Case Report

Giant cell carcinoma of endometrium: A rare case report and review of literature

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ABSTRACT

Giant cell carcinoma of uterus is an aggressive form of endometrial carcinoma. It can be confused on histopathology with other giant cell containing lesions including trophoblastic tumors, certain primary sarcomas, and malignant mixed müllerian tumors. Due to the paucity of cases of this rare subtype, the prognostic parameters are difficult to assess. We describe here one such case in a 60-year-old female who presented with postmenopausal bleeding. To the best of our knowledge, this is the 13th case being reported in world literature. We intend to describe this case due to its rarity, failure to recognize this tumor as a subtype, and lack of definition and guidelines in the literature for accurate classification.

Key words: Aggressive, endometrium, giant cell carcinoma, postmenopausal bleeding

INTRODUCTION

Endometrial carcinoma is the most common invasive carcinoma of female genital tract and accounts for 7% of all invasive cancers in women.[1] Endometrial carcinomas have been classified based on tumor cell type. Several variants of endometrial carcinoma have been described in the literature, endometrioid variant being the most common.[2] Furthermore, there are poorly differentiated adenocarcinomas of specific type including endometrial adenocarcinoma with trophoblastic differentiation, giant cell carcinoma, lymphoepithelioma like carcinoma, glassy cell carcinoma, and hepatoid carcinoma.[3] However, uncommon subtypes are poorly recognized and under reported in the daily practice.

Giant cell carcinoma was originally introduced by Nash and Stout in 1958 to describe a highly aggressive primary lung cancer with a distinctive morphology.[4] Giant cell carcinoma is a recently described variant of endometrial carcinoma. It is rare and infrequently reported entity[5] with only 12 cases reported in literature so far. Hence, although this tumor seems to behave aggressively in some cases the prognosis of giant cell carcinoma remains uncertain. We report this case keeping in mind the paucity of literature due to its rarity and lack of guidelines in the literature for its accurate classification.

CASE REPORT

A 60-year-old postmenopausal female presented with bleeding per vaginum since 8 months. The bleeding was moderate, intermittent with a history of passage of blood clots. There was no significant past history. Papanicolaou cytology revealed predominantly basal and parabasal squamous epithelial cells along with few atypical glandular cells. Ultrasound revealed a bulky uterus with increased endometrial thickness of 17.2 mm. Magnetic resonance imaging revealed an oval shaped intracavitary space occupying lesion measuring 3 cm × 2.5 cm × 2 cm suggestive of endometrial carcinoma.

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Dilatation and curettage of the endometrial cavity were done, which on microscopic examination showed features of endometrioid adenocarcinoma with numerous pleomorphic multinucleated giant cells. However, due to the paucity of material no attempt was made to subtype the tumor. Total abdominal hysterectomy with bilateral salpingo-oophorectomy was performed.

On gross examination, the endometrial cavity was covered with a fleshy gray white, friable growth measuring 3 cm in its greatest dimension. The growth was invading less than inner half of the myometrium grossly. The uterus was also studded with multiple intramural and serosal fibroids varying in diameter from 1 cm to 3 cm. Cervix, ovaries, and fallopian tubes were within normal limits.

Microscopically, the tumor was composed of nests, sheets as well as isolated population of multinucleated giant cells. These giant cells had abundant dense eosinophilic cytoplasm and vesicular nuclei with prominent nucleoli. The cells showed marked nuclear pleomorphism with the presence of numerous atypical mitosis. The giant cells were seen infiltrating into the myometrium and comprised approximately 60% of the tumor volume. Areas of endometrioid adenocarcinoma were also present [Figure 1a-c].

The tumor cells including the giant cells were positive for cytokeratin (CK), epithelial membrane antigen (EMA), estrogen receptor (ER), and progesterone receptor (PR). The tumor cells were negative for vimentin, desmin, smooth muscle actin (SMA), p63, CD68, α-fetoprotein, and β-human chorionic gonadotropin (βHCG) [Figure 2a-f]. Thus, a diagnosis of giant cell carcinoma of the endometrium (International Federation of Gynecology and Obstetrics Stage IB) was made.

DISCUSSION

Giant cell carcinoma of endometrium is a rare and aggressive variant of endometrial carcinoma.[6] Similarly, giant cell carcinoma has also been reported elsewhere in the female genital tract like in the cervix[7] and fallopian tubes.[8]

Definitive criteria as described by Jones *et al.* on microscopic examination includes bizarre multinucleated giant cells admixed with malignant mononuclear cells. It should be distinguished from other endometrial tumors with a prominent giant cell component including trophoblastic tumors, malignant giant cell tumors, primary sarcomas, and malignant mixed müllerian tumors on the basis of morphology and immunohistochemistry.[5] Trophoblastic giant cells can be seen in uterine choriocarcinoma or endometrial carcinoma showing choriocarcinomatous differentiation. However, these tumors have a characteristic biphasic pattern of cytotrophoblasts and syncytiotrophoblasts, which are positive for βHCG.[9] Giant cells can also be frequently seen in malignant mixed mullerian tumors or carcinosarcomas, and positivity for vimentin in the mesenchymal (sarcomatous) component of this tumor aids in differentiating it from giant cell carcinoma of the endometrium.[10]

Jones *et al*.[5] reported a short series of six patients with giant cell carcinoma. The patients ranged in age from 43 to 85 years (mean 65). All the patients presented with vaginal bleeding. All the tumors of their series had giant cell component with at least focal areas of endometrial adenocarcinoma of one usual type. While four cases showed a predominance of giant cells, two cases showed only 15% of the tumor volume composed of multinucleated giant cells. Occasional giant cells were positive for CK and EMA, whereas desmin and SMA were negative in all tumors. Four of six patients in whom tumor invaded more than superficially, developed recurrent tumor and three patients died of disease within 3 years.

In another short series[11] of five patients, the age ranged from 53 to 83 years with a mean of 64 years. Three of the patients presented with vaginal bleeding, one with anemia, and one with a pelvic mass. Giant cell component in these tumors varied from 30% to 100%. One patient in

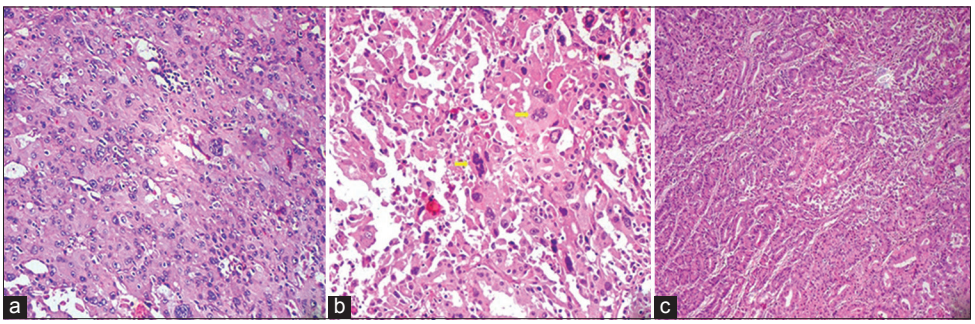

Figure 1: (a) Sheets of pleomorphic tumor cells (H and E, ×200). (b) Sheets as well as the isolated population of multinucleated giant cells with abundant dense eosinophilic cytoplasm and pleomorphic vesicular nuclei with prominent nucleoli (H and E, ×400). (c) Areas of endometrioid adenocarcinoma of usual type (H and E, ×200)

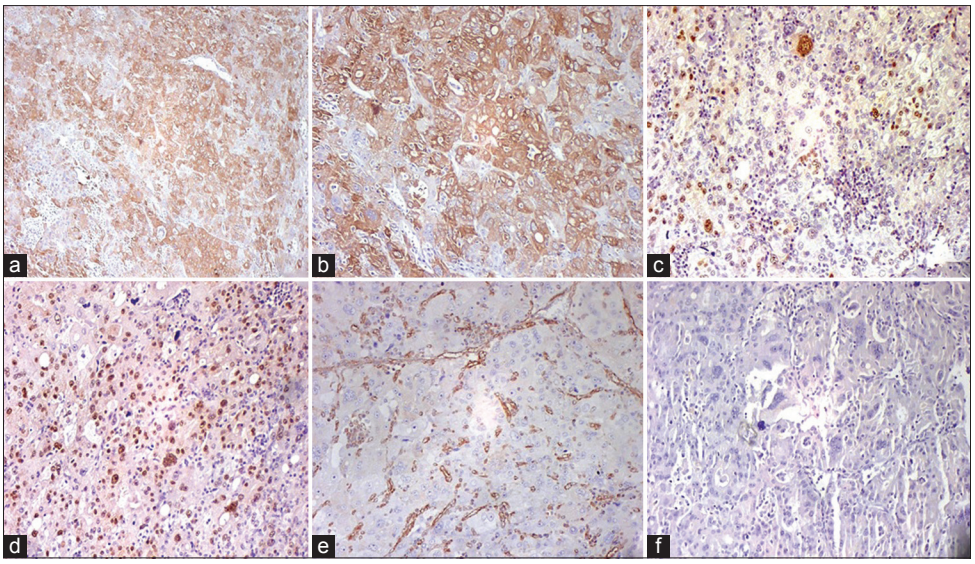

Figure 2: The tumor cells including the giant cells showed immunohistochemical positivity for cytokeratin (a), epithelial membrane antigen (b), estrogen receptor (c), progesterone receptor (d) and negative for vimentin (e) and human chorionic gonadotropin (f)

Table 1: Clinical features and histopathological features of patients with giant cell carcinoma of endometrium

Patient	Age	Symptoms	FIGO (%)	Giant cell component (%)	Conventional cell type (%)
Jones *et al.*					
Case 1	43	Vaginal bleeding	IA (superficial invasion)	15	Endometrioid (85)
Case 2	66	Vaginal bleeding	IA (superficial invasion)	Predominant	Endometrioid (minor)
Case 3	64	Vaginal bleeding	IA (superficial invasion)	Predominant	Endometrioid (minor)
Case 4	85	Vaginal bleeding	IIIA	Predominant	Endometrioid (minor)
Case 5	63	Vaginal bleeding	IVB	15	Endometrioid (85)
Case 6	71	Vaginal bleeding	IVB	Predominant	Endometrioid (minor)
Mulligan *et al.*					
Case 7	53	Vaginal bleeding	IA (<50)	70	Clear cell
Case 8	60	Anemia	IB with positive peritoneal cytology	100	Not present
Case 9	58	Vaginal bleeding	IA (<50)	50	Endometrioid with spindled areas
Case 10	83	Pelvic mass	IIIC2	30	Endometrioid
Case 11	67	Vaginal bleeding	IA (confined to endometrium)	90	Serous
Bhattarcharya *et al.*					
Case 12	70	Vaginal bleeding	IB	80	Endometrioid
Present case					
Case 13	60	Vaginal bleeding	IB	60	Endometrioid

FIGO: International Federation of Gynecology and Obstetrics

whom the tumor was exclusively of the giant cell type developed lung metastasis 4 years after diagnosis and another patient remained disease free after 14 years. The remaining 3 patients showed no evidence of disease with 15–32 months of follow-up [Table 1]. They recommended that the presence of giant cell component should be mentioned even if it is <10% clearly stating that its biologic significance is uncertain. The present case was composed predominantly of giant cells comprising more than 60% of the total tumor volume.

The usual treatment of endometrial carcinoma is panhysterectomy with or without pelvic and paraaortic lymphadenectomy depending upon grade of the tumor. Hormone therapy in endometrial carcinomas is a well-established treatment modality for primary, metastatic, and recurrent cases. However, the role of hormone therapy in this rare and aggressive subtype of endometrial carcinoma still remains unstudied. Till date, there is no data on the receptor (ER and PR) status of this tumor, positivity of which in our study could have a therapeutic implication.

CONCLUSION

Giant cell carcinoma of endometrium is a rare and aggressive tumor, diagnosis of which can only be established by histopathological examination. The cut-off percentage of giant cell component required to classify a tumor as giant cell carcinoma of endometrium has not yet been defined. In addition, awareness of this entity is important to prevent its misclassification due to a wide range of differential diagnosis and poor prognosis of these cases.

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Conflicts of interest
There are no conflicts of interest.

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