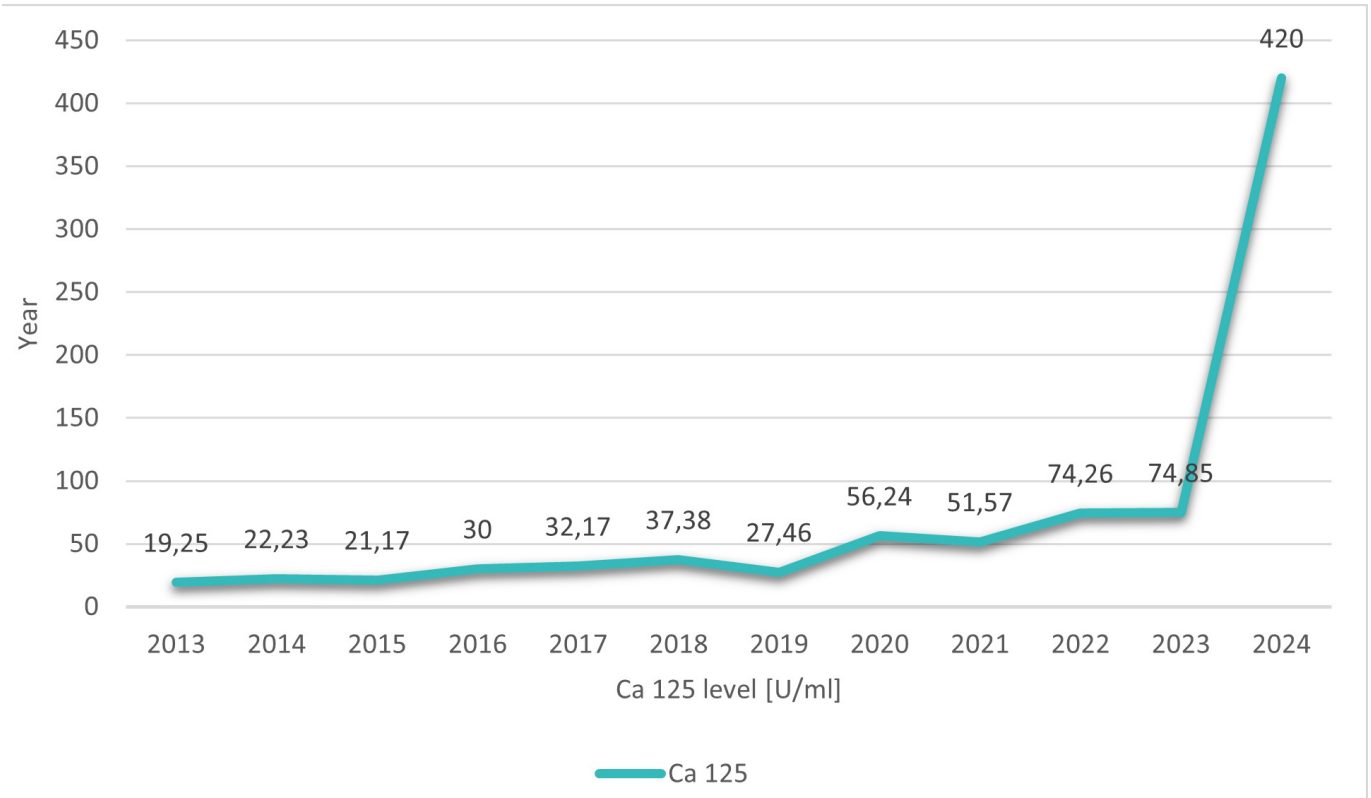

FIGURE 2. CA125 levels changes across the years of 2013–2024. CA125: cancer antigen 125.

sion tomography/computed tomography (PET-CT) examination due to the findings of possible recurrence in control CT scans. The following changes were detected in control CT:

(1) Peritoneal implant in the retrocecal area with small calcifications measuring 47 × 22 mm,

(2) Hypodense mass in the right mid-abdomen below the transverse colon, measuring 48 × 35 mm,

(3) Mass in the left ovary area with small calcifications measuring 25 × 19 mm,

(4) In the genital area, a heterogeneously hypodense area with scattered small calcifications measuring 83 × 33 mm.

PET-CT confirmed abdominal and pelvic adhesions and active tumor growth process staged FIGO IIIC. In 2016 she was given a second-line chemotherapy with 6 cycles carboplatin/paclitaxel, again with a good response. In control CT scans after the second-line chemotherapy lesions' dimensions remained stable. Interestingly, in the years 2018–2019 the abdominal lesions gradually decreased, then became stable. The exact dimensions are presented in Table 1. In addition to the lesions listed in the table, numerous other implants appeared from 2019, including a 77 × 37 mm lesion in the pouch of Douglas.

In 2020–2024, the CA125 levels started to increase moderately. In 2023, the CT imaging showed a new minor cystic intraperitoneal metastatic lesion. We performed an exploratory laparoscopy with sample retrieval from the greater omentum for histopathological assessment. Laparoscopic control revealed extensive intestinal adhesions and brown cloudy fluid in the peritoneal space, as well as peritoneum and omentum with small punctate changes corresponding to cancer recurrence. Histological examination of the excised fragments confirmed

TABLE 1. Dimension changes in years 2016–2020 of the first four lesions found in 2016 on the control CT scan.

Date (mon/yr)	Dimensions (mm)			
	(1)	(2)	(3)	(4)
10/2016	47 ×22	48 ×35	25 ×19	83 ×33
01/2017	46 ×21	46 ×27	25 ×17	83 ×33
05/2017	47 ×21	45 ×32	25 ×19	83 ×33
12/2017	50 ×22	47 ×40	25 ×22	83 ×33
07/2018	57 ×22	45 ×32	23 ×21	69 ×33
01/2019	52 ×27	25 ×34	23 ×22	58 ×31
04/2019	51 ×27	39 ×30	24 ×21	51 ×27
12/2019	51 ×27	36 ×28	26 ×21	49 ×35
05/2020	55 ×36	38 ×24	28 ×24	50 ×36

an ovarian tumor of the same type as diagnosed 45 years before—a low-grade serous OC, hence excluded a secondary disease. In next-generation sequencing (NGS) determinations the tumor was *BRCA1* and *BRCA2*-mutations and homologous recombination deficiency (HRD) test negative. The patient was successfully subjected to the third line of platin-based chemotherapy, doing fine and symptoms-free till the end of 2023. In the beginning of 2024, CA125 levels increased again and the patient reported some abdominal discomfort. Fig. 3 depicts the changes in lesions in the years 2013–2024. Fig. 4 depicts the chosen histological slides of the patient's ovarian tumor biopsies performed in 2013 and 2023. At the time of submission of this report (2024), the patient is 77 years old, awaiting to receive the fourth-line platin-based chemotherapy

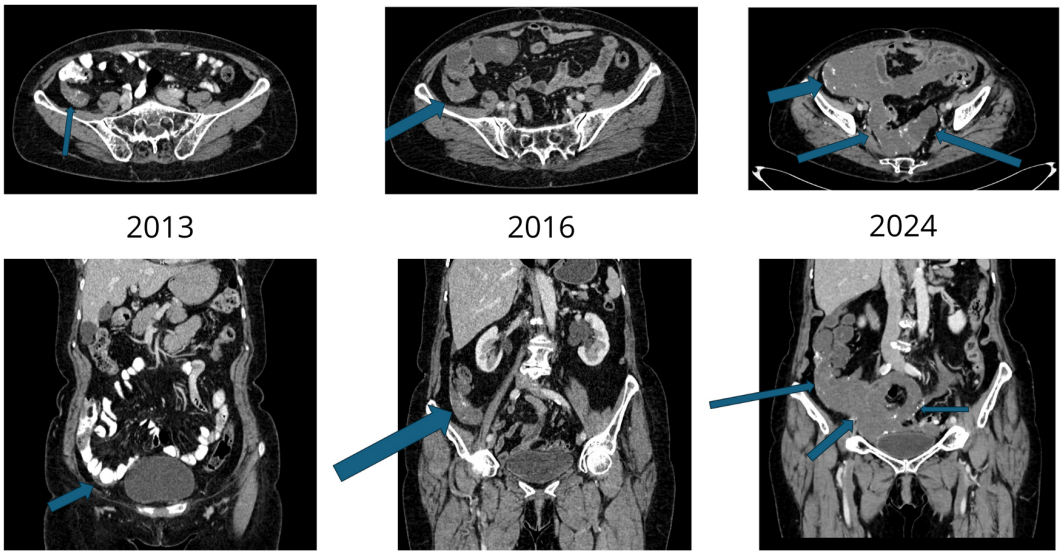

FIGURE 3. CT scans of patient's ovarian lesions in years 2013, 2016 and 2024. Blue arrows pointing at tumor mass found on the CT scans.

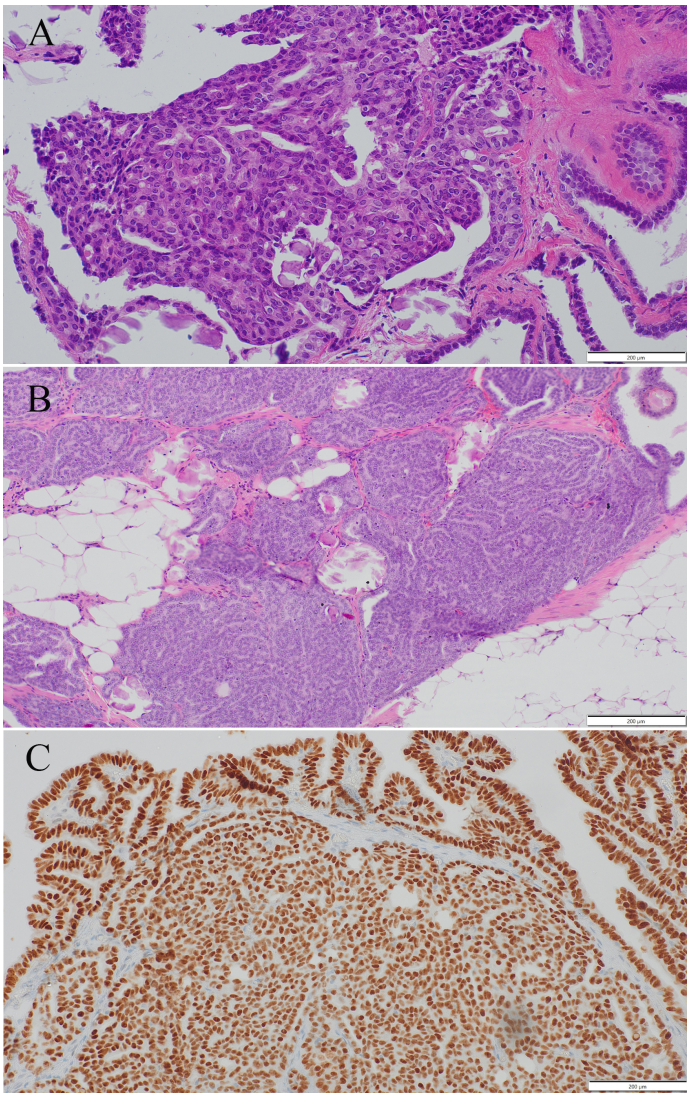

FIGURE 4. Histology Slides of ovarian tumor. (A) the year 2013, (B) the year 2023, (C) PAX8 positive.

and she declares doing fine.

3. Discussion

To the best of our knowledge, this is the longest reported survival of a patient with serous OC, as the tests applied to our patient confirmed an unchanged histological type of the lesion during the 45-year observation. Survival beyond five years post-diagnosis has been achieved in less than 50% of individuals diagnosed with advanced-stage SOC. Long-term survivors are considered patients who have survived for more than 10 years from a cancer diagnosis. The median survival for epithelial OC is under 5 years and around 15% of patients can expect to survive beyond 10 years, while for LGSOC median survival reaches approximately 10 years [19–21].

The survival rates in OC patients are typically low, but casuistic reports on longer-than-average survival in patients with OC may be spotted. In Huang *et al.* [22] report, the patient survived 9 years from the first findings of the disease in stage IV, without complete remission during observation time. The patient was treated with neoadjuvant chemotherapy, interval cytoreductive surgery, and postoperative long-term chemotherapy, and the disease was well-controlled during this time. Even with positive response attributes, the majority of women diagnosed with advanced-stage OC are likely to experience a recurrence. The sensitivity of LGSOC to chemotherapy remains under consideration. Di Lorenzo *et al.*'s [23] comparison of outcomes from other authors confirms that LGSOC has a different sensitivity to chemotherapy compared to HGSOC, which strengthens doubts about the effectiveness of this therapeutic approach. Overall, LGSOC is a rare subtype of ovarian cancer characterized by a high recurrence rate and limited effective systemic therapies [24].

Patients with LGSOC are typically diagnosed at a younger age and have longer survival compared to those with high-grade serous ovarian cancer HGSOC. Wong *et al.* [25] refer to a study in which the 5-year survival rate was 62.3% for 33 patients with LGSOC and 43.9% for 241 patients with HGSOC. Despite the difference in 5-year survival, the 10-year survival rates were nearly equivalent, with 21.2% for LGSOC and 22.7% for HGSOC. Only 10–20% of these patients survive for more than 10 years after diagnosis [26]. Other studies provide median survival rates for patients with LGSOC, such as the study by Grisham and Iyer, which reports the median survival in LGSOC ranges from 82 to 126 months, with the upper limit of 126 months being just over 10 years [27]. Other study shows that follow-up rates range up to 377 months and the median overall survival was 142.3 months (range: 48.8 months to not reached) for patients without the residual disease, 86.4 months (range: 54.1–163.3 months) for patients with residual disease between 1 and 10 mm, and 35.2 months (range: 15.6–49.9 months) for patients with residual disease greater than 1 cm [23]. However, there is a lack of studies that present the longest possible survival. Our patient survived 45 years with recurrent LGSOC, which significantly exceeds the average values reported in the literature. Her remissions were complete and symptom-free. In literature, an extended survival is linked to prognostic factors that have been validated at the primary diagnosis, such as being younger age, presenting at an earlier clinicopathologic stage, non-serous histology of OC, lacking ascites, undergoing primary surgery, response to the platin-based chemotherapy, and achieving optimal cytoreduction during the initial surgery. Patients with advanced LGSOC have a median survival of around 10 years and typically undergo multiple lines of therapy [20]. OC is often asymptomatic in early stages, wherefore it is usually diagnosed as an advanced tumor or accidentally during routine examinations. Our patient was young and asymptomatic when first diagnosed with cancer. Of note, therapeutic management depends on the character and size of the lesion. Ovarian tumors smaller than 5 cm are often treated conservatively, while bigger tumors are treated surgically with laparoscopy or laparotomy, which enhances diagnosing [28].

The laparoscopic approach's advantages over classic open surgery are fewer complications, lower overall blood loss, shorter postoperative hospital stay, faster patient recovery, and superior cosmetic results, but to date, laparoscopy has been limited to unadvanced cases. Moreover, incorporating diagnostic laparoscopy into the decision-making process appears essential for accurately directing OC patients to appropriate treatment strategies [29]. In the progressed disease, the preferred operative method remains laparotomy. The operative staging of serous OC includes a comprehensive surgical assessment of the peritoneal cavity: total hysterectomy, bilateral salpingo-oophorectomy, omentectomy, iliac and paraaortic lymphadenectomy, with maximal cytoreductive surgery for all visible peritoneal disease. The evaluation of the peritoneal surface, including the diaphragm, paracolic gutters, and the mesentery of the intestines is performed. Pelvic peritoneal washing should be conducted to completely evaluate the stage of the disease. When possible, the recommended initial treatment for advanced SOC is surgery followed by chemotherapy, but when it comes to LGSOC chemotherapy has long been considered ineffective, and still available reports have differing opinions on this matter. However, most authors and the latest expert consensus report indicate that LGSOC is regarded as having low sensitivity to chemotherapy. Achieving complete cytoreductive surgery, which involves removing all visible tumor lesions, is linked to improved overall survival. Conversely, any remaining tumor after surgery is considered a negative prognostic factor for survival [30]. Other treatment options for SOC are neo-adjuvant platinum/taxane-based chemotherapy and palliative chemotherapy, as well as angiogenesis- and Poly (ADP-ribose) polymerase (PARP) inhibitors, however, there is still a paucity of information regarding the efficacy of PARP inhibitors in the case of LGSOC [31–33].

The results of the recently published Gynecologic Oncology Group (GOG)-0213 study on the treatment of recurrent OC showed no advantage in overall survival in patients treated with secondary cytoreductive surgery over the patients receiving the chemotherapy alone. The authors suggest that secondary cytoreductive surgery may be considered in the cases of the absence of postoperative residual tumor, good general condition of the patient, and single recurrence in platinum-sensitive ovarian recurrence [18, 34]. The significance of neoadjuvant chemotherapy in the overall survival rates of patients with OC is still controversial and clinical trial results are

inconsistent. Some authors report an improvement in the prognosis of patients with the use of adjuvant chemotherapy, while others show no changes in whether chemotherapy is implemented before the surgery or not [22]. Other recent trials are SOC-1 and the Descriptive Evaluation of Preoperative Selection Criteria for Operability in Recurrent Ovarian Cancer (DESKTOP) III [35]. SOC-1 was a phase 3 trial, multicenter, open-label, randomized, controlled, and was conducted at four academic centers in China. This clinical trial registration number is National Clinical Trial (NCT) 01611766. Outcomes of SOC-1 proved that in patients with platinum-sensitive relapsed ovarian cancer, secondary cytoreduction followed by chemotherapy led to significantly longer progression-free survival compared to chemotherapy alone [36]. DESKTOP III trial (NCT01166737) was performed in 2022, and its results confirm that the cytoreductive surgery for later ovarian cancer relapse seems feasible and has low mortality in selected patients who received non-surgical treatment for their first relapse. Surgery should be considered as an option for carefully selected patients at later stages within a specialized gynecological cancer setting [37, 38]. The justification for secondary cytoreductive surgeries in recurrent ovarian cancer is currently still under consideration; however, our patient, since the relapse in 2013, has been given three chemotherapies with carboplatin/paclitaxel, and she now receives another such chemotherapy.

New immunotherapy treatment strategies for SOC are being rapidly investigated. Targeted therapy is a fast-growing modality for cancer treatment, which might enhance surgical treatment and delay cancer relapse [39–41]. These groups of substances include specific antibodies influencing tumor cell biology. For example: an angiogenesis inhibitor bevacizumab has been applied in OC patients. Bevacizumab binds to the vascular endothelial growth factor (VEGF) protein and inhibits the vascularization process in tumors, slowing tumor growth [42]. Other examples of targeted drugs used in OC treatment, some still under study are olaparib, rucaparib, niraparib, mirvetuximab soravtansine, larotrectinib and entrectinib [43–48]. Their effectiveness remains to be assessed.

4. Limitations of the study

This report focuses on an isolated case, thus its applicability to the broader population of ovarian cancer patients is limited. The unique clinical course of this patient may not be representative of others with serous ovarian carcinoma. While the patient's case is remarkable, the follow-up after her last recurrence may not fully reflect the lasting effects of treatment or the potential for future disease progression. These limitations emphasize the need for additional research, including long-term large cohort studies in ovarian cancer survivors, to deepen our understanding of the factors contributing to prolonged life expectancy.

5. Conclusions

OC is still one of the most common causes of cancer deaths in women's population worldwide. Unfortunately, there is still no screening test for OC. Commonly used detection methods are ultrasound or CA125 biomarker level testing in patients' blood serum, but they did not prove screening value, and still many patients are diagnosed at advanced stages of the disease. Overall survival in SOC patients is relatively low and long survival in affected patients is still very rare. The most optimal treatment method has to be appropriately matched to the patient's needs. In the treatment of LGSOC, the rationale for secondary cytoreductive surgeries in recurrent OC is still being evaluated. Opinions on the effectiveness of neoadjuvant chemotherapy are still divided. The factors contributing to long-term survival remain unclear. The improvement of SOC biology and therapeutic methods may help better understand why some OC patients have privilege over others.

ABBREVIATIONS

BRAF, v-raf murine sarcoma viral oncogene homolog B; *BRCA1*, Breast Cancer Type 1; *BRCA2*, Breast Cancer Type 2; BRCA, Breast cancer; BRIP, *BRCA1*-interacting protein; CA125, Cancer antigen 125; CA19-9, Cancer antigen 19-9; CEA, Carcinoembryonic antigen; CK7, Cytokeratin 7; CT, Computed Tomography; DESKTOP, Descriptive Evaluation of Preoperative Selection Criteria for Operability in Recurrent Ovarian Cancer; ER, Estrogen receptors; *ERBB2,* Receptor tyrosine-protein kinase erbB-2; FIGO, International Federation of Gynecology and Obstetrics; GOG, Gynecologic Oncology Group; HE4, Human epididymis protein 4; HGSOC, High-Grade Serous Ovarian Cancer; HRD, Homologous recombination deficiency; Ki67, Antigen Kiel 67; *KRAS*, Kirsten rat sarcoma viral oncogene homolog; LGSOC, Low-Grade Serous Ovarian Cancer; MRI, Magnetic Resonance Imaging; NCT, National clinical trial; NGS, Next-generation sequencing; *NRAS*, Neuroblastoma RAS viral oncogene homolog; OC, Ovarian Cancer; PARP, Poly (ADP-ribose) polymerase; PAX8, Paired-box gene 8; PET/CT, Positron emission tomography/Computed tomography; PR, Progesterone receptors; SOC, Serous Ovarian Cancer; *TP53*, Tumor protein 53; VEGF, Vascular endothelial growth factor; WT1, Wilms' Tumor 1.

AVAILABILITY OF DATA AND MATERIALS

The data are contained within this article.

AUTHOR CONTRIBUTIONS

MD, JW and MJ—designed the research study, analyzed the data, and wrote the manuscript. MD and MJ—performed the research. JW and MJ—provided supervision and advice on editing and preparing the final form. MD—wrote the original draft. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was conducted in accordance with the Declaration of Helsinki. According to the Regulations of the Bioethics Committee of Poland, this does not require the consent of the bioethics committee, as this case was not an experimental procedure. Informed consent has been obtained from the patient to publish this paper.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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