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Original Research Article

Spindle cell tumours of the female genital tract

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ABSTRACT

Background: Our aim is to describe the clinicopathology features of spindle cell tumors of the female genital tract seen in our hospital and to compare the findings with what is seen in other parts of the world.
Methods: We conducted a cross-sectional study of all spindle cell tumors diagnosed in the department of Morbid Anatomy and Forensic medicine of Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Nigeria from January 1, 2017, to December 31, 2022.
Results: Leiomyoma was the most common spindle cell tumour seen. Only 570 cases met the inclusion criteria. Only one nodule was removed in 130 cases (22%) while greater than one nodule was excised in 432 cases (75.8%). The mean age of patients was 40.77 years while the age range was 19-79 years. About three-quarters of leiomyomas are removed in the age-group 31-50. There was no correlation between the number of nodules removed and the age of the patient. The next second most common spindle cell tumor seen was malignant mixed mullerian tumour. Eleven cases were seen in the study period, The average age was 57.7 years. The age range of cases was 27-72 years.
Conclusions: Our study supports the general observation that leiomyomas commonly cause symptoms in the reproductive age group and that most patients with leiomyoma frequently have more than one nodule. Our study further reinforces the widely established knowledge that MMMT is found in older post-menopausal women and can occasionally be seen in younger pre-menopausal women.

Keywords: Spindle cell, Leiomyoma, Leiomyosarcoma, Mullerian

INTRODUCTION

Spindle cell tumors are neoplastic lesions made up in part or whole of proliferating elongated cells with tapering nuclei and bipolar cytoplasm. They are found in many parts of the body and are mesenchymal in origin. Diagnosis of these tumors can sometimes be challenging, especially in core needle biopsies where major architectural configurations that may be diagnostic or highly suggestive of disease entities may be lacking. The spindle cell tumour most encountered in the female genital tract is leiomyoma. Leiomyoma is a benign spindle cell tumour with smooth muscle differentiation. It is most found in the uterus where it can be subserosal, submucous or intramural. It is a major cause of morbidity in women and accounts for most hysterectomies.[1-7] It can be in the uterine corpus or cervix. It can sometimes prolapse to form a leiomyomatous cervical polyp. Leiomyoma can be found in other organs of the female genital tract particularly the ovary and the wall of the vagina. Leiomyoma is very common in Nigerian women and can usually be identified either clinically or following ancillary investigations.[8,9] However histologic examination is required for confirmation of the tumour and to exclude other masses like its malignant form, Leiomyosarcoma and a form of endometriosis known as Adenomyoma. Leiomyoma is not usually removed except if it presents with some complications.

Leiomyosarcoma is a malignant smooth muscle tumour that can result from transformation of a leiomyoma. It is distinguished from leiomyoma by the presence of atypical nuclei that is frequently very bizarre, necrosis and frequent mitotic figures. Its identification can be challenging if the tumour is bizarre. In this case, immunohistochemical identification of SMA, Desmin, and Caldesmon can be helpful. Endometrial stroma tumors and Cellular Angiofibroma are rare mesenchymal tumors that are found in the female genital tract, particularly in the endometrium and vulva, respectively. These tumors can have prominent spindle cell morphology and can mimic other spindle cell lesions. It is necessary to note that malignant epithelial tumors of the female genital tract including the derivatives of the mullerian epithelium can undergo malignant transformation. These include squamous cell carcinoma particularly of the uterine cervix and malignant mixed mullerian tumour. The aim of our study is to describe the clinicopathology features of spindle cell tumors of the female genital tract seen in our hospital and to compare the findings with what is seen in other parts of the world. Our findings will provide baseline data for future works in this area.

METHODS

We did a cross-sectional study of all spindle cell tumors diagnosed in the department of Morbid Anatomy and Forensic medicine of Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile-Ife, Nigeria from January 1, 2018, to December 31, 2022 (Five-year period). Obafemi Awolowo University Teaching Hospitals Complex is situated in the southwestern part of Nigeria. All the information on the biodata of the patients was extracted like duration of symptoms, size and number of the masses and the nature of surgery from the departmental records. Each case was evaluated to confirm the diagnosis seen in the records. We cut and stained the tissue blocks of each case with hematoxylin and eosin.

Inclusion and exclusion criteria

All cases with biodata and available histopathology reports were included. Cases with missing biodata and tissue were excluded. We studied 570 cases of leiomyoma and eleven cases of malignant mixed mullerian tumour seen during the study period. These were all the cases that met the inclusion criteria.

Statistical analysis

Extracted data was compiled in Microsoft excel and analyzed using Microsoft excel and statistical package for social sciences (SPSS) version 20.

RESULTS

Five hundred and seventy-four cases of Leiomyoma were seen during the study period. However only 570 cases met the inclusion criteria. Four cases were excluded from the study. Only one nodule was removed in 130 cases (22%) while greater than one nodule was excised in 432 cases (75.8%). All the cases of leiomyoma seen were in the corpus uteri. There were no cases in the ovary, fallopian tube, or vagina. The mean age of patients was 40.77 years while the age range was 19-79 years. The age-group 31-40 years accounted for 40.5% of cases, which was the most frequent case. This was followed by the age group 41-50 which accounted for 195 cases (34.2%). Hence about three-quarters of leiomyomas are removed in the age-group 31-50 years. The age distribution is shown in (Figure 1).

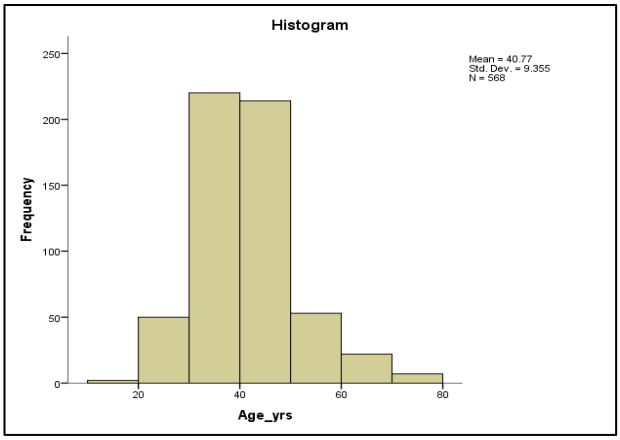

Figure 1: Age distribution of cases.

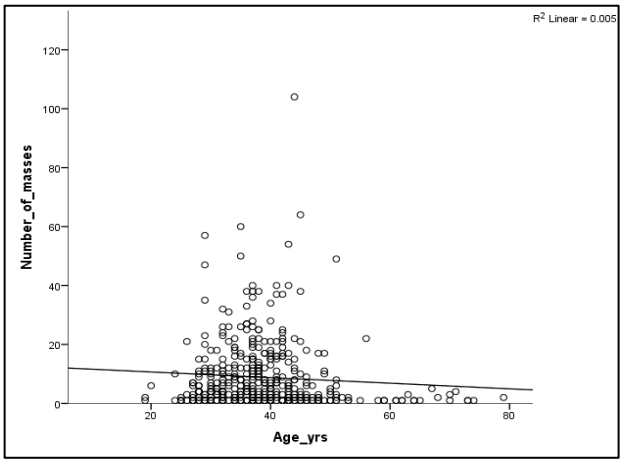

Figure 2: The number of masses versus the age of the patient.

Further age group analysis shows that most leiomyoma nodules (75%) are removed in the reproductive age period of 15-45 years. As shown in (Figure 2), there was no correlation between the number of masses removed and the age of the patient (R^2=0.005). There was no correlation between the number of masses and the widest diameter of the largest mass (R^2=0.013). This is shown in (Figure 3). There was no correlation between the age of the patient and the widest diameter of the largest mass (R^2=0.036). This is shown in (Figure 4). The most common surgical procedure used was myomectomy which accounted for

383 cases (67%). Hysterectomy was done for 183 cases (32%).

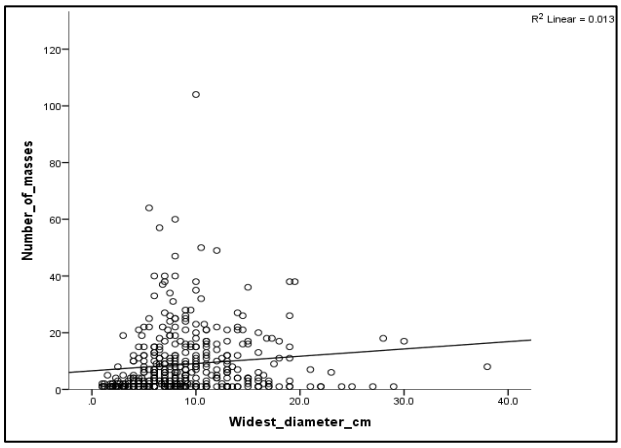

Figure 3: The number of masses versus the widest diameter of the largest mass.

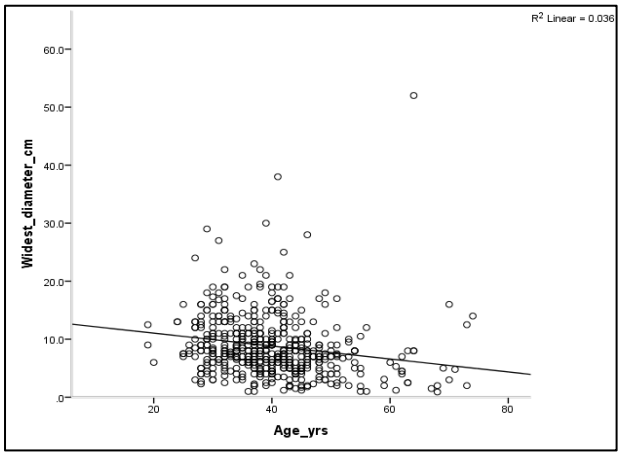

Figure 4: The widest diameter of the largest mass versus the age of the patient.

There were no adequate details for four cases. The type of surgery done is associated with the multiplicity of the masses ($p<0.0001$) with hysterectomy more common in cases of multiple masses than in patients with single nodules. Myomectomy tends to be more common than hysterectomy in the reproductive age group while hysterectomy is more commonly done in the post and peri-menopausal age groups (Figure 5). A typical case of leiomyoma is shown in (Figure 6).

Most cases are in the 30-to-50-year age group. The ages of two of the patients are unknown. The scatter diagram in (Figure 2) shows no relationship between the number of leiomyomatous nodules and the age of the patients. The scatter diagram in (Figure 3) shows no relationship between the number of leiomyoma nodules and the widest diameter of the biggest nodule. The scatter diagram shows no relationship between the widest diameter of the largest leiomyoma nodule and the age of the patients. The scatter diagram in (Figure 5) myomectomy is frequently done in reproductive age groups while hysterectomy is the procedure of choice in older age groups.

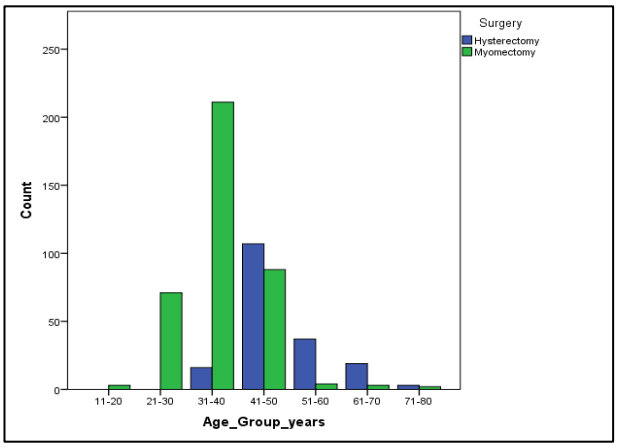

Figure 5: The frequency of types of surgery for removing the leiomyoma nodule in each age group.

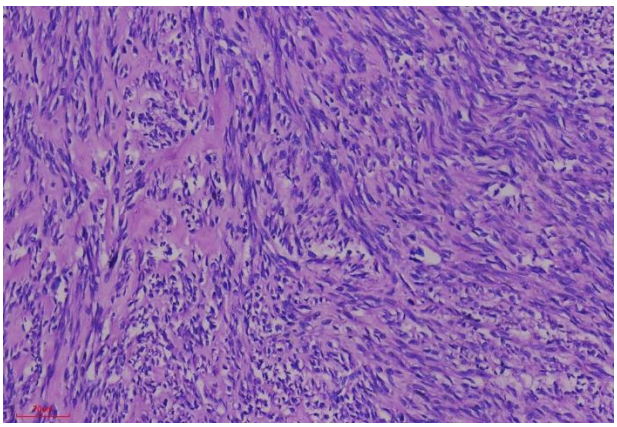

Figure 6: A typical case of leiomyoma.

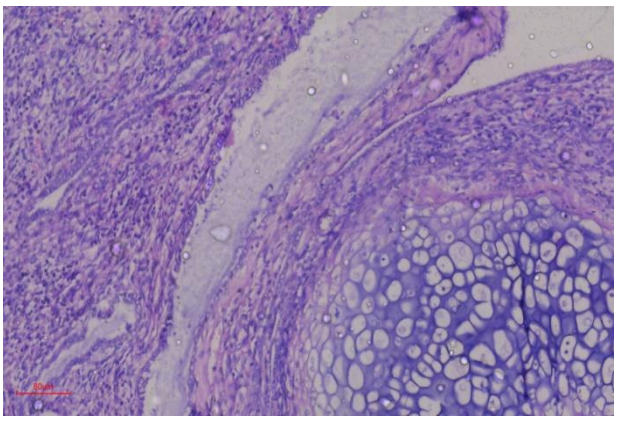

Figure 7: Malignant mixed mullerian tumour with heterologous element.

The photomicrograph shows leiomyoma with areas of hyalinization. The next most common spindle cell tumour seen was malignant mixed mullerian tumour. Eleven cases were seen in the study period, The average age was 57.7 years. The age range of cases was 27-72 years. Two of the

patients had hypertension and type 2 diabetes mellitus (ages 65 and 72 years). One of the patients had chronic liver disease and tuberculosis. Only two of the cases showed heterologous elements on microscopy. All the affected patients had hysterectomy. The duration of symptoms before presentation in the hospital ranges from 2-12 months with an average of 5.6 months. The (Figure 7) shows a typical case of a malignant mixed mullerian tumour. We saw only one case of leiomyosarcoma. It was found in a 42-year-old woman. There were no cases of spindle cell carcinoma of the cervix, cellular angiofibroma or any endometrial stroma tumour. The (Figure 7) shows a malignant mixed mullerian tumour seen to form cartilaginous tissue.

DISCUSSION

Leiomyoma

About three-quarters of leiomyomas are removed in the age-group 31-50 years. Our study supports the general observation that leiomyomas commonly cause symptoms in the reproductive age group. This is because one of its main symptoms, heavy menstrual bleeding, is found in pre-menopausal women. Submucous leiomyomas can increase the surface area of the endometrium thereby increasing the surface area of tissue shed during menses and contributing to the degree of blood loss. Infertility has also been associated with leiomyomas. Both infertility and heavy menstrual bleeding are not direct problems of post-menopausal women, hence problems caused by leiomyomas decrease after menopause. Moreso, it is known that leiomyomas grow in response to oestrogen.[10–12] Loss of oestrogen at menopause is believed to be linked with reduction in size of the nodules and resolution of symptoms that might have been present before attainment of menopause. More than one leiomyoma nodule was removed from the uterus of a substantial percentage of patients (>75%). This is consistent with the well-known fact that most patients with leiomyoma frequently have more than one nodule. Even patients who had one nodule removed could have more nodules. It is likely that only the nodule seen to pose a problem to the patient was removed. An imaging study to directly assess the number of nodules in patients will be more informative. We did not find any correlation between the age of the patient and the number of masses removed or the widest diameter of the largest mass. This suggests that the number of leiomyomas that are removed do not increase as the patients grow older. It also implies that the masses do not get larger as the patient's age increases. Although it seems as though an expected increase in diameter of the mass before menopause will be neutralized by the expected decrease after menopause and hence erode any correlation between the size of the leiomyoma nodule and the age of the patient, we did not find any correlation between the two variables even when cases of pre-menopausal women were selected and analyzed separately. However, to make a conclusive statement about this, it is necessary to directly measure the size of the mass in-situ using imaging techniques and then follow it up over time.

The most common surgical procedure used to remove leiomyoma during the study period was myomectomy as it is often desirable not to remove the uterus of women of reproductive age, most affected by leiomyoma, who may be desirous of more children. Myomectomy can be complicated by haemorrhage, especially in large masses that are embedded within the muscle wall. Gynaecologists commonly opt for hysterectomy if the risk of haemorrhage is remarkably high, particularly if the number of leiomyoma nodules to be removed are numerous. Expectedly, we found that the proportion of hysterectomy increased significantly in the post-menopausal women where it might even be more beneficial to remove the reproductive organs and further reduce risks of malignancy in the reproductive organs.[13,14] All the cases of leiomyoma seen in the female genital tract were in the corpus uteri. There were no cases in the ovary. It is well known that leiomyoma of the ovary is very rare.[15-18] It is therefore not surprising that we did not find any case during the study period. Leiomyoma of the ovary can easily be misclassified as subserous uterine leiomyomas hence effort should be made to extensively section the nodule to identify native ovarian tissue that might be compressed and pushed to the periphery in such cases. It is also important identify cases of leiomyoma of the ovary as removal of such may be associated with premature menopause especially if the other ovary has been rendered non-functional by destructive chronic tubo-ovarian inflammation or had been removed for other reasons. Identifying this may help gynaecologists to explain symptoms of ovarian failure which may develop in such patients.

Expectedly we did not find any case of leiomyoma of the fallopian tube as it is well known to be rare.[19-21] Theoretically, leiomyoma of the fallopian tube can predispose patients to ectopic gestation. This will be seen as a surgical emergency that commonly results in excision of the affected tube. The extensive haemorrhagic necrosis commonly found in histology of such specimens may prevent the identification of pre-existing leiomyoma. Although cases of fallopian tube are likely to be extremely rare, the few cases that exist might be easily missed, making identification of any case almost impossible. We did not identify any case of leiomyoma of the vagina during the study period. Vaginal leiomyoma is very rare.[22-24] The upper part of the vagina develops from the mullerian epithelium and is expected to have similar lesions to the upper part of mullerian derivatives. Although leiomyoma is a mesenchymal derivative, it will not be unusual to find it in the upper vaginal wall. The vagina is very elastic and capable of wide expansion. Hence a leiomyoma in this location will have to be larger than that of the uterus to come to clinical attention as it is unlikely to cause significant symptoms.

Malignant mixed mullerian tumour

The second most common spindle cell tumour seen during the study period was malignant mixed mullerian tumour (MMMT). Only one case of leiomyosarcoma was seen in our study. Although this tumour is derived from mullerian epithelium and not mesenchymal, it usually has a high proportion of spindle shaped cells that can mimic a sarcoma. From our experience, you sometimes need to examine many tissues to identify the epithelial component. Sometimes the epithelial component is not seen in biopsies but only seen after hysterectomy. Our finding implies that pathologists should endeavor to exclude MMMT in uterine biopsies that show malignant spindle cells as MMMT is much more common than leiomyosarcoma.

Most of the cases of MMMT seen in our study were in women in their 60s and 70s. Only two cases were found in younger women, one in a 27-year-old woman and another in a 42-year-old woman. This is consistent with pre-existing facts. Our study further reinforces the widely established knowledge that MMMT are found in older post-menopausal women and can sometimes be seen in younger pre-menopausal women. Endometrial cancers are known to be associated with hypertension and diabetes mellitus. This has also been found to be the case with MMMT.[25,26] The finding of the two patients that had concomitant hypertension and diabetes conforms to well established knowledge. However, we are not aware of any association between MMMT and chronic liver disease or tuberculosis. Although there were no cases of spindle cell carcinoma of the cervix seen in our study, it is necessary to emphasize that spindle cell carcinomas from the cervix can locally infiltrate the uterine corpus and mimic sarcomas. Many cases have areas with classical malignant squamous epithelial cell nests that can enhance easy identification of the entity. However, in tru-cut biopsies only spindle cells may be seen. Pathologists need to be aware of this.

Limitations

Current study is limited to being a retrospective study in which the data was not proactively collected. The size of the uterine nodules was measured after fixation in formalin. This may cause a small degree of shrinkage of tissues. Our study is also limited by assessment of nodules excised rather than assessment of the masses insitu using imaging techniques.

CONCLUSION

Current study supports the general observation that leiomyomas commonly cause symptoms in the reproductive age group and that most patients with leiomyoma frequently have more than one nodule. There is no correlation between the age of the patient and the number of masses removed or the widest diameter of the largest mass. The most common surgical procedure used to remove leiomyoma was myomectomy All the cases of leiomyoma seen in the female genital tract were in the corpus uteri. The second most common spindle cell tumour seen during the study period was malignant mixed mullerian tumour. Pathologists should endeavor to exclude MMMT in uterine biopsies that show malignant spindle cells as MMMT is much more common than leiomyosarcoma. Current study further reinforces the widely established knowledge that MMMT are found in older post-menopausal women and can sometimes be seen in younger pre-menopausal women.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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