Synchronous endometrial and ovarian carcinoma (SEOC): case series and literature review

Shahzarul Fazril Lin1,1, Zainab Yahaya1,1, Nuraini Ramli1,1, Habibah Abdul Hamid2, *

1 Obstetrics & Gynaecology Department, Hospital Serdang, Serdang, 43400 Selangor, Malaysia
2 Obstetrics & Gynaecology Department, Faculty of Medicine & Health Sciences, Universiti Putra Malaysia (UPM), Serdang, 43400 Selangor, Malaysia

*Correspondence: habib@upm.edu.my (Habibah Abdul Hamid)
† These authors contributed equally.

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Objectives: Synchronous endometrial and ovarian cancer (SEOC) is a rare female reproductive malignancy comprising ovarian and endometrial cancer. Precise diagnosis is crucial for treatment and prognostication, as overall outcome and treatment is differ from those of metastatic endometrial cancer (EC) or ovarian cancer (OC). In this review based on 4 case series of SEOC, we aim to discuss the clinical characteristic, accurate diagnosis using advance molecular analysis techniques and immunohistochemistry (IHC) tests and treatment modalities of SEOC. Method: Case series and literature review. Results: In our report, SEOCs are more prevalent in young premenopausal women with obesity, nulliparous and hereditary predisposition as risk factors. Abnormal menses, abdominal distention and abdominal pain were the common presenting symptoms. It made all diagnosis for SEOCs histologically based on established criteria. Surgery remains the main treatment modality with the goal for treatment and achieving diagnosis. All of our patients had an endometrioid type histology with early stage and low grade histology for both endometrial carcinoma (EC) and ovarian carcinoma (OC) except two patients had concomitant seromucinous ovarian carcinoma (OC). We perform a review of the literature highlighting the characteristic and management of SEOC, particularly emphasizing the importance of IHC test on the histological confirmatory diagnosis and molecular studies. Conclusion: It is very essential to gain an accurate diagnosis, treat and prognosticate this disease as overall outcome and treatment is different compared to metastatic EC or OC.

Keywords
Endometrial cancer (EC), Ovarian cancer (OC), SEOC, Metastatic disease, Outcome; Synchronous primary cancer

1. Introduction
The advancement of molecular testing and diagnostics has allowed us to better understand the relationship between tumors and determine its origin accurately. Techniques such as massive parallel sequencing would allow us to identify genetic mutation and ultimately determine cancer origin and development. Studies from Angelisio et al. 2016 [1] and Schulteis et al. 2016 [2] into SEOC cases, has demonstrated genetic clonality in clinically independent tumors to be actually molecularly related [1]. Based on this paradigm shifting evidence, we have retrospectively evaluated four of our cases to hopefully provide us with new perspective when dealing with dual primary malignancy.

It is known that synchronous primary tumours of the female genital tract are relatively rare, comprising 1.7% of all genital neoplasms [3]. They occur in 10% of cases of ovarian cancer and in 5% of women with endometrial cancer [4]. The most predominant cancer is synchronous endometrial and ovarian cancer (SEOC), which accounts for 51.7% of all synchronous genital tumours [3]. The restricted dissemination phenomenon according to Angelisio et al. 2016, suggests that SEOC tumor cells is capable of separating from the primary site, avoid apoptosis, spread through open spaces and colonize exclusive sites (endometrium and ovary) [1]. The indolent nature of the spread means any spread beyond the primary sites is not associated with metastasis. Women with SEOC are typically diagnosed with disease confined to the pelvis, microscopically limited to the uterus and ovary with low histologic grade which has better prognosis and surgical resectability compared to metastatic disease of single origin malignancy. It is reported in one study that women with stage I endometrioid endometrial carcinoma and stage I endometrioid ovarian carcinoma have similar survival outcomes to those with stage I endometrioid endometrial cancer with synchronous ovarian cancer, with a 10-year rate overall survival rate of 88.2% versus 89.1%, P = 0.40 [5]. Other studies have also reported favourable prognosis of 73.3% for a five-year survival rate [3].

The most common histology type of SEOC is endometrioid adenocarcinoma in both endometrium and ovary which accounts for 60.47% [6]. Other histologic types are serous adenocarcinoma, clear cell carcinoma, adenosquamous and acanthoadenocarcinoma. In the past SEOC diagnosis was based on clinicopathology criteria. When histologic types are discordant, the diagnosis of SEOC is precise; however, the dilemma occurs for concordant histologic types because the treatment, prognosis and overall survival differs significantly from SEOC and metastatic disease. It is thus necessary to employ more sophisticated methods for the analysis of tissue and immunohistochemistry (IHC) to distinguish these two entities.
In this retrospective case series, we present four patients diagnosed with SEOC who underwent definitive treatment at Serdang Hospital for two years (2018 to 2020). We critically discuss the presentation, diagnostic characteristics, management, clinical outcome and clinicopathological characteristics of these women.

2. Case reports

2.1 Case 1

A 40-year-old single, nulliparous, obese woman with a body mass index (BMI) of 31 kg/m², presented with a history of abnormal uterine bleeding and abdominal distention for the past two years. She has a strong family history of carcinoma where both of her sisters had endometrial and ovarian carcinoma, and four paternal uncles and grandfather had colon carcinoma. Clinical examination showed a large cystic abdominal mass corresponding to a 24-week size gravid uterus.

Abdominal ultrasound scan showed 2 malignant ovarian tumour features; an irregular multiloculated solid-cystic mass measuring 11 cm × 8 cm with multiple, (>4) papillary projections, and the uterus was normal-sized with an irregular mixed echogenic endometrial lining of 24 mm and no ascites. The computed tomography (CT) scan of the thoraco-abdomen-pelvis area revealed a large multi-septated solid cystic mass measuring 9.7 cm × 13.3 cm × 16.5 cm (AP × W × CC) with an enhancing peripheral solid component and internal septations. There was the presence of hydrometra with an ill-defined bulky cervix measuring about 4.5 cm (AP) × 5.5 cm (W) × 3.4 cm (CC). There were also multiple small nodules along the pelvic iliac chain. Endometrial sampling performed and the histopathology reported endometroid carcinoma of the endometrium.

The tumour markers, CA-125 and CA19-9 both were raised at 52.6 U/mL and 61.9 U/mL respectively. The CEA and AFP levels were normal. The clinical diagnosis was an endometrial carcinoma with ovarian metastasis or synchronous endometrial and ovarian malignancy.

She underwent a total abdominal hysterectomy, bilateral salpingo-oophorectomy, pelvic lymph nodes dissection, omentectomy and appendectomy on September 2019. The final histological report confirmed an endometrioid adenocarcinoma of the endometrium with less than 50% myometrial invasion (stage IIA, Grade 1). Subsequently, the patient had undergone six cycles of adjuvant chemotherapy of carboplatin and invaded the right fallopian tube and adjacent fatty tissue (stage II A, Grade 1). Subsequently, the patient had undergone six cycles of adjuvant chemotherapy of carboplatin (AUCS) and paclitaxel (175 mg/m²). Currently, she is still alive and recurrence-free at this point of reporting.

2.2 Case 2

A 38-year-old married lady, obese body mass index (BMI) 28 kg/m², nulliparous presented with a history of abnormal uterine bleeding and abdominal distension for two months. She has a background history of primary infertility secondary to polycystic ovarian syndrome (PCOS) and endometriosis. Clinical examination showed a mobile cystic abdominal mass corresponding to a 30-week gravid uterus.

An abdominal ultrasound scan revealed 2 malignant ovarian tumour features (M3, M4). There was a huge irregular multiloculated solid-cystic mass measuring 25 cm × 18 cm, with multiple papillary projections (>4) and no ascites present. The uterus was normal-sized with an irregular hyperechoic endometrial lining of 17 mm. The computed tomography (CT) scan of the thoraco-abdomen-pelvis revealed a large multiloculated cystic mass occupying almost half of the abdomen arising from the right ovary. It measured approximately 26.0 cm × 19.0 cm × 24.0 cm with multiple internal septations and thickened cyst wall. The uterus is bulky with a thick endometrial lining. There was no pelvic lymphadenopathy, omental infiltrations or any distant lesions to suggest metastasis. Her serum CA125 levels were at 206 U/mL and other tumour markers such as CA 19-9, CEA and AFP were normal. A diagnostic hysterectomy, dilatation and curettage was performed and the histopathology reported complex hyperplasia with atypia associated with focal adenocarcinoma. Clinical diagnosis preoperatively was endometrial carcinoma with ovarian metastasis.

This patient underwent a total abdominal hysterectomy, bilateral salpingo-oophorectomy, pelvic lymph nodes dissection and omentectomy. The final histological report confirmed an endometrioid adenocarcinoma of the endometrium with less than 50% myometrial invasion (stage 1A Grade 1) with no lymphovascular invasion and both corona showed absence of tumour involvement. Also, her right ovarian endometrioid carcinoma had breached the capsule and invaded the right fallopian tube and adjacent fatty tissue (stage II A, Grade 1). Subsequently, the patient had undergone six cycles of adjuvant chemotherapy of carboplatin (AUCS) and paclitaxel (175 mg/m²). Currently, she is still alive and recurrence-free at this point of reporting.

2.3 Case 3

A 46-year-old, nulliparous and obese woman with Body Mass Index (BMI) of 30 kg/m² presented with a history of abnormal uterine bleeding and abdominal pain for one week. Her clinical examination was unremarkable.

The abdominal ultrasound scan showed normal size uterus with an irregular, mixed echogenic endometrial lining of 15 mm. There was one benign ovarian and no malignant features present; bilateral smooth multiloculated cystic mass, the right mass measuring 6 cm × 5 cm, the left ovarian mass measuring 5 cm × 4 cm. Both ovarian masses had no papillary projection nor strong blood flow on colour doppler. There was no ascites present. A computed tomography (CT) scan reported bilateral adnexa cystic lesions mea-
The endometrioid carcinoma of ovary is composed of complex tubular glands with focal squamous differentiation. The tumour cells show grade 2 nuclear features. The uterine tumour is composed of neoplastic glands with occasional solid growth pattern. Tumour cells invade superficial myometrium, and display grade 2 nuclear features. (A and B: Haematoxylin and Eosin stain, 100×).

Note—Assessment of both tumours favour independent primary tumour based on superficial myometrial invasion of the endometrium with coexisting atypical hyperplasia and no presence of tubal involvement or lympho-vascular invasion.

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A total abdominal hysterectomy, bilateral salpingo-oophorectomy and pelvic lymph nodes dissection was performed. The final histological report confirmed a well-differentiated endometrioid endometrial carcinoma with less than 50% myometrial invasion and endocervical stroma involvement with a background of complex atypical hyperplasia and no lymphovascular invasion (stage 2, grade 1). Besides, she also had bilateral endometrioid ovarian carcinoma with right tumour surgical spillage (stage 1c, grade 1). The histology favoured two independent tumours given the histologic dissimilarity of both the ovarian and uterine tumours and no lymphovascular invasion. She completed six cycles of adjuvant chemotherapy of carboplatin (AUC5) and paclitaxel (175 mg/m²) with external radiotherapy of 23F and brachytherapy 2F. At the time of writing, this patient is alive and under gynaec-oncology surveillance.

2.4 Case 4

A 53-year-old lady with underlying diabetes, hypertension, chronic kidney disease (CKD) stage III and obesity BMI 33 kg/m², presented with abdominal distension and umbilical swelling for the past one month. Clinical examination showed a distended abdomen and an irregular cystic periumbilical mass measuring 2 cm × 2 cm. The abdominal ultrasound revealed a normal size uterus with an irregular mixed echogenic endometrial thickness of 11 mm. There was a bilateral ovarian tumour with 2 malignant features; irregular multiloculated solid mass of the right ovary measuring 15 cm × 9 cm and 10 cm × 8 cm on the left ovary. There was no papillary projection or ascites seen. The CT scan reported bilateral ill-defined heterogeneous mass with solid and cystic component. The mass on right side measures 11.8 cm × 15.1 cm × 14.9 cm and on the left side was 11.4 cm × 11.7 cm × 13.9 cm. There are two cystic lesions with minimal soft tissue component: in the subcutaneous tissue of the umbilical region and involved the...
umbilicus; and at the right inguinal area anterior to the symphysis pubis. The mass measured 6.1 cm × 6.0 cm and 2.4 cm × 2.6 cm respectively. There were enlarged bilateral inguinal lymph nodes noted. The impression favoured bilateral ovarian malignancy with umbilical and inguinal lymph node metastasis.

Cytology fluid taken from periumbilical mass were suggestive of metastatic adenocarcinoma. The immunohistochemistry (IHC) profile and cytomorphological features were suggestive of a gynaecological tract or breast primary. Subcutaneous nodules with one nodule involving the umbilicus is likely a Sister Mary Joseph nodule. Her tumour markers are CA 125 was 2007 U/mL, CA 19-9 was more than 12000 U/mL, CEA was 31 U/mL, and AFP was normal.

The patient had a total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy, appendicectomy, pelvic lymph nodes dissection and excision of umbilical mass in April 2018. The final histology report confirmed a case of synchronous tumours of endometrial (well-differentiated endometrioid, Grade 1) with invasion less than one half of myometrium. There was no lymphovascular invasion found, and the resection margin is free of tumour. Both ovarian tumours are well-differentiated endometrioid, Grade1 carcinoma. A capsular breach noted in the left ovarian tumour, and both fallopian tubes showed tumour involvement in the mucosa, given the presence of complex atypical hyperplasia in endometrium and less than one half of myometrial invasion of the endometrial tumour; which favours a double primary tumour. The umbilical nodule is moderately differentiated metastatic endometrioid carcinoma. Peritoneal tissue, omentum and appendix are free of tumour.

The final diagnosis is synchronous endometrioid of endometrial and bilateral ovarian carcinoma with skin metastases (Sister Mary-Joseph nodule). Adjuvant chemotherapy was not given due to her low ECOG status (grade 3) and multiple co-morbidities. She was disease free for the past 17 months and was diagnosed with the recurrent disease on September 2019 based on increasing CA125 levels from 182 U/mL to 1469 U/mL and on CT scan showed an increased size of metastatic nodules of the right inguinal, left axillary and iliac lymph nodes. She was given six cycles of single agent carboplatin and is currently on gynaec-oncology surveillance follow up.

3. Discussion

In our case series, the majority of patients were below the age of 50 years old with obesity and nulliparity present in 3 out of 4 cases. One patient had a strong family history of endometrial and ovarian carcinoma. The most common symptom presented were abnormal uterine bleeding and abdominal distension. The ultrasound findings of the ovarian tumours in 3 cases were suspicious of ovarian malignancy, while one patient had benign features based on the simple ultrasound rules for diagnosis of ovarian cancer. Three patients had endometrial biopsies based on abnormal uterine bleeding symptom with the results reported as complex hyperplasia with atypia with focal adenocarcinoma (n = 2) and endometroid carcinoma (n = 1). Tumour markers taken showed remarkably elevated CA 125 in all the patients, while the CA 19-9 levels taken for three patient also demonstrated raised values. Preoperatively three cases were diagnosed with endometrial carcinoma with ovarian metastasis (ECOM) or suspected SEOC and one patient as ovarian cancer. All of our patients had undergone abdominal hysterectomy with pelvic lymph node dissection. Post-operative histology in all patients reported as synchronous endometroid carcinoma of the endometrium and ovarian in all the patients. Three patients were diagnosed with stage 1A endometrial cancer, and one patient with stage 2. Adjuvant chemotherapy was given to 3 patients using the carboplatin (AUC5) and paclitaxel (175 mg/m²) regiment for six cycles while one patient only received six cycles of single agent carboplatin (AUC5) during recurrence.

There are various limitations in our case series, such as the retrospective data collected and the small number of patients. The molecular or immunohistochemistry (IHC) testing was not carried out due to the limited availability of laboratories and the high cost in our local setting.

In our case series, 3 out of 4 women were aged less than 50 years old and nulliparous at the time of diagnosis which concurs with previous studies that SEOC is more prevalent in younger, premenopausal and nulliparous women [6–9]. The presence of obesity in all these women is a known risk factor for EC, as BMI of more than 28 kg/m² increases the risk for developing endometrial cancer [6] and potentially concomitant OC.

SEOC is the most common synchronous malignancy of the genital tract, accounting for 51.7% of all genital tract synchronous tumours [7]. The incidence of EC has increased over the past two decades, mainly due to obesity and physical inactivity. Various studies confirmed that SEOC is more prevalent in younger, premenopausal, nulliparous and obese women [6–9]. In our case series, 3 out of 4 women were nulliparous and aged less than 50 years old, and all of them were premenopausal at the time of diagnosis, which corresponds with the above data.

In our report, the most common presentations were abnormal uterine bleeding and abdominal distention which concurs with known data that the most common clinical symptoms were abnormal uterine bleeding (65.12%), abdominal pain and abdominal fullness (39.53%), followed by the presence of a palpable abdominal mass (25.58%) [6].

The radiologic distinction between SEOC from ECOM is uncertain although three patients demonstrated signs of malignant adnexal mass on ultrasound. Serum tumour markers such as CA 125 (normal value CA125 < 35 U/mL) are high in all our patients, which is similar in the majority of reported cases of SEOCs (76.9%) [6].
<table>
<thead>
<tr>
<th>No</th>
<th>Age</th>
<th>Race</th>
<th>Para</th>
<th>BMI (kg/m²)</th>
<th>Other risk factors</th>
<th>Presenting symptoms</th>
<th>Tumour markers</th>
<th>Surgery</th>
<th>EC Histology (Stage/Grade)</th>
<th>OC Histology</th>
<th>Adjuvant chemo/radiotherapy</th>
<th>Recurrence</th>
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<tbody>
<tr>
<td>1</td>
<td>41</td>
<td>Malay</td>
<td>0</td>
<td>31</td>
<td>Family history of malignancy: Abnormal menstrual bleeding</td>
<td>CA125: 52.6</td>
<td>TAHBSO + PLND + omentectomy + appendicectomy</td>
<td>Endometrioid</td>
<td>(Stage IA, G2)</td>
<td>Endometrioid</td>
<td>Chemotherapy</td>
<td>No</td>
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<td></td>
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<td></td>
<td>2 sisters had endometrial and ovarian carcinoma</td>
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<td></td>
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<td></td>
<td>4 Paternal uncles and grandfather had colon carcinoma.</td>
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<tr>
<td>2</td>
<td>38</td>
<td>Malay</td>
<td>0</td>
<td>28</td>
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<td>Abdominal distention</td>
<td>CA125: 206</td>
<td>TAHBSO + PLND + omentectomy</td>
<td>Endometrioid</td>
<td>(Stage IA, G1)</td>
<td>Endometrioid + endometriosis</td>
<td>Chemotherapy only</td>
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<td>Endometriosis.</td>
<td>Constitutiona...</td>
<td>Endometrioid</td>
<td>(stage IIA, G1)</td>
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<tr>
<td>3</td>
<td>46</td>
<td>Chinese</td>
<td>0</td>
<td>30</td>
<td>Infertility</td>
<td>Abnormal menstrual bleeding</td>
<td>CA125: 205</td>
<td>TAHBSO + PLND</td>
<td>Endometrioid adenocarcinoma with squamous differentiation with extension to cervical stroma</td>
<td>Endometrioid</td>
<td>Chemotherapy</td>
<td>No</td>
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<td></td>
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<td></td>
<td>(Stage 2, G1)</td>
<td>(Stage IC, G1)</td>
<td>Pelvic radiotherapy</td>
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<tr>
<td>4</td>
<td>53</td>
<td>Malay</td>
<td>1</td>
<td>33</td>
<td>Diabetes Abdominal distention</td>
<td>CA125: 2007</td>
<td>TAHBSO + PLND + omentectomy + appendicectomy + excision of umbilical mass</td>
<td>Endometrioid</td>
<td>(Stage IA, G1)</td>
<td>Endometrioid</td>
<td>Sister-Mary Joseph nodule</td>
<td>Yes (after 17 months of surgical treatment)</td>
</tr>
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<td></td>
<td>Hypertension</td>
<td>Umbilical mass</td>
<td>CA19-9: 12000</td>
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</table>
All SEOC diagnosed in the early stages and adequately treated by surgery alone, followed by surveillance [5, 10]. In our case series, all patients underwent a staging procedure; hysterectomy, bilateral salpingo-oophorectomy and bilateral pelvic lymphadenectomy with or without omentectomy and appendicectomy. Subsequently, all patients required adjuvant chemotherapy and one patient required radiotherapy due to disease stage (Table 1). These additional treatments, however, does not correlate with available literature regarding SEOCs, which beckons the review for new evidence to explain the findings.

The histology subtype of all the patients in this case series had concordant endometrioid adenocarcinoma of the endometrium and ovary. It is the typical histology for SEOCs in up to 60–70% of cases, and most of them are diagnosed in early stages with low histologic grade [3, 4, 6, 8, 11]. This concurs with the hypothesis of “microenvironment restriction” where the two primaries would be in the early stage with a low-grade histology [4, 12, 13]. However, three patients had ovarian carcinoma of stages 2–4, which does not reflect the pattern of most SEOCs despite low-grade histology in the endometrium.

In our cohort of patients, the results and treatment outcome was different from available literature on SEOCs, and this poses a question of clinical and pathologic importance. Currently, the histologic diagnosis of a synchronous tumour is according to the Ulbright and Roth criteria for SEOC [14, 15]. These criteria, however, may not always be applicable. When molecular testing was carried out on clinicopathology diagnosed SEOC cases, a large proportion was found to be metastatic disease [12]. In our patients, no immunohistochemistry (IHC) or molecular testing was done, thus metastatic disease could not be ruled out nor confirmed.

In this case series, we need to acknowledge that by performing advance molecular analysis techniques and IHC tests would enable us to determine the accurate diagnosis and explain the disease pattern observed. By using high-depth targeted parallel sequencing we can confirm the relationship between synchronous uterine and ovarian lesion, and whether they are clonally related or distinct tumours. High-depth targeted massively parallel sequencing can determine that these tumours are clonally related and metastasis can occur from either the endometrium to the ovaries or vice versa [2, 13]. In patients with concordant endometrioid histology, massively parallel sequencing (MIPS) and molecular inversion probe microarrays can better demonstrate the presence of similar somatic mutation to confirm clonality or single origin [16]. Another determinate is the copy number analysis (CNA), where the presence of a significant number of overlapping copies are present between tumours may indicate a single origin and patients who would require adjuvant treatment [16].

Immunohistochemistry testing for vimentin should also be carried out in our patients to assess the pattern of expression. A negative stain has a sensitivity and specificity to predict primary ovarian carcinoma at 97% and 82% [13]. While a positive vimentin staining had an 82% sensitivity and 97% specificity in predicting a uterine carcinoma [15]. Paired-box gene 8 (PAX8) is another marker that can be useful in distinguishing between EC and OC. It can diagnose gynecological malignancy of ovarian in origin primarily and used before receiving neoadjuvant chemotherapy in cases of advanced ovarian carcinoma [17], this is because primary ovarian cancers express PAX-8 but not OC metastases [8].

The role of genetic testing in our setting is limited and only performed to individuals with family history of malignancy. It is known that patients with Lynch syndrome or hereditary non-polyposis colorectal cancer (HNPCC) would present with a molecularly concordant disease which suggests a single origin rather than SEOC [18]. One of our patients would benefit from this application as young women with SEOC have a higher prevalence for HNPCC. However, it is worth noting that microsatellite instability and subsequent mutations in genes mismatch repairs compatible with HNPCC were also present in 40% of women with SEOC [8, 19, 20]. Patients with a family history of HNPCC and EC may benefit from additional counselling regarding the higher risk of developing colon carcinoma within five years following a hysterectomy at 2% and 6% respectively [9].

Surgical staging remains the mainstay treatment for SEOCs and the majority of metastatic disease cases. In cases where the origin of the primary tumour is uncertain, it is best to perform surgical staging and pelvic lymphadenectomy where lesions are confined to the uterus and endometrium [16]. SEOC patients with tumours localized to the uterine body and adnexe (ovary and fallopian tube) show a low risk for recurrence. Therefore, adjuvant therapy for an early stage and low histologic grade of SEOC is not beneficial. However, the prognosis of SEOC is different from metastatic endometrial or ovarian cancer [5]; therefore, it is crucial to distinguish the diagnosis and offer appropriate treatment to improve outcomes. In our case series, molecular and IHC testing would play a significant role in determining metastatic disease or SEOC, which would enable us to recommend appropriate counselling and adjuvant treatment. A recent study by Wang T et al. [14] suggested that aggressive therapy to both SEOC, endometrial carcinoma and ovarian metastasis (ECOM) patients, especially those with menopausal status, endometrial tumours, advanced omental and lymph node metastasis for better prognosis and survival rate.

The importance of distinguishing SEOC from endometrium with ovarian metastasis is crucial as it determines management and prognosis. The prognosis of women with early stage SEOC is excellent, with overall survival of 80–90% [13]. The presence of stage 1 endometroid ovarian cancer and stage 1 endometrial cancer does not affect overall survival [12]. Nevertheless, in metastatic disease, the five year survival of FIGO stage III endometrial cancer or FIGO stage II-III of ovarian cancer is 25–70%. It is vital that molecular, and IHC (vimentin, PAX-8) testing be incorporated into our
investigation process to identify and clearly distinguish these two entities. We hope based on current literature and evaluation of previous cases, would provide new perspective into our approach of SEOC or dual primary tumours patients.

4. Conclusions
The identification of SEOC or metastatic endometrium/ovarian disease is of great clinical significance. Management, prognosis and overall survival differ substantially between the two. It poses a challenge to diagnose and thus requires more sophisticated testing. Histopathologic assessment may not suffice; thus, molecular and IHC testing would play a significant role in achieving diagnosis and establish as part of testing in the future. SEOC is prevalent in younger premenopausal women who are obese and nulliparous. Genetic testing for HNPCC should be offered to those with a family history of breast and ovarian malignancy, as it may predispose to developing into SEOC and colon cancer. We advise that adequate surgical staging with pelvic lymphadenectomy performed in situations where two primary or origin of the tumour is uncertain.

Author contributions
SFL, ZY and NR designed the case series and participated in inpatient treatment. SFL and NR analyzed the data. SFL, NR and HAH wrote the manuscript. HAH and ZY provided help and revised the corresponding sections in the manuscript. All the authors have read and approved the final manuscript.

Ethics approval and consent to participate
All subjects gave their informed consent for inclusion for their participation in this study. The study was conducted in accordance with the Declaration of Helsinki, and the study was approved by the Ethics Committee of Hospital Serdang Clinical Research Centre.

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Conflict of interest
The authors declare no conflict of interest.

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