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CASE REPORT OPEN ACCESS

Atypical (symplastic) uterine leiomyoma masquerading as endometrial malignancy in a 78-year-old post-menopausal Nigerian woman

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Abstract

Background: The atypical (symplastic) uterine leiomyoma is uncommon and is often characterized by similar macroscopic features as typical uterine fibroid but differs microscopically by having intense cytological features such as enlargement of the nucleus, hyperchromasia, and prominent nucleoli. It lacks histopathological features usually seen in leiomyosarcoma but harbours a low potential of transformation into leiomyosarcoma. Atypical leiomyoma very rarely occurs in post-menopausal women.

Case presentation: A 78-year-old postmenopausal woman presented to our gynaecology clinic with an 8-month history of post-menopausal bleeding and abdominal swelling. Physical examination revealed abdominal swelling but blood chemistry was normal. An initial diagnosis of endometrial carcinoma was made and she subsequently had a total abdominal hysterectomy with bilateral salpingo-oophorectomy. Following histopathological evaluations, a confirmatory diagnosis of atypical uterine leiomyoma was made. She has been symptom-free for two years following surgical intervention.

Conclusion: Despite their rarity in postmenopausal women, atypical fibroids should be considered in the differential diagnosis for postmenopausal bleeding. Considering the malignant transformation potential, recurrence risk of this pathology, and the completion of family size in this case, hysterectomy is the most preferred treatment option even though myomectomy can be offered to patients with plans of conception in the future.

Keywords: Atypical uterine fibroids, Leiomyoma, Post-menopausal bleeding, Nigerian woman

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Background

Uterine leiomyomas are the most prevalent benign tumors, present amongst women of reproductive age affecting about 70% of women globally. Uterine leiomyoma originates from the clonal expansion of a single cell in the myometrium. They are monoclonal tumours of the uterus's smooth muscle tissue layer; the histology shows anastomosing fascicles of uniform smooth muscle cells. Degenerative changes such as hyaline degeneration, cystic degeneration, myxoid change, fatty change, calcification, and metaplasia can be associated (1, 2, 3). Resident in the uterine wall, rare case has been reported elsewhere, including the anterior virginal lip (4).

Rarely, atypical leiomyoma, a benign variant of uterine leiomyoma is seen in histology. Unlike conventional leiomyomas, atypical leiomyomas exhibit distinct histological features, such as nuclear atypia, enlarged hyperchromatic nuclei, and irregular shapes, which may mimic more aggressive tumours like leiomyosarcomas. Despite these atypical characteristics, they generally have a benign clinical course, with a low risk of recurrence or malignant transformation. Accurate diagnosis is crucial to differentiate atypical leiomyomas from malignant counterparts, as it significantly influences patient management and prognosis (3). Uterine leiomyoma can occasionally show uncommon, unusual histological characteristics that resemble leiomyosarcoma, making diagnosis and proper management challenging (5).

We herein present an atypical clinical and histological presentation of uterine leiomyoma in a 78-year-old post-menopausal Nigerian woman. This case, to the best of our knowledge, is the first reported atypical uterine leiomyoma in a post-menopausal woman of Nigerian descent.

Case presentation:

A 78-year-old G6 (6A) who is a 12-year-old post-menopausal woman presented with 8 months history of post-menopausal bleeding and abdominal distension. Physical examination and blood chemistry were normal.

Examination

General physical examination was normal. Abdominal examination revealed a distended abdomen with an abdominopelvic mass about the size of a 32-week uterus. Other organs were not palpably enlarged, and there was ascites. A perineal and speculum examination revealed a normal but atrophic female genitalia, vaginal wall, and multiparous cervix. An abdominal computed tomography scan showed a markedly enlarged, bulky uterus with heterogeneous myometrial density and enhancement measuring 19.5 x 16.4 x 18.9 cm. It also showed amorphous calcifications and significant and significant endometrial collection. There was no ascites. A preliminary assessment of endometrial cancer in a menopausal woman was made.

Management

The patient subsequently had a total abdominal hysterectomy with bilateral salpingo-oophorectomy. Hemorrhagic peritoneal fluid and bulky, irregularly shaped uterus were seen. Cytology of blood-tinged yellowish peritoneal fluid showed cohesive clusters of markedly reactive mesothelial cells admixed with acute and chronic inflammatory cells.

Histopathology report of the uterus revealed a grossly distorted uterus with irregularly shaped submucosal masses with hemorrhagic areas (Figure 1).

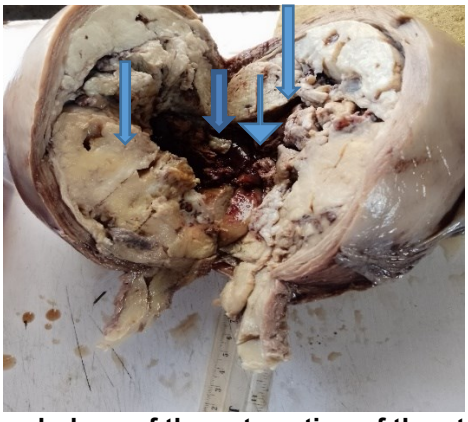

Figure 1: Showing gross morphology of the cut section of the uterus with diffuse irregularly shaped endometrial submucosal greyish white masses (long arrow) with hemorrhagic areas (short arrow)

Microscopy of the uterus showed a cellular mesenchymal lesion composed of proliferating bundles of mature smooth muscle cells disposed in interlacing fascicles and whorls with areas of

atypical cells having hyperchromatic nuclei with chromatin smudging (Figure 2). There are features of calcification, hyalinization, red, and cystic generation (Figure 3). An assessment of atypical leiomyoma was made.

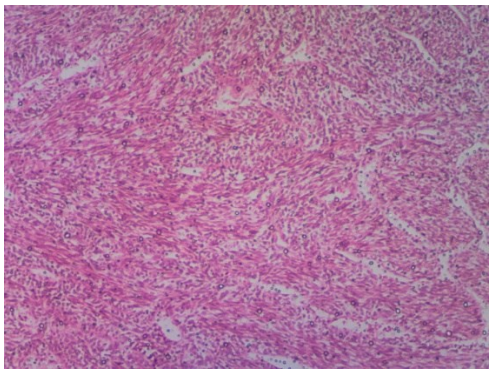

Figure 2: H & E x 100 magnification showing markedly cellular lesion composed of proliferating smooth muscle cells with mild to moderate cellular atypia, disposed in interlacing fascicles and whorls in keeping with atypical leiomyoma

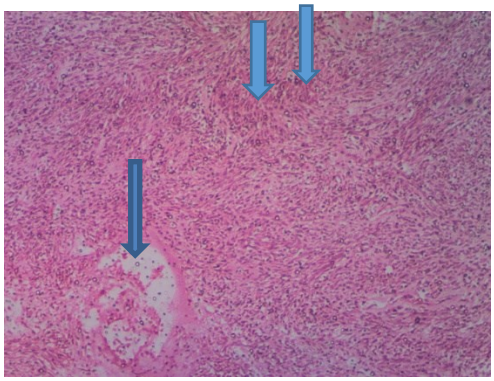

Figure 3: H & E x 100 magnification showing moderately atypical cellular leiomyomatous lesion with focal areas of mitosis (short arrows) and cystic degeneration (long arrow)

Sections of the endometrium show few atrophic unremarkable glands within a scanty stroma. No focus of atypia or malignant change is seen. Features are in keeping with endometrial atrophy consistent with the patient's age. The patient had an uneventful post-operative period and has been symptom-free for two years now.

Discussion

Uterine leiomyomas are the most common uterine neoplasms originating from uterine smooth muscle cells. They are uterine smooth muscle cell monoclonal tumours primarily composed of extracellular matrix, including proteoglycan, fibronectin, and collagen. Although the exact cause of these fibroids is unknown, there is strong evidence that progestogens and estrogens stimulate the formation of tumours, as fibroids rarely develop before menarche and disappear following menopause. They can be single or many, categorized as subserous, intramural, or submucous depending on where they are relative to the uterine layers (6).

Atypical uterine leiomyoma (ALM) (also known as pleomorphic, bizarre, or symplastic leiomyoma) is an infrequently occurring variant of uterine leiomyoma that when seen tends to occur among those in reproductive ages (age range of 25-51 years and mean age of 40.7 to 48 years) (7). Grossly and radiologically, symplastic uterine leiomyoma has the same features as typical leiomyomas (TL) such as multiple sub-centimetre to large masses in the parenchyma of the uterus and well-circumscribed lesions (5, 7), They could exhibit softening, cavitation, myxoid alteration, haemorrhages, or yellow or tan patches (3). These tumours' maximum dimensions fall between 1 and 14 cm with a mean dimension of 4.2 cm (7). In our case, however, our patient was 78 years old and post-menopausal. Although the lesion had tan patches and areas of haemorrhage expected in AUL, it was irregularly shaped (Figure 1), suggesting a malignant tumour as was diagnosed clinically.

Furthermore, ALM differs histologically from TL by having atypical features like hyperchromatic nuclei with chromatin smudging (4). Indeed, these findings were seen in our case. (Figure 2)

In 2014, WHO classified different variations of uterine leiomyoma. They include cellular

leiomyoma, cotyledonoid or dissecting leiomyoma, myxoid leiomyoma, epithelioid leiomyoma, apoplectic leiomyoma, hydropic leiomyoma, mitotically active leiomyoma and leiomyoma with bizarre nucleus (5, 8).

Cellular leiomyomata are characterized by intense hematoxylin staining, showing a higher abundance of nuclei compared to the extracellular component. They lack TP53 mutations but often have PTEN and MED12 mutations. Leiomyomata with increased mitotic activity show up to 15 mitoses per 10 high-power fields (HPF) and frequently carry MED12 mutations, with less abnormal expression of HMGA2 or FH (5).

Epithelioid leiomyomas resemble conventional leiomyomas, appearing as extracellular matrix masses surrounding small clusters of rounded smooth muscle cells, giving a pseudo-epithelioid appearance, with no cytogenetic differences from typical leiomyomas. Myxoid leiomyomas contain abundant myxoid material separating smooth muscle cells, and the presence of cytological atypia, infiltrating margins, and mitotic activity greater than 2/HPF distinguishes myxoid leiomyosarcomas from myxoid leiomyomas. Differentiation from conditions like myxoid degeneration and inflammatory myofibroblastic tumours is important (5).

Dissecting leiomyomas are named for their characteristic tongue-like projections of benign smooth muscle neoplasia with hydropic changes, dissecting the surrounding myometrium without atypia, necrosis, or mitotic activity (5).

Leiomyoma with bizarre nuclei (LM-BN) is an uncommon tumour with histologic features (mononucleated or multinucleated bizarre cells that may have a diffuse distribution, prominent nucleoli, and karyorrhectic nuclei that may mimic atypical mitoses) that often confuses with leiomyosarcoma (9).

Also, Hendrickson and Kempson described and classified primary benign smooth muscle tumours in 3 large groups as follows: 1- Leiomyomas with usual differentiation, 2- variants defined based on cytological features or cellularity, and 3- with unusual patterns of growth (10).

Our patient's histology falls under the leiomyoma with bizarre nuclei and variants defined based on cytological features or cellularity according to the World Health Organization and Hendrickson and Kempson classifications respectively. Additionally, as outlined by Ubago and colleagues (10), ALM is microscopically characterized by moderate to severe cellular atypia, <10 mitotic figures per 10 HPF, and absence of necrosis. Indeed, in the index case, there was moderate cytologic atypia and mitosis was <10 per 10HPF but there was no necrosis (Figure 2) conforming to the diagnosis of ALM.

Worthy of note is that the atypical features could mislead pathologists and lead to an erroneous diagnosis of leiomyosarcoma. Uterine leiomyosarcoma differs from atypical leiomyoma grossly with the presence of hemorrhagic and necrotic foci and invasion of myometrium. On microscopic examination, hyperchromatic atypical spindle-shaped tumour cells are seen growing in fascicles with eosinophilic cytoplasm. If tumour cell necrosis is present in a smooth muscle neoplasm with at least diffusely moderate nuclear atypia, the presence of mitotic figures is not critical for diagnosing leiomyosarcoma. However, if necrosis is absent, diagnosis requires diffuse moderate nuclear atypia and more than 10 mitotic figures per high-power field (HPF). Leiomyosarcoma typically stains positive for smooth muscle markers such as smooth muscle actin (SMA), desmin, and caldesmon, and expresses p16, p53, Ki67, ER, and PR (5, 11).

In our case, although hemorrhagic areas were seen macroscopically, there was unsurprisingly no necrosis or myometrial invasion supporting its benign nature. Indeed, the absence of necrosis and mitotic figures being <10 per HPF in the microscopy of our patient's uterine lesions further bolstered the diagnosis of ALM in the index case. Furthermore, we did not consider immunohistochemistry as the histological features were completely in tandem with ALM and for economic reasons.

The possibility and certainty of atypical uterine leiomyoma undergoing a malignant transformation are shrouded in mystery as it is unclear if they represent a completely benign variant of uterine leiomyoma or tumours of the uterine corpus that do not fulfil the histological criteria for typical uterine leiomyomas; smooth muscle tumour of unknown malignant potential (STUMPS) and clear-cut malignancies (5, 12).

The treatment of atypical leiomyoma is dependent on the desire for future fertility. In persons who do not desire fertility hysterectomy is the treatment of choice while myomectomy is the preferred modality of treatment in those still desirous of pregnancy. Furthermore, there is a low risk of recurrence which is reported to occur in 82% of patients following myomectomy but improves to 94% post-hysterectomy (5, 13). AL is also said to have a mild risk of malignant transformation (10). Due to the age, completion of the family in this case, and considering the initial malignant tumour diagnosis, she had a total hysterectomy with bilateral-salpingo-oophorectomy. She has been symptom-free for three years following surgical intervention.

In conclusion, uterine leiomyoma is an uncommon cause of postmenopausal bleeding; it should remain a critical differential diagnosis in clinical evaluations. Its potential presence underscores the necessity for comprehensive diagnostic assessments in postmenopausal patients presenting with abnormal uterine bleeding. Recognizing and considering uterine leiomyoma ensures that appropriate and timely management can be provided, ultimately improving patient outcomes.
Also, more importantly, as AL has malignant transformation potential and is also commoner in younger women, it should constitute an important differential in premenopausal women who present with bleeding par vaginum as this would determine the best choice of treatment considering that these individuals are most likely going to be still desirous of reproduction.

List of Abbreviations
ALM: Atypical uterine leiomyoma
H & E: Haematoxylin and eosin
STUMP: Smooth muscle tumour of unkown malignant potential
TL: Typical leiomyoma

Declaration
Ethics approval and consent to participate
Written informed consent for publication was obtained from the patient whose management is being reported.

Consent for publication
All the authors gave consent for the publication of the work under the Creative Commons Attribution- Non-Commercial 4.0 license.

Availability of data and materials
The essential data supporting the findings of this study are available within the article. Additional data are available upon request from the corresponding author due to confidential reasons.

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

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Authors contributions
All the authors were involved in the management of the patients and conceptualizing the report. OVC, JBB, NCD, MI, OAI and OOM wrote the first manuscript. OVC, AA, STO, and NJI, corrected the manuscript. All the authors agreed on the final manuscript. The manuscript has been read and approved by all the authors.

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