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Case report

Malignant mesenchymal vaginal tumor mimicking pedunculated submucous myoma: A case report

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ABSTRACT

Introduction: Vaginal mesenchymal cancer is one of the rarest cases, covering only 3% of all cases of vaginal malignancies. While risk factors are not heavily studied, genetic disorders and hereditary diseases have been stated to be responsible for the increasing incidence of vaginal mesenchymal carcinoma. The diagnosis of leiomyosarcoma could be done through anamnesis to find abnormal uterine discharge and pelvic pain and physical examination to find a protruding mass on the vagina, which then should be confirmed through a series of radiologic examinations and histopathological examinations. Due to its rarity, each case should be properly evaluated for its clinical manifestation, diagnostic results, and outcome of the treatment.

Case presentation: A 46-year-old woman came in with vaginal discharge and a protruding mass from the vagina without bleeding or urinary or defecation difficulties, which was suspected to be pedunculated submucous myoma. Based on pelvic USG and MRI, the mass was suspected to have originated from the vagina. Histopathology examinations from biopsy showed a possible mesenchymal malignant type. The patient then underwent total hysterectomy, bilateral salpingo-oophorectomy, and partial vaginectomy. Histopathological evaluation confirmed the diagnosis of leiomyosarcoma in the patient.

Discussion and conclusion: The patient was diagnosed with a vaginal malignant mesenchymal tumor stage II intraoperatively and underwent total hysterectomy and bilateral salpingo-oophorectomy. Leiomyosarcoma is not commonly diagnosed preoperatively, hence implying the importance of radiologic examination to do an early diagnosis prior to the histopathological analysis. Due to the rarity of vaginal mesenchymal malignancy, further studies are needed to increase understanding of this case.

1. Introduction

Vaginal mesenchymal cancer is one of the rarest cases of malignancy, with a rate of 3% from all cases of vaginal malignancies. Genetic disorders are one of the risk factors that cause leiomyosarcoma. The loss of chromosomes 10q (PTEN) and 13q (RB1), the addition of 17p (TP53), and mutations in the PTEN gene are thought to be some of the triggers for the development of leiomyosarcoma. With poor response to chemoradiation treatment, surgery is still the primary option in this condition. This study has been reported in line with the SCARE 2020 criteria [1].

2. Case presentation

A 46-year-old woman came to the hospital with a chief complaint of a mass protruding from her vagina and vaginal discharge. There was no abnormal vaginal bleeding and no complaint about defecation or urination. Physical examination showed protruding mass from vagina sized 15 cm × 10 cm × 10 cm, with a bumpy surface. The mass is depicted in Fig. 1. Based on the chief complaint and physical examination, the patient was first suspected to have a pedunculated submucous myoma, due to the characteristic of a protruding mass without abnormal vaginal bleeding found.

Ultrasound showed a hypo-hyperechoic mass protruded in the vagina with some part in front of the vulva with vascularization (see Fig. 2).

MRI on April 22, 2021, showed a solid mass with a minimal cystic component, lobulated, and suspected from the middle of vagina extended super posteriorly between the uterus and the rectum and inferiorly until out of perineum and perianal. The mass changed to be

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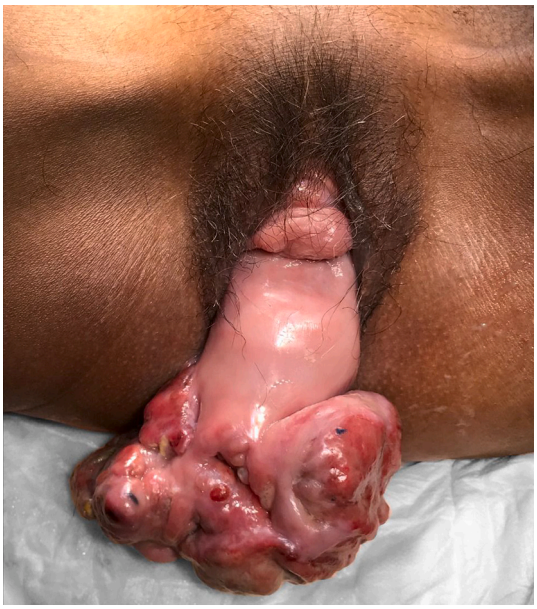

Fig. 1. Mass found on inspection.

slightly enhanced after contrast injection (Fig. 3). Histopathological examination on April 21, 2021, showed endometrial and a vaginal polyp with a mesenchymal malignant tumor and possible leiomyosarcomas.

Based on the data, the patient was diagnosed with a vaginal malignant mesenchymal tumor. She underwent total hysterectomy laparotomy and bilateral salpingo-oophorectomy and partial vaginectomy (tumor debulking), as depicted in Fig. 4.

Pathology examination from the operative procedure showed proliferating myoma with necrotic mixed with hemorrhagic area. Cells with round to spindle nuclear – vesicular pleomorphic and hyperchromatic with marked nuclei and atypical mitoses. Several endocervical glands were seen with tumor tissue proliferating blood vessels with fibrotic walls. The incision margins and parametrium are free of tumors, with endometrium within normal limits (Fig. 5 and Fig. 6).

3. Discussion

The vagina is a copulation organ extending from the perineum toward the pelvic cavity. The inner end of the vagina enlarges, forming a region called the vaginal vault. Vaginal introitus running super posteriorly into the pelvic cavity ended up with vaginal fornix, consisting of the vagina at the lower part and the cervix at the top. Based on the location, the vaginal fornix is divided into anterior, posterior, and two vaginal fornixes [1]. Histologically, the vagina consists of three layers, including tunica mucosa, tunica muscularis, and tunica adventitia. Tunica mucosa lining the internal layer of the vagina consisted of stratified squamous epithelium. Under the tunica mucosa is the lamina propria, enriched with elastin fiber. Tunica muscularis is predominantly formed by circular smooth muscle cells in the inner part and longitudinal in the outer. Tunica adventitia is a connective tissue containing so much elastin fiber that it is strong and elastic [2]. Mesenchymal tissue is also known as soft tissue or connective tissue, which comes from the mesoderm. Mesenchymal tissue is divided into several types of tissue, such as fibrous tissue, adipose tissue, and muscle tissue. In the vagina, mesenchymal tissue refers to muscle and fibrous tissue [3].

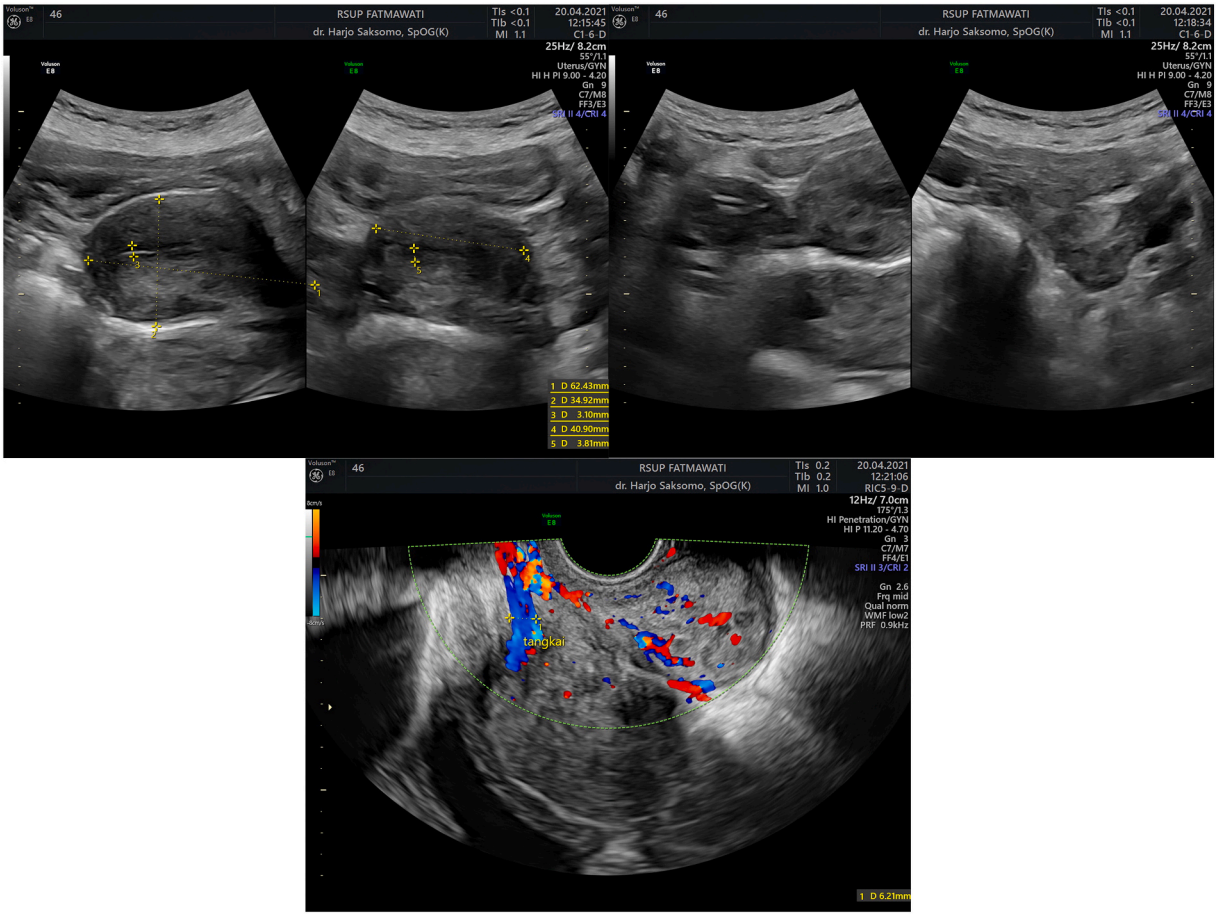

Fig. 2. Ultrasound examination on vaginal mass.

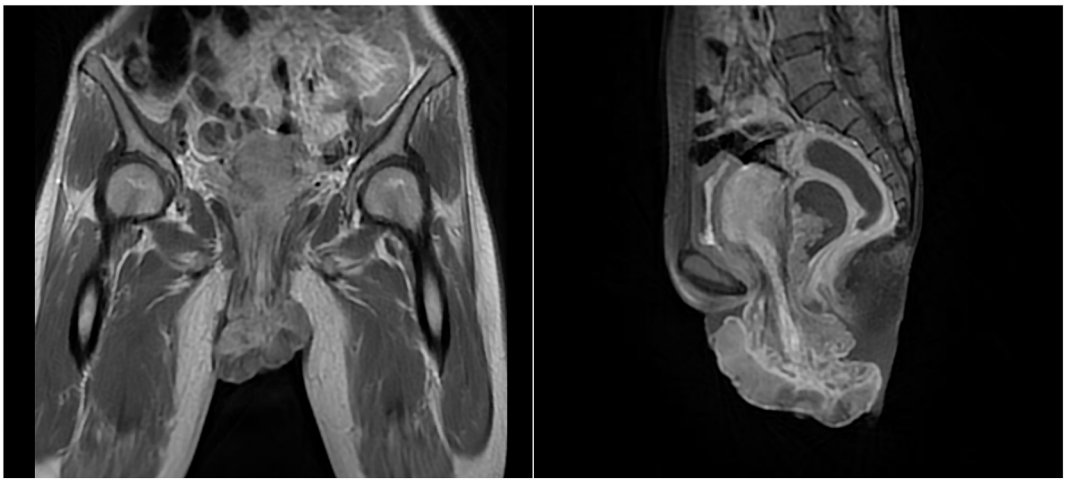

Fig. 3. Pelvic MRI with mass enhanced after contrast injection.

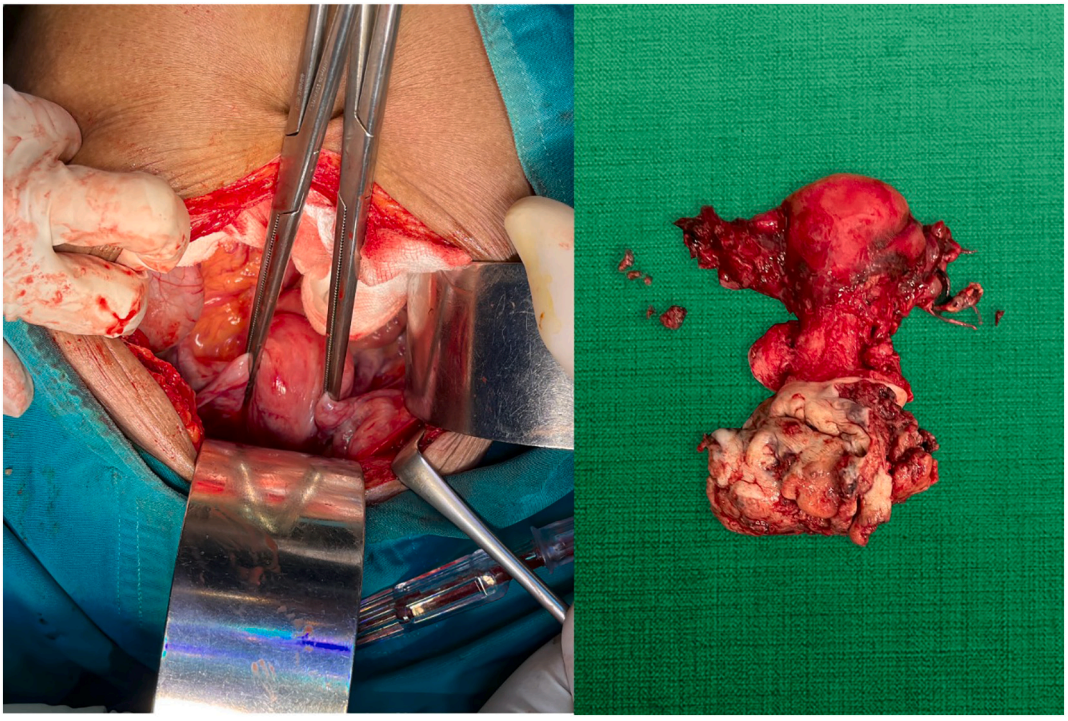

Fig. 4. Procedure and the specimen.

Under histological examinations, the appearance of each type of vaginal mesenchymal tumor is different. Generally, sarcoma in the vagina is differentiated based on the origin of the tissue; these are fibrosarcoma (malignancy originating from fibrous tissue), leiomyosarcoma (malignancy originating from smooth muscle tissue), and rhabdomyosarcoma (malignancy originating from skeletal muscle tissue). Histological images of leiomyosarcomas show abnormal cellularity with pleomorphism and hyperchromatism. Irregular mitosis can also be seen in the middle part [4].

Primary vaginal malignancy is a rare case with a prevalence of 1–2% and is more commonly caused by the spreading of malignancy from other organs. Secondary vaginal cancer comes from the cervix (32% of all cases), endometrium (18%), colon and rectum (9%), ovary (6%), and vulva (6%). Squamous cell carcinoma is the most common type of vaginal cancer, accounting for 75–90%, followed by adenoma (5–10%), melanoma, and leiomyosarcoma (1%). Leiomyosarcoma originates from smooth muscle cells of the vagina or its surrounding organs. Leiomyosarcoma is the most common vaginal mesenchymal tumor in adult females [5–10].

In 2020, the incidence of vaginal cancer in the United States was 3000 cases per year, with a mortality rate of as much as 30%. Vaginal cancer incidence is higher in Black females of 0.8 per 100,000, followed by Hispanic, White (0.6), and Asian-Pacific (0.4) [7].

Risk factors for vaginal mesenchymal cancer have not been studied extensively, due the rarity of cases. Patients with a history of radiotherapy identified on the pelvic region have a higher risk of developing leiomyosarcoma. The high energy of the radiotherapy beam can induce DNA damage and then develop into cancer. Patients with genetic abnormalities such as hereditary retinoblastoma (gene *RB1* deletion) and Li-Fraumeni syndrome (gene *TP53* mutation) also have a higher risk of developing leiomyosarcoma in the future. Leiomyosarcoma can develop from leiomyoma, although it is very rare. Therefore, leiomyoma removal

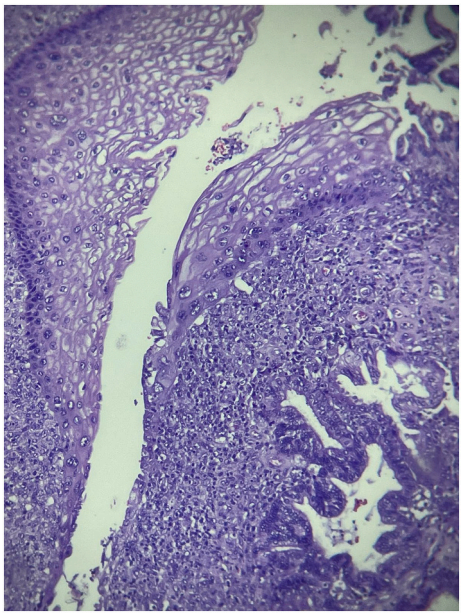

Fig. 5. Tumor extended to cervix.

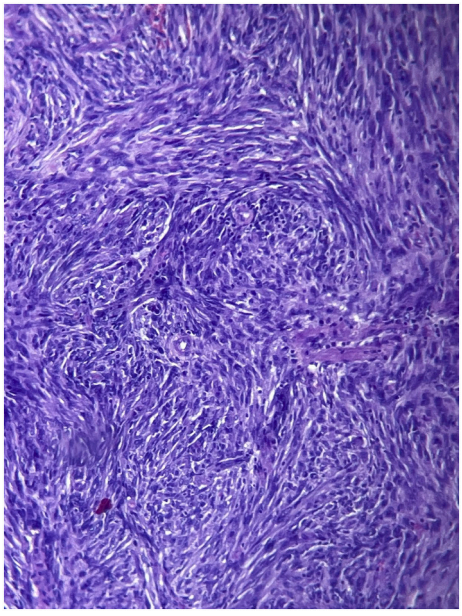

Fig. 6. Tumor area.

surgery is needed to prevent leiomyosarcoma development in the future. Leiomyoma has a high recurrence risk [3,7]. Genetic factors are thought to have an important role in the development of vaginal mesenchymal tumors. Generally, risk factors for rhabdomyosarcoma include age, gender, and some types of hereditary conditions [12–14].

Leiomyosarcoma is a group of soft tissue sarcomas with complex and unbalanced karyotypes. Cytogenetic and molecular changes in leiomyosarcoma are variable, but the most common changes are chromosome 10q deletion (*PTEN*) and 13q (*RB1*) and the addition of 17p (*TP53*). Chromosome 13 deletion causes a mutation in gene *RB1* (retinoblastoma gene), which is a tumor suppressor gene, identified in 90% of leiomyosarcoma patients. Chromosome 10q deletion causes a mutation in gene *PTEN*, which is also a tumor suppressor gene, causing activation of the phosphatidylinositol 3-kinase (PI3K)/protein kinase B AKT pathway [11,15].

Clinical signs of malignant mesenchymal vaginal tumor begin with a mass around the healthy vaginal mucosa with polypoid exophytic progression characterized by palpable necrotic vaginal mass. Malignant cancer might also involve rectum or pelvic organ invasion, which requires histopathology examination to state the diagnosis [16]. Vaginal cancer is classified according to the International Federation of Gynecology and Obstetrics (FIGO) guidelines based on Table 1 [17].

Morphologically, the vaginal tumor might be assessed by MRI as an ulcerated, ill-defined, irregular, well-defined lobulated, or circumferential thickening mass. Vaginal squamous cell carcinoma appears as an isointense to muscle on the T1 image and shows as a hyperintense in T2 [18]. The use of fat suppression in T1 examination might also produce a more precise image in early tumor mass at the first 45–90 s after the contrast injection, which plays a role in therapy evaluation [19]. Histopathology examination is required to diagnose malignancy. Spindled leiomyosarcoma is the most numerous case of a primary vaginal tumor. According to Sayeed et al., WHO uterine smooth muscle tumor criteria are also suitable for vaginal smooth muscle tumor malignancy (sensitivity 88.9%; specificity 90.2%) based on Table 2 [20].

A study proposes management options for vaginal malignancy refers to FIGO staging. Stage I malignancies in the lower vagina can be treated with mucosal surgery or radiotherapy, while stage II and III vaginal cancers require a combination of brachytherapy and external beam radiation therapy (EBRT). In certain conditions, patients need radical surgery (vaginectomy or pelvic exenteration). Patients are also recommended to receive radical postoperative neoadjuvant therapy to reduce the risk of recurrence. Meanwhile, stage IV primary vaginal cancer still has a low prevalence rate. However, extended malignancies to pelvic organs, such as the bladder or rectum, require EBRT in the interstitial, intracavitary, and external (EBRT itself) area and other treatments according to the patient's condition [17]. Other literature also states that the options for partial or radical vaginectomy, hysterectomy, or pelvic lymphatic dissection might be considered in stage I or stage II malignancies [16].

In most clinical conditions, preoperative vaginal cancer staging is not commonly practiced. Thus, a standard treatment option for vaginal malignancies is excision of the primary mass, which involves wide or radical excision to obtain clear boundaries. Total hysterectomy bilateral salpingo-oophorectomy is another option with a standard procedure using a laparotomy accompanied by an exploratory biopsy. Removal of the ovary should also be considered, as the masses are generally hormone sensitive [8].

Vaginal and vulvar malignancy patients with leiomyosarcoma can be given postoperative doxorubicin if the mass is not able to be completely resected. Doxorubicin can be given at a dose of 45–60 mg/m^2 every three weeks; the therapy is not intended for patients with congestive heart failure and reducing the dose should be considered for patients who have received pelvic radiation or other combination regimens [8]. However, the role of adjuvant chemotherapy still remains a controversy in the management of patients with vaginal malignancies; no clinical studies have demonstrated an advantage in patient prognosis [22].

Based on the examinations and tests, the patient had a solid mass

Table 1
FIGO vaginal carcinoma staging [17].

Stage	Deskripsi
I	The carcinoma is limited to the vaginal wall.
II	The carcinoma has involved the subvaginal tissue but has not extended to the pelvic wall.
III	The carcinoma has extended to the pelvic wall.
IV	The carcinoma has extended beyond the true pelvis or has involved the mucosa of bladder or rectum; bullous edema, such does not permit a case to be allotted to stage IV.
IVA	Tumor invades bladder and/or rectal mucosa and/or direct extension beyond the true pelvis.
IVB	Spread to distant organs.

Table 2
WHO uterine smooth muscle tumor criteria [20].

Any 2 of 3 warrant diagnosis of leiomyosarcoma:
1. Moderate to severe cytologic atypia
2. ≥ 10 mitotic figures/10 HPFs[a]
3. Tumor cell necrosis

[a] HPF: high power field.

with a minimal cystic component, lobulated, and suspected to originate from mid-vagina, extended super posteriorly between uterus and rectum, and inferiorly until out of perineum and perianal, enhanced after contrast injection, and seen diffusion restriction. These are suitable to vaginal tumor criteria [18,19]. However, the clinical manifestations are still in line with pedunculated submucous myoma. The myoma itself is a submucosa myoma with a peduncle that manifests from uterine submucosa and protrudes to the vagina through the cervix. Myoma is commonly seen in women aged 30–50 years old and has been found in 20–40% of women of reproductive age. It is also the cause of 2–11% of gynecologic cases in Indonesia. Pedunculated submucous myoma is often diagnosed through several clinical manifestations, including a protruding mass through the vagina, abnormal vaginal bleeding, abdominal pain, and various manifestations due to the protruding mass, such as urinary retention and obstipation, which should then be properly evaluated using USG or any other radiologic examination [23].

There had not been mass infiltration to the cervix, uterus, urethral projection, and rectum, therefore classified as stage I or II [17]. The patient underwent laparotomy total hysterectomy bilateral salpingo-oophorectomy and partial vaginectomy for tumor debulking. The specimen from the surgery was sent to histopathological test, and the result showed a mesenchymal malignant tumor that was leiomyosarcoma, with incision margin and parametrium free from tumor. The patient was then set up with adjuvant therapy to reduce recurrence risk from the same malignancy [22].

Leiomyosarcoma in the vagina originates from smooth muscle cells composing the vaginal wall, although it can also come from other surrounding organs, including the uterus, cervix, ovary, or vulva. Leiomyosarcoma most commonly occurs in the uterus and takes place sporadically, resulting from a complex genetic mutation from various genes. Malignancy requires genetic mutations involving many chromosomes; a single genetic mutation is not sufficient to develop a malignancy [21,22]. Therefore, a single genetic mutation examination is not sensitive or specific enough to be diagnostically useful [24]. Early examinations to determine the location of the primary tumor are anamnesis regarding the symptoms and the physical examination to inspect the tumor. Supporting evaluation to determine the origin and extension of the tumor is MRI with contrast, as done in this patient. The examination to confirm tissue origin and type of mesenchymal tumor is histopathology examination with immunohistochemistry testing [22].

4. Conclusion

The patient, 46 years old, came with a protruding mass and abnormal vaginal discharge with an early diagnosis of pedunculated submucous myoma, which was confirmed using USG, MRI, then suspected as malignancy of vaginal tumor. The result of histopathology examination was revealed vaginal mesenchymal malignancy (leiomyosarcoma). The patient was then treated performed with abdominal total hysterectomy bilateral salpingo-oophorectomy, and continued with total vaginectomy. Based on surgery and histopathology result (FIGO classification), the patient could be classified into stage II vaginal carcinoma. The treatments must be tailored based on personal patient conditions. Total hysterectomy bilateral salpingo-oophorectomy is considered as standard therapy of choice for vaginal carcinoma in an early stage to do a removal of mass, and further adjunctive treatment is not needed. Due to the rarity of vaginal mesenchymal malignancy, further research on its diagnosis and treatment option would considerably increase vaginal carcinoma survivability.

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Ethical approval

This study is exempt from ethnical approval.

Registration of research studies

This study was not first in man.

Guarantor

The Guarantor was also the first author.

Disclosure

None.

Informed consent statement

All the patients provided informed consent to be included in the study.

PROCESS guidelines

This paper had been in line with PROCESS guidelines [24].

Provenance and peer review

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CRediT authorship contribution statement

Fara Vitantri: study concept or design.
Chamim: data collection.
Amalia Shadrina: writing paper.

Declaration of competing interest

The authors declared have no conflicts of interest to disclose.

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