

## CASE REPORT

# Recurrent vaginal epithelioid leiomyosarcoma; a case report from Botswana and review of the literature

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Tadele Melese Benti<sup>1</sup>, Nassali Mercy<sup>1</sup>, Alemayehu. B. Eshetu<sup>2</sup>, Ibe Enyeribe Iwuh<sup>3</sup>, Mamo Woldu Kassa<sup>4</sup>

University of Botswana, Faculty of Medicine, Department of Obstetrics and Gynecology<sup>1</sup>; University of Botswana Faculty of Medicine, Department of Pathology<sup>2</sup>; Baylor College of Medicine Children's Foundation, Area 25 Hospital. Lilongwe<sup>3</sup>; University of Botswana Faculty of Medicine, Department of Anesthesia and Critical Care Medicine<sup>4</sup>

\*For Correspondence: Email: [tadele3300@yahoo.com](mailto:tadele3300@yahoo.com); [bentit@ub.ac.bw](mailto:bentit@ub.ac.bw); Phone: 00267 74231505

## Abstract

Primary vaginal leiomyosarcoma is a rare gynecological malignancy. The clinical presentation is a benign looking well circumscribed mobile mass which might however occasionally present with distant metastases. Post treatment recurrence is common, and the clinical course is often unpredictable. Primary surgical management plus radiotherapy is the commonly practiced treatment of choice. We report a case of primary vaginal epithelioid leiomyosarcoma that recurred twice after local surgical resection. The patient subsequently underwent a total abdominal hysterectomy with bilateral salpingo-oophorectomy for a recurrent vaginal leiomyosarcoma. Histopathology of the vaginal mass revealed an epithelioid leiomyosarcoma of the vagina. She also received a course of adjuvant radiotherapy. The patient was free of recurrence at 3 year follow up. Vaginal mass must be evaluated with a high index of suspicion for malignancy. Local surgical resection alone is insufficient for primary vaginal leiomyosarcoma. Surgical resection with adjuvant radiotherapy offers better treatment outcomes with decreased risk of recurrence. Empirical oophorectomy in patients with completed family size might confer additional benefit in preventing disease recurrence in resource limited settings where testing for estrogen and progesterone receptor status of the tumour is unavailable. Due to the unpredictable course of the disease, lifelong patient follow-up is critical for better outcomes. (*Afr J Reprod Health* 2021; 25[1]: 161-168).

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**Keywords:** Botswana, vaginal sarcoma, epithelioid leiomyosarcoma, vaginal mass, radiotherapy

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## Résumé

Le léiomyosarcome vaginal primaire est une tumeur maligne gynécologique rare. La présentation clinique est une masse mobile bien circonscrite d'aspect bénin qui peut cependant occasionnellement présenter des métastases à distance. La récurrence après le traitement est courante et l'évolution clinique est souvent imprévisible. La prise en charge chirurgicale primaire associée à la radiothérapie est le traitement de choix couramment pratiqué. Nous rapportons un cas de léiomyosarcome épithélioïde vaginal primitif récidivant deux fois après une résection chirurgicale locale. La patiente a ensuite subi une hystérectomie abdominale totale avec salpingo-ovariectomie bilatérale pour un léiomyosarcome vaginal récidivant. L'histopathologie de la masse vaginale a révélé un léiomyosarcome épithélioïde du vagin. Elle a également reçu un cours de radiothérapie adjuvante. Le patient était sans récurrence à 3 ans de suivi. La masse vaginale doit être évaluée avec un indice de suspicion élevé de malignité. La résection chirurgicale locale seule est insuffisante pour le léiomyosarcome vaginal primaire. La résection chirurgicale avec radiothérapie adjuvante offre de meilleurs résultats de traitement avec un risque réduit de récurrence. Une ovariectomie empirique chez les patients dont la taille de la famille est complète pourrait conférer un avantage supplémentaire dans la prévention de la récurrence de la maladie dans des contextes à ressources limitées où le test du statut des récepteurs aux œstrogènes et à la progestérone de la tumeur n'est pas disponible. En raison de l'évolution imprévisible de la maladie, le suivi des patients tout au long de la vie est essentiel pour de meilleurs résultats. (*Afr J Reprod Health* 2021; 25[1]: 161-168).

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**Mots-clés:** Botswana, sarcome vaginal, léiomyosarcome épithélioïde, masse vaginale, radiothérapie

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## Introduction

Primary vaginal malignancy is very rare and accounts for 2% of all gynaecological malignancies<sup>1</sup>. Vaginal sarcoma(VS) is even rarer accounting for only 3% of the already uncommon

vaginal malignancies<sup>2</sup>. Although the older women are more commonly affected, no age group is immune to vaginal sarcoma<sup>3</sup>. The mean age at diagnosis of VS is lower than that for squamous cell carcinoma and adenocarcinomas of the vagina<sup>4</sup>. The largest review by Ahram *et al* and small case

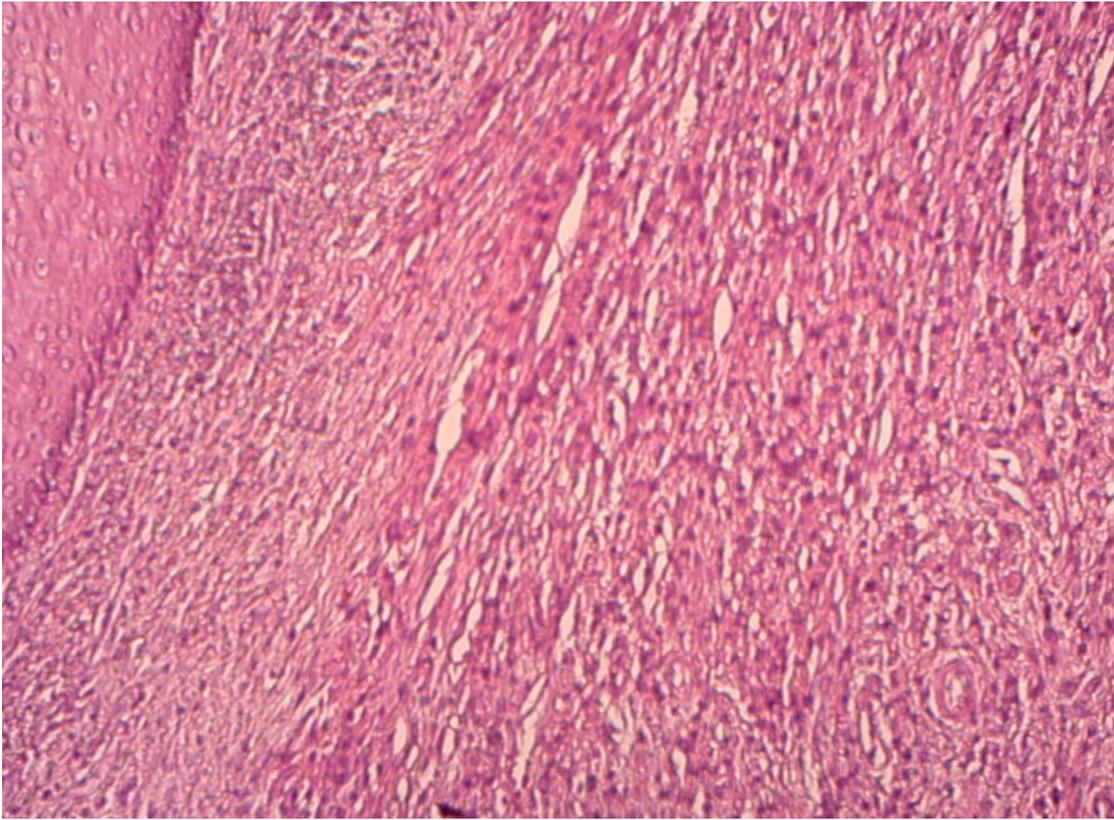
series by Wang reported the median age of patients with vaginal leiomyosarcomas to range between 44-47 years compared to squamous cell carcinoma and adenocarcinoma of the vagina which was 67.9 and 60.7 years respectively<sup>3,5,6</sup>. A report of 8 cases from China by Wang cited the youngest patient to be only 17 years old<sup>6</sup>. Vaginal sarcoma is often diagnosed at an early stage (Stage I and II) because of its unique natural disease progression pattern. Unlike carcinomas, sarcomas present with limited local extension and lymph node metastasis despite their larger tumor size<sup>4</sup>. Age at diagnosis, stage of the disease at presentation and tumour size were found to be prognostic indicators of 5-year survival<sup>4</sup>. Surgery and adjuvant radiotherapy has been associated with good prognosis<sup>4</sup>. Similarly, surgical excision with adjuvant chemotherapy has been associated with a 5 year survival rate of 90% among children younger than 5 years<sup>3</sup>. We report a case of 47 year old woman diagnosed with recurrent vaginal sarcoma; managed with surgical excision followed by adjuvant radiotherapy and remains symptom free 3 years post treatment.

## Case Presentation

A 47year old G3P3 woman presented with progressive growth of a vaginal mass for 2 months at the Princess Marina tertiary Hospital in Botswana. This was associated with perineal pain and a sensation of sitting on a mass. She also had an offensive vaginal discharge. On further evaluation, she reported a similar history of a vaginal mass at the same site for which surgical excision was performed at a primary hospital 3 years prior to the current presentation. Histopathology revealed leiomyosarcoma of the vagina. She received no further treatment and had been well till the current presentation. On examination she was in a good general condition and other systemic examination was normal. Vaginal examination revealed a 6x5x4cm midline mass protruding out of the vaginal opening with its pedicle arising from the lower third of the posterior vaginal wall. The mass was firm and mobile with a well delineated border. There was an offensive serosanguinous vaginal discharge. The anterior vaginal wall and cervix were grossly normal. The uterus was bulky and mobile. Both adnexae were

free. The rectal mucosa was smooth and free. There were no palpable inguinal lymph nodes. Pelvic ultrasound showed a coincidental finding of a 3x3cm uterine leiomyoma which was asymptomatic. Her chest X-ray was unremarkable. CT and MRI were not done due to unavailability of the service at the time. Wide resection of the protruding mass with 1 cm free margin was performed and tissue submitted for histopathology. The patient did well postoperatively and was discharged on day 7 with a follow up appointment in 3 weeks to review histology results. Frozen section procedure is not available in our setting. Unfortunately, she was lost to follow up only to return 4 months later with recurrence of a mass arising from the former surgical site; the lower third of posterior vaginal wall. The mass was however, more prominent on the right side of the vagina. Local examination, revealed a firm tender mass of 5x8cm protruding out of lower third of the posterior vaginal wall and extending to the right ischioanal fossa. The pelvic sidewalls were however free bilaterally. The mass was mobile and resectable. The mass displaced the rectum posteriorly but the rectal mucosa was smooth and free. There were no palpable inguinal lymph nodes. Although the histopathology from her second resection four months earlier revealed leiomyosarcoma with positive margins, the patient was lost to timely follow up. A provisional diagnosis of recurrent vaginal leiomyosarcoma was made. Although we were unable to perform estrogen and progesterone receptor status of the tumor, a local wide resection of the mass together with a total abdominal hysterectomy and bilateral salpingo-oophorectomy was performed. Using the International Federation of Gynecology and Obstetrics (FIGO) clinical staging system the disease was at stage II<sup>7</sup>. She did well postoperatively and was discharged on day 8 with follow up appointment after 2 weeks.

At the 3-week postoperative review, uterine histopathology reported uterine leiomyoma. Tissue from the vaginal mass consisted of a lobulated brownish soft tissue covered by vaginal mucosa. Cut section showed a white polypoid mass with areas of hemorrhage and edema measuring 6x5cm. The tumour mass showed pleomorphic cells with areas of necrosis and hemorrhage covering <50% of the tumor.



**Figure 1:** Tumour blending with vaginal mucosa H &E stain x10 Objective

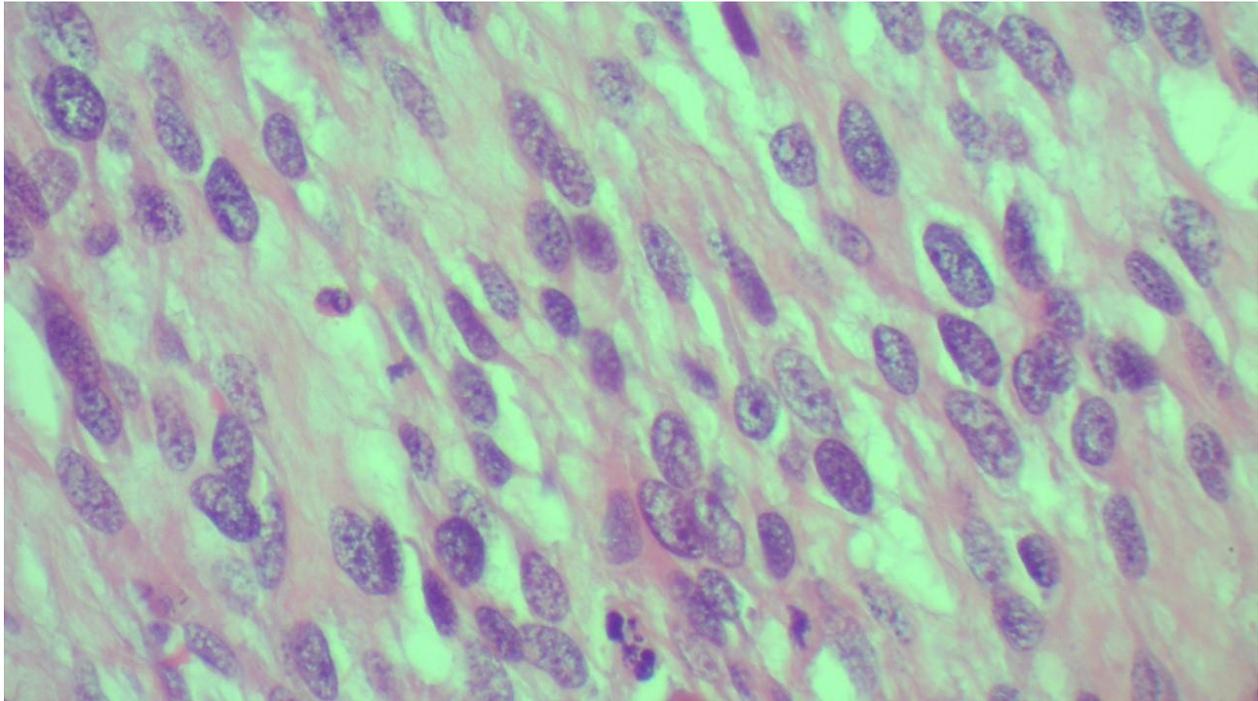
It was a spindle cell tumor with overlying stratified squamous epithelium (Figure 1). The tumor cells exhibited large blunt ended and coarse chromatic nuclei with moderate amount of eosinophilic cytoplasm. There were 17 mitotic figures per 10 high power fields (HPFs) (Figure 2). No lymphovascular invasion was seen. The surgical margin was positive. Using the most commonly used sarcoma grading system devised by the French Federation of Cancer Centers Sarcoma Groups (FNCLCC) the tumour was graded as grade 2<sup>8</sup>. The tumour cells stained positive with SMA and Desmin. The Pancytokeratin and S100 stains were negative. The histopathologic diagnosis was thus consistent with an epithelioid leiomyosarcoma. She was reviewed in the Gynaecologic oncology multidisciplinary clinic with the above results and subsequently followed up there. In view of the two previous recurrences and positive surgical margins she was initiated on adjuvant pelvic radiotherapy at a dose of 4,500 CGy and brachytherapy 2100 CGy. There were minimal local side effects including

skin discoloration and vaginal stenosis. She is currently undergoing regular follow up with no evidence of recurrence at 3 years post treatment.

## Discussion

Leiomyosarcoma is defined based on tumor size of more than 5cm and histopathological findings of more than 5 mitotic figures per 10 high power fields, positive margins or cellular atypia<sup>9,10</sup>. Our patient had a vaginal mass of 5x8 cm, positive margins, and mitotic figures of 17 per 10 HPFs with cellular atypia which were consistent with the diagnosis.

The clinical presentation of vaginal sarcoma varies from an asymptomatic coincidental finding in early stage of disease to nonspecific symptoms including vaginal serosanguinous discharge, vaginal or rectal pain and urinary retention. On physical examination, the vaginal mass appears as a well circumscribed mass. In the absence of clinical evidence for malignant disease,



**Figure 2:** Spindle cell tumour H & E stain X40 objective

the diagnosis is solely dependent on histopathology. Based on a case reported by Çobanoğlu *et al*<sup>11</sup>, due to the absence of clinical features suspicious for malignancy, cases can be misdiagnosed as a benign vaginal mass more so if there is an inaccurate histopathological examination. For this reason, any vaginal mass should be treated with a high index of suspicion for malignancy regardless of the nature of the mass unless proven to be inflammatory in nature. According to Talayeh *et.al*<sup>4</sup> in their retrospective analysis of vaginal malignancy, vaginal sarcoma tends to affect younger women compared to squamous cell or adenocarcinoma of the vagina. Patients with primary vaginal sarcoma present with a larger tumour size but with less local extension or lymph node metastasis<sup>4</sup>. Our patient's initial diagnosis of primary vaginal sarcoma in 2013, was at the age of 44 years. Although her tumour size was big, she had no evidence of distant metastases. The mass was well circumscribed and easy to excise with no rectal involvement.

Due to the rare occurrence of VS, there is no evidence based structured guidelines for its definitive management. According to Ciaravino *et al*<sup>12</sup> surgical management has been associated with higher five year survival rates compared to primary

radiotherapy and/or chemotherapy. Their review did not demonstrate any survival benefit of adjuvant radiotherapy or chemotherapy. This was attributed to the small number of case reports reviewed<sup>12</sup>. From a review of pooled cases over 12 years in USA, majority of cases of vaginal sarcomas were treated with surgical intervention<sup>4</sup>. Our patient was initially managed with local surgical excision alone. Upon disease recurrence she had a repeat excision in combination with total abdominal hysterectomy plus bilateral salpingo-oophorectomy. This was followed by adjuvant radiotherapy. Unlike the two previous unfavorable outcomes with tumour recurrence 3 years and then 4 months after local excision respectively, she remains free of recurrence three years later following surgery and adjuvant radiotherapy. Our patient was managed and followed in a gynaecologic cancer multidisciplinary clinic which ensured she received holistic integrated care that contributed to her improved follow up.

William *et al*<sup>3</sup> after analysing pooled data from National cancer data base reported that children with vaginal sarcoma treated with chemotherapy had a 5 year survival rate of 90%. On the other hand, women aged 20 -70 years treated primarily with surgery and some of them

receiving adjuvant chemotherapy or radiotherapy had a five year survival rate of 84%<sup>3</sup>. Ahram *et al*<sup>5</sup> from their own experience and review of 138 heterogeneous cases of vaginal leiomyosarcoma in terms of stage and grade of disease, were unable to make a definite recommendation as to the best treatment plan. They however suggested that local excision with radiotherapy should still be a feasible approach. There is however, limited supportive data for the use of adjuvant chemo-radiation<sup>5</sup>. In another case report by Suh, VS successfully managed by wide surgical excision and radiotherapy resulted in a 5 year disease free survival<sup>13</sup>. A report by Zheng *et al*<sup>14</sup> similarly presents a successful surgical excision with adjuvant chemotherapy and the patient was free of disease recurrence up to one year follow up.

Ahram *et al*<sup>5</sup> reported a case of poorly differentiated leiomyosarcoma where the patient presented with a mobile vaginal mass. Surgical resection with adjuvant radiotherapy was offered but she died within 4 months of the onset of the disease due to lung metastases<sup>5</sup>. Some vaginal sarcomas can be aggressive with early haematogenous spread despite presence of a localized and well encapsulated primary tumour. Given such aggressive nature of the disease, most published reports have demonstrated aggressive management approaches that include surgical resection with local radiation and consideration of chemotherapy in event of distant metastasis<sup>5</sup>. Similarly, in a report of 8 cases by Wang, surgical resection was the mainstay of therapy and radiotherapy or chemotherapy was only offered in cases of high grade and /or advanced stage of disease<sup>6</sup>.

Radiotherapy has been recommended by Hensley *et al*<sup>15</sup> with the aim of reducing local recurrence in patients with high grade disease, advanced stage and positive margins after surgical resection. Divya *et al*<sup>16</sup> reported a case of recurrent vaginal leiomyosarcoma who was disease free 29 months after surgical excision and adjuvant radiation. Another report by Suh *et al*<sup>13</sup>, reported successful treatment of vaginal leiomyosarcoma after surgical resection and radiotherapy. The patient was free of recurrence 5 years after treatment. Our patient had a repeat wide local excision of the vaginal leiomyosarcoma with positive margins, a total abdominal hysterectomy and bilateral oophorectomy. This was followed by adjuvant local radiation resulting in a better

treatment outcome compared to only local resection performed previously.

While adjuvant chemotherapy had a major role in the management of vulvo vaginal rhabdomyosarcoma, such chemotherapy did not confer any advantage in terms of overall survival rate in other histologic types of sarcomas of the vagina and vulva<sup>15</sup>. Punnonen *et al*<sup>17</sup> also reported unsuccessful chemotherapy in a patient with leiomyosarcoma with distant bone metastasis. This indicates that chemotherapy alone may not be a feasible option of treatment. Chemotherapy however, remains an option for salvage therapy in cases of unresectable tumour, persistent or recurrent disease<sup>15</sup>.

Ayatallah *et al*<sup>18</sup> reported successful hormonal management of indolent recurrent Estrogen and Progesterone receptor positive leiomyosarcoma of the vagina. They also recommended an individualized approach to cases of vaginal sarcoma<sup>18</sup>. As early as 1988, Meng-Mei Liu reviewed a small number of cases and proposed the estrogen dependent nature of vaginal sarcomas following a review of cases of regression of vaginal myoma after menopause. He then recommended consideration of oophorectomy in cases of recurrent leiomyoma or leiomyosarcoma<sup>19</sup>. Later on, Ayatallah *et al*<sup>18</sup> reported a case of a recurrent estrogen and progesterone receptor positive vaginal sarcoma managed conservatively with an aromatase inhibitor (letrozole)<sup>18</sup>. This approach was then reported as a possible option in selected cases with unresectable uterine leiomyosarcoma that is positive for estrogen and progesterone receptors in more than 90% of the tumour cells. A disease progression free survival of more than 24 months has been reported from this study<sup>20</sup>. Our patient underwent a hysterectomy based on the unpredictable course of the pre-existing uterine leiomyoma in the presence of a recurrent vaginal leiomyosarcoma. Although we were not able to test for estrogen and progesterone receptors in the specimen, due to unavailability of the service, empirical removal of both ovaries could have contributed to her longer recurrence free interval.

Disease recurrence is common among patients with vaginal sarcomas. Moller *et al*<sup>21</sup> reports a case managed with surgical excision with positive tissue margins followed by radiotherapy who was disease free for only for 5 months. Nathan *et al*<sup>22</sup> also reported a case of vaginal leiomyosarcoma treated with total

abdominal hysterectomy and bilateral salpingo-oophorectomy in addition to resection of the sarcoma. The tissue margins were positive and the patient was given adjuvant chemoradiotherapy. The recurrence free survival was only 18 months<sup>22</sup>. Another long term recurrence free survival of 6 years and eventual death of the patient 8 years after initial diagnosis of leiomyosarcoma of the vagina, due to recurrence has been reported by Punnonen and Kudo<sup>17</sup>. Wang from china reported disease free survival of up to 81 months after diagnosis of leiomyosarcoma of the vagina. One of the cited cases however, with stage I high grade leiomyosarcoma, had recurrence of disease 3 months post-operative<sup>6</sup>. These findings are consistent with our case report where our patient had two episodes of recurrence 3 years and then 4 months after the first and second local excisions respectively. Long recurrence free survival of 3 years has been achieved after wide resection of vaginal leiomyosarcoma in combination with total abdominal hysterectomy, bilateral salpingo-oophorectomy and radiotherapy. A report by Ngan addresses disease recurrence 21 years after the initial diagnosis of vaginal leiomyosarcoma<sup>23</sup>. This implies that patients with diagnosis of vaginal leiomyosarcoma can have recurrence any time in their life even decades post diagnosis and should be counselled about the importance of lifelong follow up. This also indicates that the postoperative course after vaginal sarcoma is quite unpredictable. While some patients have a less aggressive disease with longer intervals between diagnosis and time of recurrence and/or death, it can be quite aggressive in others with disease recurrence in less than 3 months. Based on this evidence, Gynaecologists should understand that long term close follow-up must be a standard of care in view of the unpredictable and less understood clinical course of vaginal leiomyosarcoma.

Low cost interventions such as telephone reminders, home visits and treatment buddies are worth exploring by cancer treatment units even in resource limited settings to minimise losses to follow up that adversely impact patient outcomes.

In regards to prognosis, vaginal leiomyosarcoma is more aggressive with 69% greater risk of cancer related mortality compared with vaginal squamous cell carcinoma<sup>4</sup>. In one retrospective review, age of the patient was found to be an independent predictor of 5year survival. Patients younger than 50 years have a 51% five-

year survival rate compared to 26% among those aged 50 and above. Stage I and II disease has 44-55% five year survival compared to 25% for stage III and IV disease<sup>12</sup>. Another report by Ngan and Curtin *et al*<sup>23,24</sup> cites grade and stage of the disease as significant predictors of treatment outcome. Our patient at the age 47 years, with FIGO stage 2 disease and grade 2 epithelioid leiomyosarcoma is expected to have a good prognosis.

From most reports, surgical management remains the mainstay of treatment of vaginal sarcoma. Based on our case report, recurrence of vaginal sarcoma can be prevented using radiotherapy especially for cases with positive surgical margins. Empirical removal of ovaries could have a role in the prevention of recurrence though we have limitation of confirming the estrogen or progesterone receptor status of the tumour in our case. Based on our review, adjuvant chemotherapy appears to have less impact in the treatment of vaginal sarcoma with the exception of rhabdomyosarcoma of the vagina. Lifelong patient follow-up is recommended given the unpredictable course of the disease.

## Conclusion

Any vaginal mass should be managed with a high index of suspicion for possible malignancy as most vaginal leiomyosarcomas often appear clinically as a benign mass. Patients and family members must be counselled for lifelong follow up in view of the unpredictable course of vaginal leiomyosarcoma, its prognosis and potential recurrence any time in life. Oophorectomy may be considered in the absence of estrogen and progesterone receptor testing in resource limited settings for premenopausal women or those with a completed family size. Such patients must be duly counselled about the sequelae of the oophorectomy. Timely referral to tertiary care and a multidisciplinary approach to the management of VS helps to have a better plan of patient care and follow up there by optimizing clinical outcomes.

## Consent for Publication

Written consent was obtained from the patient.

## Competing Interests

All the authors declare that they have no competing interest.

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## Contribution of Authors

TMB and IE operated the patient and TBM prepared the manuscript draft. MN, IE and MK were involved in pre and post-operative management of the patient and reviewed the manuscript. AE read and reported the final histopathology and reviewed the manuscript. All authors have reviewed the draft manuscript and approve the final version of the manuscript.

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