

Case Report

Giant Cell Carcinoma of Endometrium: a Rare Clinical Entity

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ABSTRACT

Giant cell carcinoma of the endometrium is a rare and an aggressive tumor that should be distinguished from other endometrial tumors with a prominent giant cell component, including trophoblastic tumors, certain primary sarcomas, and malignant mixed müllerian tumors. At present, cumulative data on this rare histological variant is limited and the prognostic significance of the presence and the extent of a giant cell component in endometrial carcinoma remain uncertain. We report giant cell carcinoma of endometrium in an Indian female, which according to our best knowledge, is the first case being reported from Indian Subcontinent.

Key words: Giant Cell Carcinoma, Endometrium

Introduction

Endometrial carcinoma is the most common invasive carcinoma of female genital tract and accounts for 7% of all invasive cancers in women, excluding skin cancer (1). Women have a 2.5 percent lifetime risk of developing endometrial cancer, which accounts for 6% of all cancers in women (2).

Endometrial carcinomas are classified based on tumor cell type; tumors of different cell types are associated with different natural histories, treatment regimens, and prognoses (3). However,

uncommon subtypes are poorly recognized and under reported in the daily practice.

One such tumor is the Giant cell carcinoma of endometrium, first described by Jones *et al.* in 1991 as a tumor composed of sheets or nests of poorly cohesive bizarre multinucleated giant cells admixed with mononucleate tumor cells (4). It is a rare histological variant of high-grade endometrial carcinoma with only a few cases reported in the literature.

We hereby report a case of giant cell carcinoma in an elderly Indian female keeping in mind the paucity of literature due to its true rarity, failure

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to recognize this tumor as a specific subtype and lack of definition and guidelines in the literature for accurate and reproducible classification. In addition, to the best of our knowledge, this is the first case of giant cell carcinoma of endometrium being reported from the Indian Subcontinent.

Case History

A 70 years old female presented with bleeding per vaginum since 2 months. Patient was post-menopausal for the last 20 years. The bleeding was moderate, intermittent with history of passage of blood clots. There was no significant past history. Routine hematological and biochemical investigations were within normal limits apart from mild anemia with Hb-10.5 gm%.

On local examination, uterus was slightly bulky. Cervical fornices were slightly tender. Simultaneously, PAP smear from the cervix was taken as first line screening modality. PAP cytology revealed predominantly basal and parabasal squamous epithelial cells with mild neutrophilic infiltrate and a few atypical glandular cells along with an occasional multinucleated cell. In view

of suspicious glandular cells, biopsy was advised to reach at a definitive diagnosis.

Dilatation and curettage of the endometrial cavity was done which on microscopic examination showed features of Poorly Differentiated Carcinoma with many pleomorphic multinucleated giant cells.

With a provisional clinical diagnosis of endometrial carcinoma, total abdominal hysterectomy with bilateral salpingoophorectomy was done and the specimen was sent to the Department of Pathology for histopathological examination.

Pathological Examination

On gross examination, the total hysterectomy specimen measured 8x4x4 cm. On cut section, the endometrial cavity contains a polypoid mass measuring 4 cm in its greatest dimension. The mass was fleshy and grey white without any evidence of hemorrhage and necrosis invading the inner half of myometrium (Fig. 1). The cervix was atrophic and both adnexa were grossly unremarkable. Representative sections were taken and routinely processed for the histopathological examination.



Fig. 1- Polypoid Endometrial mass within the endometrial cavity

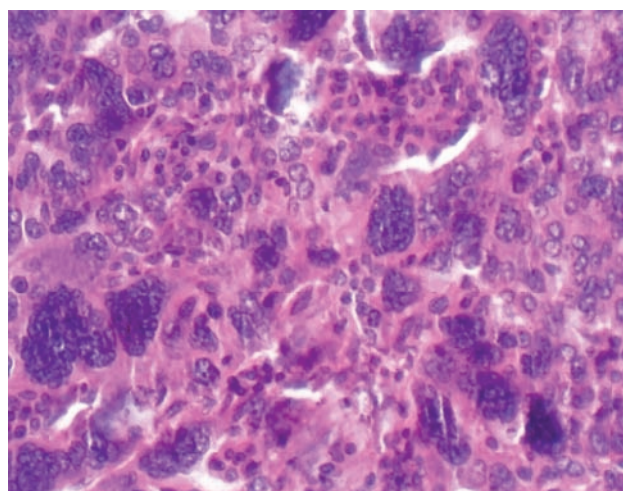


Fig. 2- Pleomorphic multinucleated giant cell distributed amidst mononuclear tumor cell without glandular differentiation. (H&E, ×400)

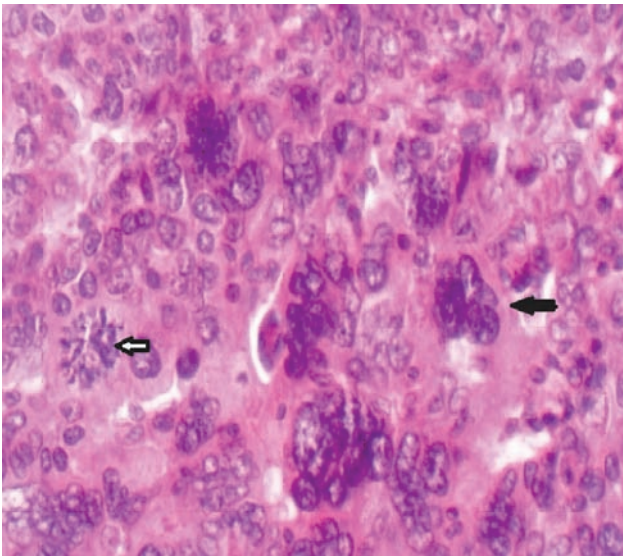


Fig. 3- Pleomorphic multinucleated giant cell (thick arrow). Note an abnormal mitotic figure (thin arrow). (H&E, $\times 400$)

On microscopic examination, the growth comprised predominantly multiple pleomorphic multinucleated giant cells interspersed between malignant cells exhibiting no particular arrangement. The giant cells were distributed throughout the tumor and were invading the inner half of the myometrium as well (Fig. 2 & 3). The diagnosis of giant cell variant of endometrial carcinoma FIGO stage IB was made.

Discussion

Giant cell carcinoma of endometrium is a rare and aggressive variant of endometrial carcinoma with unknown biological significance.

Endometrial carcinoma is uncommon in women younger than 40 years of age group with peak incidence being 55-65 years. Although it may be asymptomatic for a period, it usually produces irregular or postmenopausal vaginal bleeding with excessive leucorrhea (1).

Mulligan *et al.* had described five cases of endometrial carcinoma with giant cell component with an age range of 53 to 83 years, presenting with vaginal bleeding, anemia, or a pelvic mass

(5). This case was also within their age range but had only presented with postmenopausal vaginal bleeding.

The diagnosis of endometrial cancer should ultimately be established by biopsy or curettage and histological examination of the tissue (1) as done in the present case also, where confirmative diagnosis could be achieved only on histopathological examination. 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, certain primary sarcomas, and malignant mixed müllerian tumors (4).

Conditions with osteoclast like giant cells are easily distinguished from those in giant cell carcinoma by morphology. These giant cells have small round to oval bland nuclei and are benign in nature while those in giant cell carcinoma are highly pleomorphic and malignant in nature. Trophoblastic giant cells can be seen in endometrial choriocarcinoma or endometrial carcinoma showing choriocarcinoma or trophoblastic differentiation. However, typical biphasic pattern of cytotrophoblast and syncytiotrophoblast helps to distinct it from giant cell carcinoma.

An algorithmic approach to the diagnosis of giant cell containing lesions of the endometrium is described (Fig. 4) (5). In the present case, no other component apart from pleomorphic giant cells interspersed with scattered mononuclear cells was seen even with repeated sections.

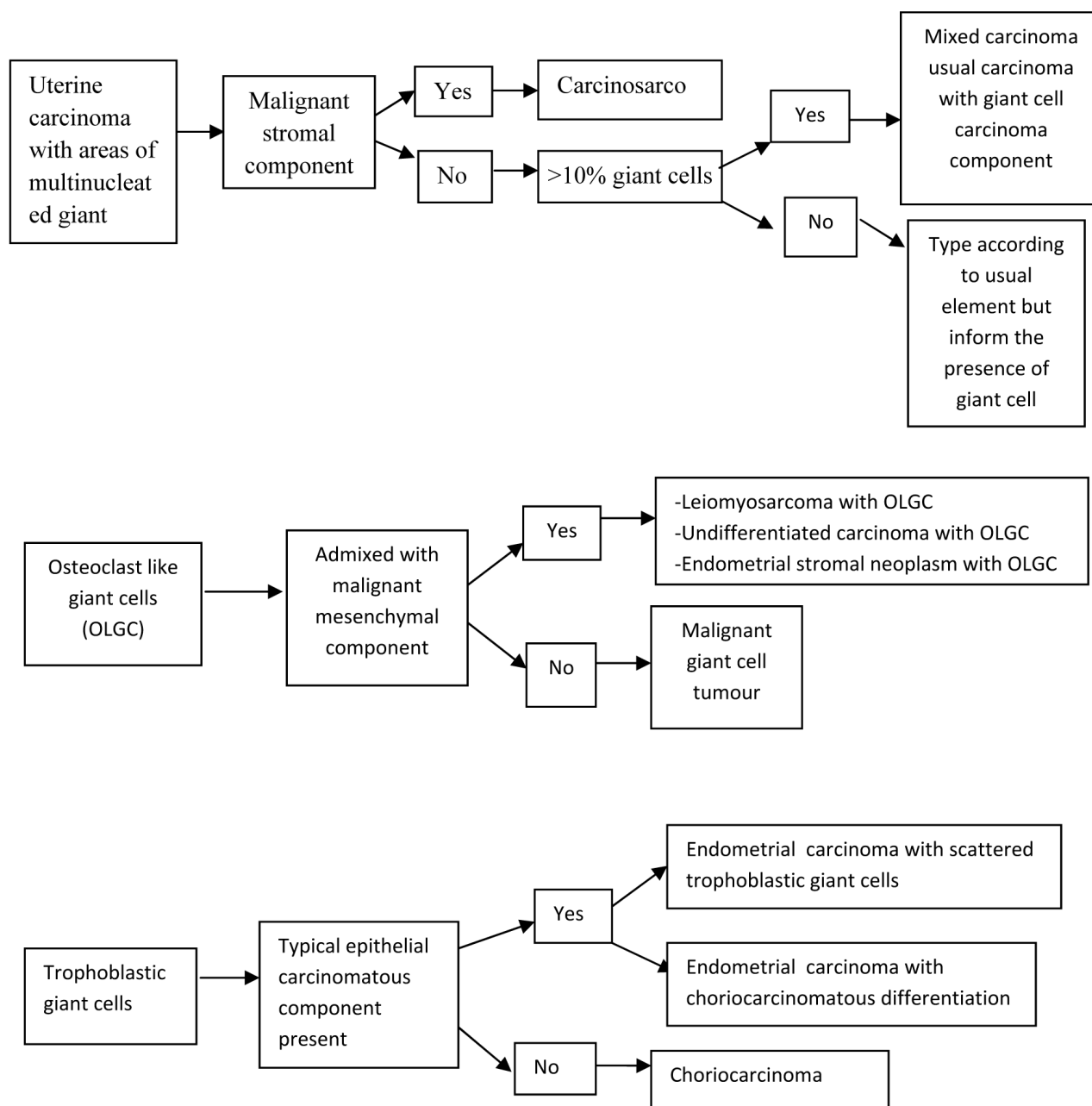


Fig. 4- Algorithmic approach to the diagnosis of giant cell containing lesion of the endometrium

Pleomorphic multinucleated giant cells in all the above-mentioned tumors exhibit variable expression for different immunohistochemical markers and hence can be differentiated from those found in giant cell carcinoma of endometrium. Waldmann *et al.* reported three cases of leiomyosarcoma with multinucleated giant cells, which on immunohistochemistry showed positivity for vimentin, CD 68, and lysozyme (6). Immunohistochemical stain like cytokeratin and Epithelial Membrane Antigen (EMA) for epithelial component and

vimentin for mesenchymal component can help differentiate the mixed mullerian tumors (7). immunohistochemistry for keratin, human Chorionic Gonadotropin (hCG) and human Placental lactogen (hPL) are helpful in differentiating a trophoblastic tumor from a non trophoblastic tumor (8). Mulligan *et al.* reported in endometrial carcinoma with giant cell component the giant cells showed focal staining for epithelial markers namely, AE1/AE3 and CAM 5.2 (5). Because of the economical constraint and the characteristic morphology of giant cell

carcinoma of endometrium on microscopical examination, immunohistochemistry was not done in the present case.

As histotype supplemented by staging information is critical in selection of treatment modalities and in prognostication in uterine malignancies, accurate classification is mandated (5). The present case was classified as FIGO stage IB as the tumor had invaded inner one-half of the myometrium. Accurate classification can be achieved by histopathological examination, which is the gold standard.

In endometrial carcinoma pleomorphic multinucleated giant cells may be the predominant component or can be a part of other histological variants. Giant cell was a predominant component of endometrial carcinoma in 4 out of 6 cases reported by Jones *et al.* and 3 out of 5 cases reported by Mulligan *et al.* (4, 5). Part of other histological variant was present in all the cases except one by Mulligan *et al.* and it included endometroid type, clear cell type, serous component, and spindle cell component. Mulligan *et al.* recommended that the presence of giant cell component should be mentioned even if it is less than 10% clearly stating that its biologic significance is uncertain. The present case was composed predominantly of giant cells comprising more than 80% of the total tumor volume. At this time, the cumulative data on endometrial Giant Cell Carcinoma are limited and the prognostic significance of the presence and the extent of a giant cell component in endometrial carcinoma remain uncertain (5). Even with extensive search of the literature, we have not come across about the percentage of giant cells to be present in the tumor, to be classified as giant cell carcinoma of endometrium.

Prior to treatment, a complete pelvic and general physical examination should be performed, with particular attention to the size and mobility of the uterus and the presence of extrauterine masses or ascites; potential sites of nodal metastases should also be examined (e.g., supraclavicular nodes) (9). In this case, uterus was mobile with no ascites

or extra-uterine mass and lymphadenopathy.

The usual treatment of endometrial carcinoma is total abdominal hysterectomy with bilateral salpingo-oophorectomy which should be supplemented by pelvic and para-aortic lymph node biopsy if grade III tumor, >50% myometrial invasion, extrauterine spread or unfavourable histologic type is present (10). Since the present case was Stage I, total abdominal hysterectomy with bilateral salpingo-oophorectomy was done in this case also and until now patient is doing fine.

To conclude, giant cell carcinoma of endometrium is a rare and aggressive tumor, diagnosis of which can only be established on histopathological examination. Even if the component of giant cell is minimal, it should be mentioned in the pathological report as percentage of giant cell component required to classify, as giant cell carcinoma of endometrium has not yet been documented, clearly stating that the biologic significance of giant cell is uncertain. In addition, awareness of this entity is important to prevent its misclassification due to wide range of differential diagnosis.

Acknowledgments

The authors declare that there is no conflict of interests.

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