Clinical analysis of 12 cases of ovarian neuroendocrine carcinoma

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Abstract

Background

Neuroendocrine neoplasms (NENs) of the female genital tract are rare. This study aims to enhance our clinical understanding of neuroendocrine carcinoma of the ovary.

Methods

A retrospective review was conducted on 12 patients diagnosed with neuroendocrine carcinoma of the ovary, analyzing clinicopathological characteristics, treatment modalities, and survival status.

Results

The median age at diagnosis was 34.5 years (range: 20 to 62 years). Among the 12 cases, 9 were small cell carcinoma of the ovary (SCCO) and 3 were large cell neuroendocrine carcinoma (LCNEC). Five cases were stage I tumors, one case was stage IV, and six cases were stage III. Eleven patients underwent surgery as part of their treatment. All patients received adjuvant chemotherapy. Among the 12 patients, one patient received radiotherapy, and one patient with a BRCA2 mutation was administered PARP inhibitor maintenance after chemotherapy. The median progression-free survival was 13 months, and the median overall survival was 19.5 months. Four cases remained disease-free, while eight cases experienced tumor recurrence, including three cases that resulted in death due to disease recurrence.

Conclusion

Neuroendocrine carcinoma of the ovary is a rare condition that is more common in women of childbearing age and is associated with aggressive behavior and poor clinical outcomes. Surgical resection remains the mainstay of treatment, with some patients benefiting from adjuvant chemoradiation therapy.

1. Introduction

Neuroendocrine neoplasms (NENs) of the female genital tract are rare, accounting for only 1–2% of gynecological malignancies [1]. Among these, primary ovarian NENs are even rarer, as most gynecological NENs are located in the uterine cervix. NENs are a heterogeneous group of diseases. Neuroendocrine carcinoma (NEC) of the ovary represents the highly malignant end of this spectrum, characterized by high-grade tumors that often exhibit aggressive clinical behavior and unfavorable outcomes [2]. NEC of the ovary can be further classified into two subtypes: large cell neuroendocrine carcinoma (LCNEC) and small cell carcinoma of the ovary (SCCO) [3]. Diagnosis of NEC primarily relies on histology, which includes immunohistochemistry. Common markers used for diagnosis include chromogranin A (Cg-A), synaptophysin (Syn), neuron- specific enolase (NSE), and CD56. The histologic origin of NEC is believed to be either from the ovarian surface epithelium or associated with the dedifferentiation of a de novo carcinoma, as they have often been associated with epithelial neoplasms[4, 5]. Currently, there are no established treatment guidelines for NEC of the ovaries due to limited knowledge about this rare entity. Most patients are treated based on guidelines for ovarian epithelial malignancies, which typically involve debulking surgery followed by adjuvant chemotherapy (carboplatin and paclitaxel). The lack of clinical data and evidence-based protocols may contribute to unsatisfactory outcomes in relation to this condition.

In this study, we presented a series of 12 cases of NEC of the ovary, which is one of the largest series reported from a single institution. We analyzed the clinical, pathological, radiological, and survival data of these cases to provide a reference for future therapeutic approaches.
2. Materials and Methods

2.1 Materials

A database search was conducted to identify patients with primary ovarian neuroendocrine carcinomas who were treated in the Department of Gynecology at the First Affiliated Hospital of Zhengzhou University from August 2015 to May 2020. A total of 12 cases were identified with a confirmed diagnosis of NEC through postoperative pathology. The pathological interpretation was conducted by a pathologist specialized in gynecologic malignancies and verified by a second gynecological pathologist. Patients with incomplete clinical data and/or who were lost to follow-up were excluded from the study.

2.2 Methods

Clinical data were obtained through a retrospective chart review, which included information such as age, chief symptoms, auxiliary examination results, FIGO stage, pathology, and treatment. The follow-up period was defined as the time between the initial diagnosis of NEC of the ovary and the last date of contact or death. The performance status was assessed using the Eastern Cooperative Oncology Group (ECOG) score standard. Tumors were staged according to the 2014 FIGO staging classification for ovarian carcinomas. The follow-up period concluded on May 1, 2021. The collection and analysis of data were approved by the Ethics Committee of the First Affiliated Hospital of Zhengzhou University.

3. Results

3.1 Clinical characteristics

The incidence of NEC of the ovary among all ovarian malignancies in this series was 0.59% (12/2048). The median age at diagnosis was 34.5 years (ranging from 20 to 62 years). None of the patients had a family history of ovarian cancers. The initial presentations included abdominal pain (5/12), pelvic mass (4/12), vaginal bleeding (2/12), and abdominal distention (1/12). None of the patients in the study group presented with paraneoplastic syndrome. Eleven out of twelve cases showed an increase in preoperative cancer antigen 125 (CA-125) levels, with a median level of 146.6 U/ml (range: 38.63 to 401.2 U/ml; normal range: 35 U/ml). Neuron specific enolase (NSE) levels, which are normally approximately 13 ng/ml, increased in 5 cases. However, after treatment, all elevated tumor markers returned to normal levels. None of the patients showed an increase in CA199 or HE4 levels. Based on the FIGO 2014 staging standard, 5 cases were classified as stage IA, 1 case as stage IVB, and 6 cases as stage IIIC disease. The clinical features can be found in Table 1.
<table>
<thead>
<tr>
<th>Case</th>
<th>Age (years)</th>
<th>Symptom</th>
<th>CA125(U/ml)</th>
<th>NSE(ng/ml)</th>
<th>Size(cm)</th>
<th>Location</th>
<th>Diagnosis</th>
<th>Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>28</td>
<td>Mass</td>
<td>91.4</td>
<td>N/A</td>
<td>12</td>
<td>Right</td>
<td>SCCO</td>
<td>IA</td>
</tr>
<tr>
<td>2</td>
<td>62</td>
<td>Pain</td>
<td>38.63</td>
<td>N/A</td>
<td>14</td>
<td>Left</td>
<td>LCNEC</td>
<td>IA</td>
</tr>
<tr>
<td>3</td>
<td>29</td>
<td>Pain</td>
<td>46.4</td>
<td>189.7</td>
<td>8</td>
<td>Right</td>
<td>SCCO</td>
<td>IA</td>
</tr>
<tr>
<td>4</td>
<td>37</td>
<td>Mass</td>
<td>42.13</td>
<td>N/A</td>
<td>8</td>
<td>Right</td>
<td>SCCO</td>
<td>IA</td>
</tr>
<tr>
<td>5</td>
<td>20</td>
<td>Pain</td>
<td>401.2</td>
<td>50.65</td>
<td>20</td>
<td>Bilateral</td>
<td>SCCO</td>
<td>IC</td>
</tr>
<tr>
<td>6</td>
<td>54</td>
<td>Bloating</td>
<td>170.6</td>
<td>N/A</td>
<td>5</td>
<td>Bilateral</td>
<td>LCNEC</td>
<td>IIIB</td>
</tr>
<tr>
<td>7</td>
<td>26</td>
<td>Pain</td>
<td>150.7</td>
<td>27.02</td>
<td>5</td>
<td>Bilateral</td>
<td>SCCO</td>
<td>IIIC</td>
</tr>
<tr>
<td>8</td>
<td>31</td>
<td>Mass</td>
<td>61.25</td>
<td>N/A</td>
<td>10</td>
<td>Left</td>
<td>SCCO</td>
<td>IIIC</td>
</tr>
<tr>
<td>9</td>
<td>32</td>
<td>Pain</td>
<td>146.6</td>
<td>N/A</td>
<td>10</td>
<td>Bilateral</td>
<td>SCCO</td>
<td>IIIC</td>
</tr>
<tr>
<td>10</td>
<td>46</td>
<td>Mass</td>
<td>191.0</td>
<td>46.44</td>
<td>13</td>
<td>Bilateral</td>
<td>LCNEC</td>
<td>IIIC</td>
</tr>
<tr>
<td>11</td>
<td>58</td>
<td>Bleeding</td>
<td>14.5</td>
<td>N/A</td>
<td>4</td>
<td>Bilateral</td>
<td>SCCO</td>
<td>IIIC</td>
</tr>
<tr>
<td>12</td>
<td>62</td>
<td>Bleeding</td>
<td>166.5</td>
<td>370</td>
<td>15</td>
<td>Bilateral</td>
<td>SCCO</td>
<td>IVB</td>
</tr>
</tbody>
</table>

### 3.2 Radiological Characteristics

Abdominal ultrasound (US) was performed on all 12 patients, and computed tomography (CT) was performed on 10 patients. Abdominal ultrasound showed that the masses were typically solid or cystic-solid with abundant blood supply within the lesion, occupying the pelvic cavity. The borders of the masses were clearly defined with irregular contours (Fig. 1). The CT scan typically revealed a soft tissue mass with varying density in the pelvic cavity. Contrast-enhanced CT demonstrated slight enhancement or uneven enhancement of the solid components (Fig. 2).

### 3.3 Pathologic evaluation and classification

Out of the 12 primary ovarian NEC patients, 9 had SCCO and 3 had LCNEC. The median greatest dimension of the ovarian tumor was 10.4 cm, ranging from 4 to 20 cm. The tumor was unilateral in 5 cases and bilateral in 7 cases. The neoplastic cells were positive for CD56 in all cases (Fig. 3c), Cg-A in 5 out of 10 cases (Fig. 3d), and Syn in 9 out of 11 cases (Fig. 3e). Additionally, CK was positive in 5 out of 6 cases (Fig. 3f), with CK7 being positive in 4 out of 6 cases, CK20 being positive in 1 out of 3 cases, EMA being positive in 6 out of 7 cases, and PAX-8 being positive in 4 out of 8 cases. The immunohistochemical results are listed in Table 2.
### Table 2

<table>
<thead>
<tr>
<th>case</th>
<th>CD56</th>
<th>Syn</th>
<th>Cg-A</th>
<th>CK</th>
<th>NSE</th>
<th>KI-67</th>
<th>CK7</th>
<th>CK20</th>
<th>EMA</th>
<th>PAX-8</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>90%</td>
<td>N/A</td>
<td>-</td>
<td>-</td>
<td>N/A</td>
</tr>
<tr>
<td>2</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>N/A</td>
<td>70%</td>
<td>+</td>
<td>N/A</td>
<td>N/A</td>
<td>+</td>
</tr>
<tr>
<td>3</td>
<td>+</td>
<td>+</td>
<td>focal+</td>
<td>N/A</td>
<td>N/A</td>
<td>70%</td>
<td>N/A</td>
<td>N/A</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>N/A</td>
<td>80%</td>
<td>-</td>
<td>N/A</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>+</td>
<td>+</td>
<td>focal+</td>
<td>N/A</td>
<td>N/A</td>
<td>70%</td>
<td>N/A</td>
<td>N/A</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>focal+</td>
<td>+</td>
<td>focal+</td>
<td>N/A</td>
<td>N/A</td>
<td>70%</td>
<td>+</td>
<td>+</td>
<td>N/A</td>
<td>+</td>
</tr>
<tr>
<td>7</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>N/A</td>
<td>70%</td>
<td>+</td>
<td>N/A</td>
<td>N/A</td>
<td>-</td>
</tr>
<tr>
<td>8</td>
<td>+</td>
<td>-</td>
<td>N/A</td>
<td>+</td>
<td>-</td>
<td>90%</td>
<td>N/A</td>
<td>N/A</td>
<td>+</td>
<td>N/A</td>
</tr>
<tr>
<td>9</td>
<td>+</td>
<td>-</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>40%</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>10</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>N/A</td>
<td>90%</td>
<td>N/A</td>
<td>N/A</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>11</td>
<td>+</td>
<td>N/A</td>
<td>-</td>
<td>N/A</td>
<td>N/A</td>
<td>80%</td>
<td>+</td>
<td>N/A</td>
<td>N/A</td>
<td>-</td>
</tr>
<tr>
<td>12</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>N/A</td>
<td>N/A</td>
<td>100%</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>N/A</td>
</tr>
</tbody>
</table>

### 3.4 Therapies

Surgery was performed by gynecological oncologists with the primary goals of achieving complete tumor resection and adequate staging, following the FIGO guidelines. Primary surgery was conducted in 10 patients, with one patient having received neoadjuvant chemotherapy (TCx3), and one patient (case 12) declining surgery due to extensive metastasis. Out of the 11 patients, 8 underwent bilateral salpingo-oophorectomy (BSO) and hysterectomy. Fertility was preserved in two patients (case 3 and 5), while one patient (case 7) only underwent omentectomy and peritoneal biopsy as their family refused debulking surgery. Systemic pelvic and paraaortic lymphadenectomy was performed in all 9 patients. To achieve optimal tumor debulking, omentectomy was performed in all nine patients, with additional extra-ovarian debulking in five patients. After surgery, 10 out of 11 patients showed no visible tumors. Prior to chemotherapy, all patients were evaluated for their performance status using the ECOG 0–1 scale. The chemotherapy regimens used are listed in Table 3. The time interval between surgery and the start of chemotherapy ranged from 2 to 4 weeks. Six patients received etoposide/cisplatin (EP), while the remaining cases were treated with paclitaxel/cisplatin (TC) or carboplatin (TP), as indicated. Among the 6 patients treated with TP or TC, patient 10, who requested genetic testing, was found to have a BRCA2 mutation. After chemotherapy, this patient received PARP inhibitor maintenance. However, the tumor recurred 2 months post-chemotherapy. Patient 11 received radiotherapy after chemotherapy and remained disease-free during the 49-month follow-up period.

### 3.5 Survival

The follow-up time for the 12 cases ranged from 9 to 49 months, with a median of 19.5 months. Out of the patients, 3 expired due to tumor recurrence, while 9 patients were still alive during the follow-up period. Among the patients, 8 experienced recurrence and/or disease progression, with recurrences observed in the liver, bones, pelvis, and inguinal lymph nodes. Due to the limited number of cases, we were unable to determine the impact of FIGO stage, tumor pathological type, and different chemotherapies on prognosis.
Table 3
Therapy and follow-up.

<table>
<thead>
<tr>
<th>Case</th>
<th>Operation</th>
<th>Chemotherapy</th>
<th>Recurrence(site)</th>
<th>PFS(months)</th>
<th>Survival State</th>
<th>Follow-up (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>BSO/TAH/OM/LN</td>
<td>EP×6</td>
<td>N</td>
<td>34</td>
<td>NED</td>
<td>34 m</td>
</tr>
<tr>
<td>2</td>
<td>BSO/TAH/OM/LN</td>
<td>TC×6</td>
<td>N</td>
<td>37</td>
<td>NED</td>
<td>37 m</td>
</tr>
<tr>
<td>3</td>
<td>USO</td>
<td>EP×7</td>
<td>Y, brain</td>
<td>9</td>
<td>DOD</td>
<td>10 m</td>
</tr>
<tr>
<td>4</td>
<td>BSO/TAH/OM/LN</td>
<td>EP×7</td>
<td>Y, Liver</td>
<td>13</td>
<td>AWD</td>
<td>13 m</td>
</tr>
<tr>
<td>5</td>
<td>BSO/OM/LN</td>
<td>EP×6</td>
<td>Y, Bones</td>
<td>17</td>
<td>AWD</td>
<td>25 m</td>
</tr>
<tr>
<td>6</td>
<td>NACT + BSO/TAH/OM/LN</td>
<td>TC×8</td>
<td>Y, pelvic</td>
<td>13</td>
<td>AWD</td>
<td>15 m</td>
</tr>
<tr>
<td>7</td>
<td>OM/PB</td>
<td>TC×3</td>
<td>Y, pelvic</td>
<td>3</td>
<td>DOD</td>
<td>10 m</td>
</tr>
<tr>
<td>8</td>
<td>BSO/TAH/OM/LN</td>
<td>EP×6</td>
<td>N</td>
<td>15</td>
<td>NED</td>
<td>26 m</td>
</tr>
<tr>
<td>9</td>
<td>BSO/TAH/OM/LN</td>
<td>TP×6</td>
<td>Y, lymph</td>
<td>6</td>
<td>AWD</td>
<td>17 m</td>
</tr>
<tr>
<td>10</td>
<td>BSO/TAH/OM/LN</td>
<td>TP×6 + PARPi</td>
<td>Y, liver</td>
<td>9</td>
<td>AWD</td>
<td>22 m</td>
</tr>
<tr>
<td>11</td>
<td>BSO/TAH/OM/LN</td>
<td>TC×6 + Radiotherapy</td>
<td>N</td>
<td>49</td>
<td>NED</td>
<td>49 m</td>
</tr>
<tr>
<td>12</td>
<td>-</td>
<td>EP×6</td>
<td>Y, pelvic</td>
<td>6</td>
<td>DOD</td>
<td>9 m</td>
</tr>
</tbody>
</table>

EP: Etoposide/Cisplatin; TC: Paclitaxel/Carboplatin; TP: Paclitaxel-Cisplatin; Y: Yes; N: No; DOD: Dead of disease; AWD: Alive with disease; NED: No evidence of disease; Om: Omentectomy; USO: Unilateral salpingo-oophorectomy; BSO: Bilateral salpingo-oophorectomy; LN: Lymph node dis-section; m: months; PB: Peritoneal biopsy; NACT: Neoadjuvant chemotherapy.

4. Discussion

4.1 Diagnosis of ovarian neuroendocrine carcinoma

Patients with neuroendocrine carcinoma of the ovary tend to be younger than those with other histologic subtypes of ovarian cancer. Some studies have also suggested that neuroendocrine carcinoma of the ovary can occur after menopause[6, 7]. In our study, the main symptoms observed were abdominal pain and pelvic mass. Additionally, a majority of the cases (7 out of 12) were diagnosed at an advanced stage, which aligns with findings in the existing literature[2]. The rate of lymph node metastasis in neuroendocrine carcinoma of the ovary has rarely been reported in previous studies. In our study, only one case showed lymph node metastasis, indicating a potentially low rate of lymph node metastasis for this type of tumor. This suggests that lymphatic metastasis may not be the primary route of metastasis for neuroendocrine carcinoma of the ovary.

The diagnosis of neuroendocrine carcinoma of the ovary often lacks specific findings on US and CT scans alone[8]. However, CT scans can provide valuable information about the location, size, and presence of distant metastasis of the lesion. Therefore, CT scans are of great significance for preoperative staging and determining surgical methods. In this study, it was observed that serum CA-125 levels increased in most cases (11 out of 12), suggesting a potential link between CA-125 and neuroendocrine carcinoma of the ovary. Previous studies have confirmed that CA-125 levels are closely associated with epithelial ovarian cancers and can be utilized for monitoring and diagnosing such cancers[9, 10]. The
elevation of serum CA125 in ovarian neuroendocrine carcinoma has been reported in the literature\[11\]. In our study, CA-125 levels increased in 11 out of 12 cases, with an average of 126.7 U/ml. However, the CA125 level in ovarian neuroendocrine carcinoma was found to be lower than that in ovarian epithelial carcinoma. Therefore, further studies are needed to analyze the relationship between CA-125 and neuroendocrine carcinoma of the ovary. Ascitic fluid cytology was also performed, and only two cases showed the presence of malignant cells in ascites or peritoneal lavage fluid. This demonstrates that identifying malignant cells derived from neuroendocrine carcinoma of the ovary in ascitic fluid may be challenging.

Histopathological analysis of tissue specimens is crucial for diagnosing neuroendocrine carcinoma of the ovary. Immunohistochemistry is necessary to confirm the diagnosis \[4\]. The results of immunohistochemistry revealed that tumors expressed at least one neuroendocrine marker (Cg-A, CD56, or Syn). In this study, CD56 was expressed in all cases, suggesting that it was the most sensitive marker for demonstrating the neuroendocrine nature of these tumors. However, the lack of specificity of CD56 was observed as it was also expressed in nonendocrine tissues such as renal tubules, ovarian sex cord-stromal, and thyroid follicular cells\[12–14\]. For this reason, some authors did not recommend relying solely on CD56 to demonstrate neuroendocrine components\[11–12\]. Therefore, immunohistochemistry plays a crucial role in the diagnosis.

4.2 Therapy of ovarian neuroendocrine carcinoma

The current main treatment for neuroendocrine carcinoma of the ovary is typically surgical resection followed by adjuvant chemotherapy. However, there is currently no standard guideline in place\[15\]. The goal of surgical resection is to remove all visible lesions. A recent study has shown that surgeries can significantly improve survival rates, therefore complete surgical resection should be recommended as the primary treatment option\[7\]. Some young patients may wish to preserve their fertility. However, the use of fertility-sparing surgery is a topic of debate. There have been a few small case series reporting successful pregnancies in patients who underwent unilateral salpingo-oophorectomy (USO) and received adjuvant chemotherapy\[16, 17\]. In another study, 26 patients underwent USO, but none of them resulted in a successful pregnancy\[18\]. Of these cases, two opted for fertility-sparing surgery. Unfortunately, one patient who had a BSO passed away after 10 months of treatment, and the other patient who had a USO experienced recurrence after 12 months. It is worth noting that postoperative chemotherapy can potentially impact ovarian function\[19\]. To safeguard the ovary from the harmful effects of chemotherapy, clinical practice has incorporated techniques such as oocyte or embryo cryopreservation, as well as cryopreservation of the ovarian cortex. However, performing these methods may be challenging and the future use of cryopreserved germ cells is still uncertain\[20\]. Therefore, additional studies should be conducted to evaluate the feasibility of fertility-sparing surgery for patients with ovarian neuroendocrine carcinoma.

The present study refers to adjuvant therapies for lung small cell carcinoma, specifically chemotherapy and radiation\[2\]. The literature suggests that EP and TP are the main chemotherapy regimens\[21, 22\]. Although small sample studies and case reports indicate potential benefits of chemotherapy, the lack of prospective studies hinders the availability of convincing evidence regarding its effect on the prognosis of patients with ovarian neuroendocrine carcinoma. In this study, 6 patients were treated with EP, and 6 patients received PT. Out of the total 8 patients, progression or recurrence was observed. Among these, 3 patients relapsed due to platinum resistance, while 2 patients showed progression during chemotherapy. These findings indicate a poor response of these tumors to the chemotherapy. Hence, further investigation is required to determine the sensitivity of patients to platinum drugs and identify the optimal chemotherapy regimen.

Radiotherapy has been infrequently utilized in the treatment of ovarian cancers \[2\]. In our study, only one patient received radiation therapy and was followed up for 49 months without any recurrence of the disease. The role of radiotherapy in the management of neuroendocrine carcinoma of the ovary is still not well-established, although some reports have suggested potential benefits\[23, 24\]. Therefore, further investigation is warranted to explore the potential of radiotherapy in neuroendocrine carcinoma of the ovary. Currently, there is limited research on targeted therapy in neuroendocrine carcinoma of the ovary. In this study, a single case with a BRCA2 germline mutation was treated with a PARP inhibitor.
However, the patient experienced recurrence after 2 months, suggesting that PARP inhibitors may not be beneficial for patients with neuroendocrine carcinoma of the ovary. Further recruitment of additional cases is necessary to investigate the role of PARP inhibitors in treating neuroendocrine carcinoma of the ovary.

4.3 Prognosis of ovarian neuroendocrine carcinoma

The 1-, 3-, and 5-year survival rates for patients with neuroendocrine carcinoma of the ovary were 58.3%, 33.6%, and 27.6%, respectively. Limited studies have been conducted on the prognosis of ovarian neuroendocrine cancer, with tumor staging being considered an important prognostic factor. The median follow-up time for this study was 19.5 months. Three patients died due to disease recurrence, four patients survived without evidence of recurrent disease, and five patients survived with tumor. Among patients with relapse or progression, four patients showed an increase in CA125 levels. Further data are needed to confirm whether serum CA125 levels can be used as an indicator for disease monitoring.

5. Conclusions

Neuroendocrine carcinoma of the ovary is a rare and aggressive malignant disease with a poor prognosis. The diagnosis primarily relies on histopathological analysis of tissue specimens, and immunohistochemistry plays a crucial role in both diagnosis and differential diagnosis. Surgical resection is the preferred treatment option, and adjuvant chemotherapy along with potential radiotherapy can potentially extend the survival of certain cases. Considering the rarity of primary ovarian neuroendocrine carcinoma, a future multicenter study is necessary to gain further understanding of this uncommon disease.

Abbreviations

NENs: Neuroendocrine neoplasms; SCCO: small cell carcinoma of the ovary; LCNEC: large cell neuroendocrine carcinoma; Cg-A: chromogranin A; Syn: synaptophysin; NSE: neuron-specific enolase; ECOG: Eastern Cooperative Oncology Group; N/A: Not applicable; US: ultrasound; CT: computed tomography; BSO: bilateral salpingo-oophorectomy; EP: etoposide/cisplatin; TC: paclitaxel/cisplatin; TP: carboplatin; Y: Yes; N: No; DOD: Dead of disease; AWD: Alive with disease; NED: No evidence of disease; Om: Omentectomy; USO: Unilateral salpingo-oophorectomy; LN: Lymph node dissection; m: months; PB: Peritoneal biopsy; NACT: Neoadjuvant chemotherapy.

Declarations

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Not applicable.

Authors’ contributions

Conception and design: XY, WZ. Acquisition of data: XY, WZ. Data analysis and interpretation: XY, WZ, LY, LP. Drafting of manuscript: All authors. Final approval of manuscript: All authors.

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Availability of data and materials

The datasets generated during the current study are not publicly available but are available from the corresponding author on reasonable request.
Ethic approval and consent to participate
The study was approved by Institutional Ethic Committee for Clinical Research of The First Affiliated Hospital of Zhengzhou University (2023-KY-0735-001) and individual consent for this retrospective analysis was waived.

Consent for publication
The study contained no individual person's data and individual consent for this retrospective analysis was waived.

Competing interests
The authors declare that they have no competing interests.

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References


**Figures**

![Figure 1](image-url)

**Figure 1**

US features. The tumor was solid with heterogeneous echo in case 4 (a); Color Doppler flow imaging displayed rich intralesional vascularization in the solid part of the lesion (b and c).
Figure 2

CT features. A soft tissue mass with heterogeneous density occupied the pelvic cavity in case 1(a); CT scan revealed a multiseptated mixed solid and cystic mass in case 12 (b); Enhanced CT showed marginal enhancement of the tumor in case 5 (c); Heterogenous enhancement of the solid part (d).

Figure 3

Histological and immunohistochemical LCNEC: Tumor cells are arranged in nests, with relatively abundant basophilic cytoplasm, large round-to-oval nuclei and frequent mitosis in case 10 (a); SCCO: Tumor cells are arranged in an organoid pattern, and some of the cells are spindle-shaped. The nucleus is oat-like, with abundant mitotic and apoptotic activity in case 4 (b); Neuroendocrine carcinoma positive for CD56 (c), Cg-A (d) and Syn (e); Positive for CK (f).