Advanced leiomyosarcoma of the uterus: a case report and literature review

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Received: 16 March 2021
Received: 18 April 2021
Accepted: 19 April 2021

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ABSTRACT

Uterine leiomyosarcoma is a rare malignancy accounting for 1-2% of uterine malignancies with an annual incidence of 0.5-7 per 100,000 women. It occurs mostly between the 5th to 7th decades of life hence found more among postmenopausal women. The aetiology is mostly unknown however, in 0.2% of cases, it originates from sarcomatous degeneration in a pre-existing benign uterine fibroid. Leiomyosarcoma can be mistaken for uterine leiomyoma also known as the uterine fibroid. It is an aggressive tumour that has a poor prognosis, with or without treatment. This case report aimed to report and discuss the occurrence of leiomyosarcoma as a differential diagnosis of abnormal uterine bleeding in this environment among other conditions. This will bring to the fore awareness among gynaecologists, pathologists, radiologists and oncologists that leiomyosarcoma of the uterus, though rare, should be considered in cases of menorrhagia with suspected uterine fibroid to avoid mistaking it for a diagnosis of uterine fibroid/leiomyoma. It is, therefore, imperative to consider leiomyosarcoma in a pre-menopausal and perimenopausal women diagnosed of abnormal uterine bleeding with symptomatic uterine fibroid. MRI serves as a good tool in differentiating the two pathologies.

Keywords: Leiomyosarcoma, Leiomyoma, Uterine fibroid, Leiomyoma, Menorrhagia, Radiotherapy, Chemotherapy

INTRODUCTION

Uterine leiomyosarcoma is a malignant mesenchymal tumour of the uterus originating primarily from the myometrium.¹,² Mesenchymal tumour is of three main types. These include leiomyosarcomas (LMS), endometrial stromal sarcomas (ESS) and undifferentiated uterine sarcomas (UUS).¹ Leiomyosarcoma can be found in any part of the body and it is the commonest sub-type with rare incidence and poor prognosis.² Uterine leiomyosarcoma and uterine fibroid are not only from the same source, the myometrium but also presents similarly especially in the early stage of the disease.² Thus, they are mostly diagnosed as incidental findings perioperatively.¹ The patient may be asymptomatic in most of the early cases, however other presentations include pelvic mass, haemorrhage, pressure symptoms and signs of metastasis in late cases.¹,³,⁴ The route metastasis could be haematological, peritoneal and lymphatic affecting pelvic organs, lungs and gastrointestinal organs.¹ Ultrasound scan and the endometrial biopsy are not quite helpful in making the definitive diagnosis of leiomyosarcoma.¹ However, much success has been achieved with T-weighted MRI and definitive diagnosis is made by the histological diagnosis

June 2021 · Volume 10 · Issue 6 · Page 2482
of uterine sample. Management is mostly surgical approach and adjuvant therapy such as chemotherapy and radiation.

CASE REPORT

A 42-year-old para 3+1 woman presented with heavy menstrual bleeding of a year duration with progressive abdominal swelling of six months duration in January 2020. There was a history of ultrasound diagnosis of asymptomatic fibroid of ten years duration. However, there was no history of weight loss. Her last childbirth was seven years before presentation. Past medical history revealed no significant illness and there was no history of radiation exposure. She was a sexually active woman. The family history and review of the system were unremarkable. On examination, she was pale, anicteric, afebrile. Her blood pressure was 120/80 mmHg, her pulse rate was 88/minute, and her heart sounds were normal. Upon examination, the chest was clear, and the abdomen revealed a tender uterus consistent with 22 weeks of pregnancy size. The liver, spleen, and kidneys were not palpably enlarged. There was no evidence of ascites. Vaginal examination revealed a bulky 22-week size, tender uterus. The adnexa and pouch of Douglas were free, cervical excitation tenderness was positive and examining of the gloved finger was stained with creamy vagina discharge. In the outpatient clinic, transabdominal pelvic ultrasound examination revealed an enlarged globular uterus. The endometrial cavity was thin and empty while the myometrium contained multiple circumscribed heterogeneous masses, the largest measuring 7.1 cm. The ovaries appeared sonographically normal. The overall, ultrasound diagnosis was returned as multiple uterine fibroids. Consequently, a clinical diagnosis of symptomatic uterine fibroid was made. Based on these findings, she was worked up for surgery by requesting for full blood count (FBC), fasting blood sugar (FBS), electrolyte, urea, creatinine (E/U/Cr) and chest X-ray. The haematological investigations done revealed a packed cell volume (PCV) 27%, white blood cell count (WBC) of 6500/cm³, differential counts were 64.8% neutrophils, 22.2% lymphocytes, 5.5% eosinophils, 0.8% basophils and 6.7% monocytes. Blood film appeared essentially normal with adequate Platelets of 200 X109/L. FBS was 68 mg/dl, E/U/Cr returned as being adequate, while ECG was essentially normal and showed sinus rhythm. The chest X-ray done was a normal study. Thereafter, the patient was transfused with two units of cross-matched blood. She was taken for surgery 3 weeks after stabilization with post-transfusion PCV of 35%. At laparotomy, a bulky uterus of 24-week size, a healthy left ovary, and bilateral patent tubes was seen however but the right ovary was unhealthy. She had a total abdominal hysterectomy and bilateral salpingo-oophorectomy done. Postoperative recovery was uneventful. All specimens taken were sent for histopathology. Histopathological report of the uterus endometrium showed fascicles of neoplastic smooth muscle cells arranged in whorls, with markedly pleomorphic, hyperchromatic, and vesicular spindle nuclei, numerous bizarre mitosis. No tumour infiltration on the myometrium in keeping with leiomyosarcoma with co-existing fibroid. The tubes, ovaries and omentum were normal with no evidence of tumour infiltrations. As soon as the histopathological result was obtained, postoperatively, the patient was commenced on chemotherapy using Docetaxel 100 mg/m² day1 and Gemcitabine 900 mg/m² day1 and 8, repeat every 3weeks for 6 courses. Both the pre-and post-chemotherapy blood profiles of the patient were within normal values. After the 4th course of chemotherapy, she presented with acute bleeding per vaginum. During vaginal examination, an abnormal mass detected in the vaginal vault with contact bleeding. Abdominopelvic CT scan showed a multilobulated heterogeneously enhancing intraperitoneal mass at the level of L3-L5 with infiltration of the anterior abdominal wall. There was also infiltrations and compression of the mid ureters with consequent bilateral hydronephrosis. Widespread pulmonary nodules of varying sizes were noted on each lung basis bilaterally in keeping with canin ball metastases. Overall features are indicative of metastatic disease.

She was stabilized, counselled on the prognosis, and was commenced on the haemostatic radiotherapy, 18 daily fractions of 45.00 Gy over 3.5 weeks radiation therapy. Thereafter, she continued her adjuvant chemotherapy which was still ongoing and was placed under surveillance and monitoring.

DISCUSSION

Uterine leiomyosarcoma is a rare malignancy accounting for 1-2% of uterine cancer with an annual incidence of 0.64/100000 women. It is the most common histological variant of uterine sarcomas. Leiomyosarcoma is an aggressive tumour associated with poor prognosis and has a five-year survival rate ranging from 18.8% to 68%. Leiomyosarcoma occurs in women over 40 years of age, with a median age of 60 years, as seen in the case presented who is in her 43rd year of life. Leiomyosarcoma had predilection and poor prognosis among women of African American women descent. It is usually an incidental finding in a patient who had myomectomy or hysterectomy for otherwise thought to be diagnosed with benign leiomyomas/uterine fibroid. The two main risk factors for uterine leiomyosarcoma are exposure to radiation and treatment with tamoxifen for breast cancers. Furthermore, leiomyoma may undergo mitotic changes to leiomyosarcoma. The only identifiable risk factors in our patient was a ten-year history of uterine fibroid, which could have undergone a sarcomatous change due to the prolonged duration. Before surgery, it has a similar clinical presentation with leiomyoma therefore, it is very cumbersome differentiating early stages. This diagnostic dilemma and rapid progression to the advanced stage led to its poorer prognosis. It usually presents with vaginal bleeding (56% commonest presentation), palpable pelvic mass (54%) and pelvic pain (22%), hemoperitoneum and distant metastasis. Our patient was initially diagnosed...
with symptomatic uterine fibroid pre-operatively due to the presentation typical of a symptomatic uterine fibroid. She did not have any constitutional symptoms and signs which may indicate the presence of malignant disease. Leiomyosarcoma is difficult to diagnose pre-operatively with only 0.5% of cases resected tumours being unexpectedly revealed as leiomyosarcoma after definitive histopathology. Thus, like our patient’s diagnosis, was made post-operatively from histological result of the hysterectomy specimen. Serum CA125 and serum lactate dehydrogenase level are tumour markers used in the early screening of the patient, to make a diagnosis of the disease, they however have a poor sensitivity and specificity. Most conventional screening tools such as ultrasound scan, endometrial biopsy or dilatation and fractional curettage fail to specifically diagnose leiomyosarcoma. The sonographic features of both leiomyosarcoma and leiomyoma are very similar with little differentiation both originating from the myometrium. This has made ultrasound, a baseline imaging test less sensitive and specific for the diagnosis of leiomyosarcoma. However, both CT and MRI have been proven to have increased sensitivity in diagnosing leiomyosarcoma. MRI guided biopsy can be used to diagnose a patient with a suspected case of leiomyosarcoma. MRI is the mainstay investigation for leiomyosarcoma. It showed in-depth images of myxomatous uterine tumours and contiguous spread of the disease. Both contrast-enhanced MRI including T2 and diffusion-weighted imaging (DWI) are now used as a screening tool with high specificity and sensitivity. On the MRI, the appearance of leiomyosarcoma is variable, leiomyosarcomas usually appear as a large infiltrating myometrial mass of heterogeneous low signal intensity on T1-weighted images, with irregular and ill-defined margins. On T2-weighted images, they usually show intermediate-to-high signal intensity, with central hyperintensity indicative of extensive necrosis (present in >50% of cases). Leiomyosarcoma may be submucosal, intra-mural or sub-serosal within the myometrium. Leiomyosarcomas ideally should be managed in a multidisciplinary and multimodal approach upon diagnosis. Management modalities include surgery, chemotherapy, radiation, and hormonal therapy. Surgery which includes staging hysterectomy and bilateral salpingo-oophorectomy with or without pelvic lymphadenopathy and removal of any intrabdominal masses. This is required in all stages of management. In general, there is no specific treatment protocol in the management. Our patient had a hysterectomy and bilateral salpingo-oophorectomy for symptomatic leiomyoma. Early and total resection of all metastatic site is important in surgical treatment. Leiomyosarcoma has a high recurrence rate of about 53-71% which occurs within a mean period of 18 months. The prognostic indicators are tumour size more than 5 cm, stage of the disease, depth of invasion, high mitotic indices, cellular atypia, presence of anaplasia and tumour necrosis, the extent of primary spread, tumour grade, and tumour rupture. It is a tumour that is also highly prone to local spread as well as distance metastasis, extras uterine metastases occur in 50% of cases all this affects the prognostic factor of the disease. Our patient had high mitotic indices and rapid local and distance spread to the lung bases bilaterally as well as peritoneum. Histologically, the tumours are densely cellular and are composed of bundles of spindle cells and nuclear and cellular pleomorphism, nuclear hyperchromasia, and multinucleated giant cells. The histological diagnosis of leiomyosarcoma in our patient, made us requested the CT scan, which showed metastasis to the bases of the lung and the peritoneum shown in Figure 1-2.

Figure 1: The axial view of the base of the lung showing multiple metastatic nodules, more on the right.

Figure 2: The axial view of the lower abdomen with heterogeneous peritoneal mass.

Chemotherapy such as a combination of cyclophosphamide, vincristine, doxorubicin and dacarbazine is used alone or in combination with radiation therapy. Adjuvant therapy has been used to treat individuals with leiomyosarcoma following surgery especially in the advanced stage seen in the case presented. As doxorubicin is known as the first-line choice, the preferred first and second-line choice treatment for metastatic uterine leiomyosarcoma as is the combination of a fixed-dose-rate gemcitabine and docetaxel. Radiotherapy was added to the chemotherapy to curtail the local spread as well as hemostatic.

In high-grade leiomyosarcoma, adjuvant therapy although administered has a limited role in affecting the survival rate after complete resection. She has had 7 sessions of
chemotherapy and a session of radiotherapy after the surgery and she is still undergoing surveillance and monitoring.

Table 1: 2009 International federation of gynaecology and obstetrics staging for uterine leiomyosarcoma.

<table>
<thead>
<tr>
<th>Staging</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Limited to the uterus</td>
</tr>
<tr>
<td>IA</td>
<td>Tumor ≤5 cm in largest dimension</td>
</tr>
<tr>
<td>IB</td>
<td>Tumor &gt;5 cm</td>
</tr>
<tr>
<td>II</td>
<td>Extending beyond the uterus but within the pelvis</td>
</tr>
<tr>
<td>IIA</td>
<td>Involving the adnexa</td>
</tr>
<tr>
<td>IIB</td>
<td>Involving other pelvic tissues</td>
</tr>
<tr>
<td>III</td>
<td>Infiltrating abdominal tissues</td>
</tr>
<tr>
<td>IIIA</td>
<td>In one site</td>
</tr>
<tr>
<td>IIIB</td>
<td>More than one site</td>
</tr>
<tr>
<td>IIIC</td>
<td>Regional lymph node metastasis</td>
</tr>
<tr>
<td>IVA</td>
<td>Invading bladder or rectum</td>
</tr>
<tr>
<td>IVB</td>
<td>Distant metastasis</td>
</tr>
</tbody>
</table>

CONCLUSION

Leiomyosarcoma, an aggressive tumour with a poor prognosis. Leiomyosarcoma should be considered as a differential diagnosis in patients with abnormal uterine bleeding with suspected symptomatic uterine fibroid to avoid missing the diagnosis in pre and perimenopausal women.

ACKNOWLEDGMENTS

Authors appreciate the assistance rendered by all members of staff in the department of obstetrics and gynaecology, radiology and oncology, Lagos State University Teaching Hospital, Ikeja for the active role in patient care.

**Funding:** No funding sources

**Conflict of interest:** None declared

**Ethical approval:** Not required

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