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Case Report

Large cell neuroendocrine carcinoma of the endometrium: A case report and literature review

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ABSTRACT

Objective: To report a case and review published cases of large cell neuroendocrine carcinoma (LCNEC) of the endometrium.**Case report:** A 51-year-old female presented with postmenopausal bleeding and a palpable pelvic mass. An endometrial biopsy showed a malignant mixed Mullerian tumor (MMMT). Suboptimal debulking surgery was performed. The final pathology revealed stage IVB endometrial LCNEC. Post-operative adjuvant chemotherapy with cisplatin and etoposide was administered. Two months after discontinuing adjuvant chemotherapy, salvage chemotherapy with cisplatin and ifosfamide was administered due to tumor progression; however, obstructive ileus was noted 2 months later. A segmental small bowel resection and palliative colostomy were performed. She died secondary to a post-operative infection 8 days after the operation.**Conclusion:** Endometrial LCNEC is a rare but aggressive disease. If diagnosed, combined therapies, including staging surgery, following by adjuvant radiotherapy and chemotherapy, should be performed.© 2018 Taiwan Association of Obstetrics & Gynecology. Publishing services by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

The two main types of cancer of the uterus are uterine sarcoma and endometrial carcinoma [1]. Endometrial carcinoma, which arises in the cells of the endometrium, is the most common malignancy of the female genital tract [2]. In 2015, an estimated 54,870 new cases of uterine cancer and 10,170 cancer-related deaths occurred in the United States [3]. In Taiwan, there were 1500 new cases of endometrial cancer, and the incidence continues to increase [4]. The major histologic type of endometrial carcinoma is endometrioid adenocarcinoma. Non-endometrioid histology includes mucinous, serous, clear cell, mucinous, squamous, neuroendocrine, and undifferentiated types [1].

Neuroendocrine neoplasms occur predominantly in the lung, but can be occasionally found in the gastrointestinal and genitourinary tracts. These tumors consist of a spectrum of malignancies, which are recognized by generic neuroendocrine marker

expression (i.e. synaptophysin and chromogranin detected by immunohistochemistry). Neuroendocrine tumors are classified as poorly-differentiated neuroendocrine carcinoma (NEC) and well-differentiated neuroendocrine tumor (NET) based on the differentiation grade. The former is further categorized into small and large cell neuroendocrine carcinomas (SCNECs and LCNECs, respectively). In short, a LCNEC is defined as a malignant tumor composed of large cells that show neuroendocrine differentiation [5]. LCNECs usually develop in the lungs. Within the female reproductive tract, LCNECs are always diagnosed in the uterine cervix [6] and ovary [7], and rarely in the uterine endometrium.

LCNECs of the female genital tract usually involve the uterine cervix and ovary, and rarely occur in the endometrium [8]. Only 15 cases of endometrial LCNECs have been reported in the English literature (Table 1) [9–18]. Herein we present a 51-year-old woman with the diagnosis of LCNEC of the endometrium. We also reviewed the literature pertaining to endometrial LCNECs.

Case report

A 51-year-old Taiwanese woman sought evaluation at a local hospital because of postmenopausal vaginal bleeding and a

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Table 1
Reported cases of large cell neuroendocrine carcinoma of the endometrium.

Case	Age	Initial stage	Symptoms/Signs	Immuno-profile positivity	Surgery	Further treatment (RT)	Further treatment (CT)	Follow up (Time after diagnosis)	Recurrence/Persistence	Metastatic site
1 [9]	52	IC ^a	PMB	NSE, SNP	TAH, BSO	RT (unspecified)	EPcis	Died of tumor (10 mo)	Yes	Brain, lung
2 [10]	50	IIIC ^a	PMB	NSE SNP	TAH, BSO, OMY, PPALND	RT (WP)	EPcar	Alive (12 mo)	No	None
3 [10]	80	IC ^a	PMB	NSE CGA	TAH, BSO, PLND	None	None	Died of tumor (5 mo)	Yes	Unspecified but disseminated
4 [10]	77	IIB ^a	PMB	NSE SNP CGA CD56	TAH, BSO	RT (WP)	None	Died of tumor (23 mo)	N/A	N/A
5 [10]	79	IIIA ^a	PMB	NSE CGA CD56	TAH, BSO, biopsies of omentum and peritoneum	RT (WP)	None	Alive (2 mo)	No	None
6 [10]	88	IIIC ^a	PMB	NSE CGA CD56	TAH, BSO, PLND	RT (WP)	None	Alive (1 mo)	No	None
7 [11]	42	IC ^a	AUB	SNP CGA CD56	RH	None	Platinum-based combination therapy	Alive (9 mo)	No	None
8 [12]	59	IIIB	AGC	NSE SNP CD56	RH, BSO, OMY, PPALND	RT (WP + B)	Unspecified	Alive (5 mo)	No	None
9 [13]	40	IB	AUB	SNP CD56	TAH, BSO, PLND, OMY	None	None	Alive (16 mo)	No	None
10 [14]	70	IB	PMB, mild abdominal pain	SNP CGA CD56	TAH, BSO, OMY	None	EPcis	Alive (6 mo)	Yes	Liver
11 [15]	59	IIIC2	PMB	NSE SNP CGA CD56	TAH, BSO, OMY, PPALND, APPY	RT (WP + B)	TC, PLD, EP + Oct	Died of tumor (12 mo)	Yes	None
12 [16]	73	IVB ^b	Lumbago, abdominal distention	NSE SNP CGA#2	None	None	None	Died of tumor (1 mo)	N/A	Bone, right supraclavicular lymphadenopathy
13 [16]	73	IIIC1	PMB	SNP CGA CD56	TAH, BSO, OMY, PPALND	None	IP, EPcar	Died of tumor (19 mo)	Yes	Kidney, lung
14 [17]	71	IVB	PMB	SNP CGA CD56	RH, BSO, OMY, PPALND	None	None	Died of tumor (1 mo)	N/A	N/A
15 [18]	51	IIIA	Uterine tumor at transvaginal sonography	SNP CGA CD56	RH, BSO, OMY, PPALND	None	IP	Alive (20 mo)	No	None
16 [Present case]	51	IVB	PMB, pelvic tumor, AGC	SNP CGA CD56	TAH, BSO, OMY	None	EPcis, ifosfamide + cisplatin	Died of tumor (9 mo)	Yes	Intraabdominal dissemination

AUB, abnormal uterine bleeding; AGC, atypical glandular cells; CGA, Chromogranin A; CT, chemotherapy; B, vaginal brachytherapy, EPcar, etoposide/carboplatin; EPcis, etoposide/cisplatin; IP, irinotecan/cisplatin; N/A, not available or not applicable; NSE, neuron-specific enolase; Oct, octreotide; OMY, omentectomy; RH, radical hysterectomy; PLD, pegylated doxorubicin; PLND, pelvic lymph node dissection; PMB, postmenopausal bleeding; PPALND, pelvic and paraaortic lymph node dissection; RT, radiotherapy; SNP, synaptophysin; TC, paclitaxel/carboplatin; WP, whole pelvic radiotherapy; mo, month.

^a 1998 FIGO staging; otherwise, 2009 FIGO staging.

^b Tissue diagnosis from autopsy.

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