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High-Grade Undifferentiated Vaginal Sarcoma: A Case Report and Literature Review

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Abstract **Case Report**

Primary vaginal sarcomas are rare gynecologic tumors of unknown etiology, characterized by aggressive behavior, a high risk of recurrence, and a poor prognosis. Undifferentiated vaginal sarcoma is an exceptionally uncommon subtype, with no prospective trials or standardized guidelines specifically addressing its management. Surgery is considered the mainstay of therapy for localized and recurrent disease. However, for locally advanced tumors or when surgery would result in excessive morbidity, radiotherapy is considered the standard alternative. We report the case of a 19-year-old woman diagnosed with high-grade undifferentiated vaginal sarcoma, who showed no response to six cycles of VAC chemotherapy and was subsequently treated with exclusive 3D conformal radiotherapy to a total dose of 70 Gy with concomitant chemotherapy, achieving significant clinical improvement. This case illustrates the therapeutic challenges of such rare tumors and highlights the need for individualized management and systematic reporting to improve knowledge and outcomes.

Keywords: rare case, Primary vaginal sarcoma, undifferentiated tumor, Surgery, Radiotherapy, Chemotherapy, Prognosis.

INTRODUCTION

Primary vaginal cancer is rare, constituting only 1%–2% of all female genital tract malignancies globally and only 10% of all vaginal malignant neoplasms. [1-3] It is strictly defined as a cancer found in the vagina without clinical or histologic evidence of cervical or vulvar cancer, or a prior history of these cancers, within 5 years [2]. To support this, most suspicious lesions of malignancy in the vagina will correspond to metastatic lesions of cervical or vulvar cancer, or others metastasizing to the vagina [4]. The most common histological type is squamous cell carcinoma (75-90%) followed by adenocarcinomas [5,6] Sarcomas, lymphomas, and melanomas of the vagina are extremely rare [4].

Sarcomas constitute 2 % to 3 of malignant vaginal lesions [7,8], with leiomyosarcomas being the most common type of sarcoma [5,9].

Primary vaginal sarcomas are aggressive neoplasms with different presenting characteristics and increased adjusted risk of mortality as compared to squamous cell and adenocarcinoma subtypes [10] Unfortunately, most of the sarcomas are diagnosed at an advanced stage. Histopathological grade appears to be the most important predictor of outcome.

Due to their extremely low incidence and the absence of prospective studies, there are no standardized guidelines for the optimal management of vaginal sarcomas, making treatment strategies heterogeneous and conclusions regarding best practices difficult to establish. We report here a case of High-Grade Undifferentiated Vaginal Sarcoma, contributing to the sparse literature on this rare entity. This case highlights the importance of documenting and sharing such experiences, as it concerns a patient treated and followed in the Radiation oncology Department of the Oncology and Haematology Hospital, Mohammed VI University Hospital.

CASE PRESENTATION

This is a 19-year-old woman, married, nulligravida, with no significant past medical, surgical, or family history, who presented with a two-month history of metrorrhagia of moderate abundance associated with foul-smelling leucorrhea, evolving in a context of asthenia but without fever. On admission, she was in good general condition (ECOG performance status 1). Gynecological examination had found a friable, budding tumor adherent to the vagina and bleeding on contact, the examination of the lymph nodes showed no palpable adenopathy, in particular no inguinal adenopathy, the rest of the general clinical examination was unremarkable

A pelvic ultrasound revealed a heterogeneous intravaginal mass measuring 6 × 4 cm. Pelvic magnetic resonance imaging (MRI) demonstrated a large tissue mass filling the upper two-thirds of the vaginal lumen, relatively well defined but with irregular contours, measuring 78 × 66 × 80 mm. The lesion appeared hypointense on T1-weighted images, heterogeneously hyperintense on T2, with diffusion restriction and intense heterogeneous enhancement after gadolinium injection. It was attached to the posterior lip of the cervix, without extension into the uterine body or cavity. Minimal perilesional fat infiltration was observed, as well as two small bilateral pelvic lymph nodes, the largest measuring 6.5 mm. A thoraco-abdominopelvic computed tomography (CT) scan performed subsequently confirmed a voluminous endovaginal tumor process measuring 85.5 × 97 × 126.6 mm, in contact with the bladder anteriorly and the cecum posteriorly with loss of the fatty interface, associated with lombo-aortic and interaortocaval lymph nodes (largest 12.5 × 8.5 mm). No distant metastases were identified.

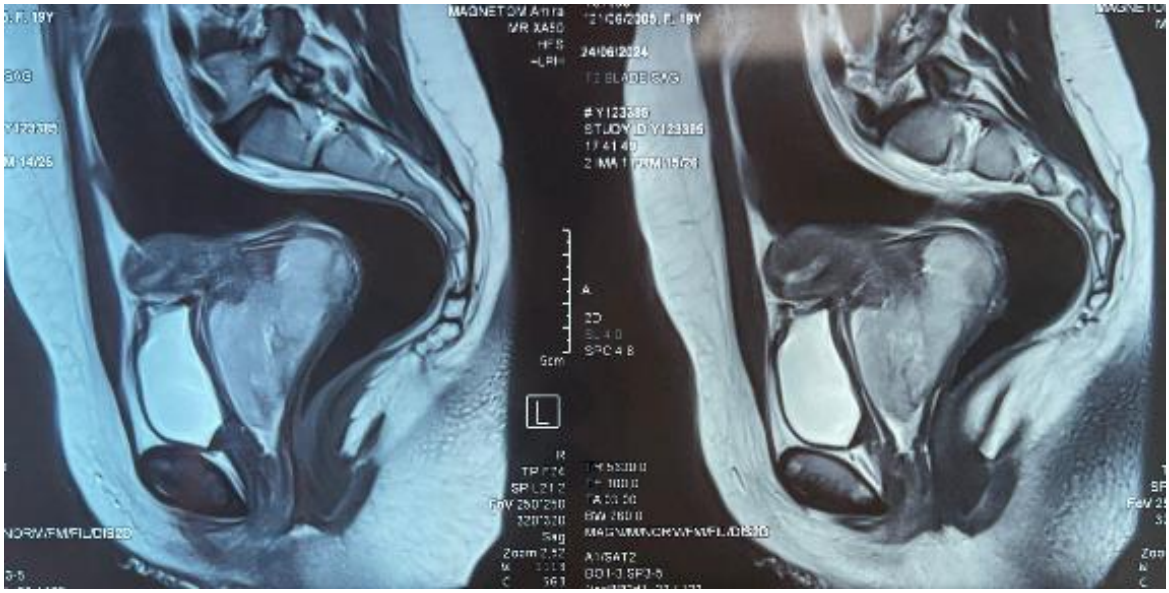

Figure 1 Sagittal pelvic MRI (T2-weighted sequence) showing a bulky compressing adjacent structures with loss of the fat interface with the bladder and rectum

A biopsy was performed, and the histopathological and immunohistochemical findings revealed a highly cellular undifferentiated tumor proliferation arranged in solid sheets, with anisokaryotic, hyperchromatic nuclei, eosinophilic cytoplasm, frequent abnormal mitoses, and tumor necrosis involving approximately 20% of the surface. were in favor of a high-grade undifferentiated vaginal sarcoma (Fig 2,3).

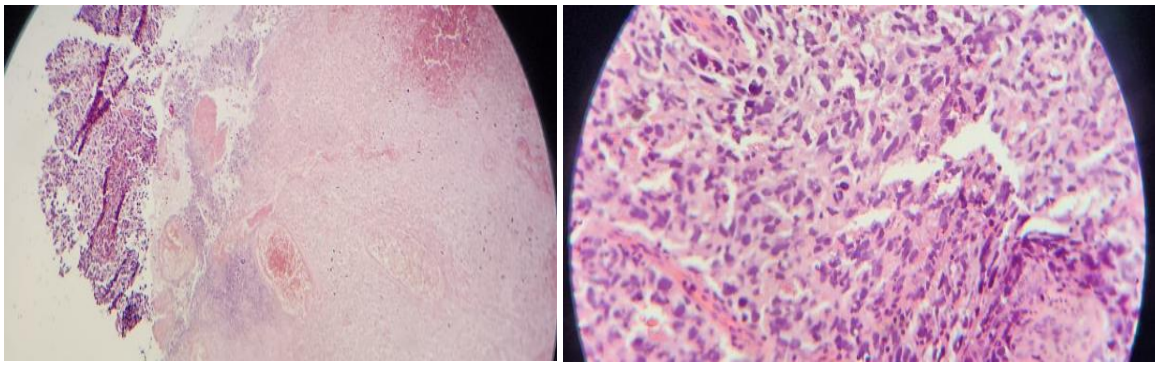

Figure 2: Low magnification demonstrating tumor infiltration with areas of necrosis and hemorrhage

Figure 3 High-power view revealing pleomorphic tumor cells with hyperchromatic nuclei, eosinophilic cytoplasm, marked nuclear atypia, and frequent atypical mitotic figures. Areas of necrosis are also noted, consistent with high-grade morphology.

Immunohistochemical study showed diffuse expression of vimentin and CD10, focal positivity of desmin, CD99 (Fig 4) , estrogen and progesterone receptors, and negativity for myogenin, cytokeratin (AE1/AE3), smooth muscle actin, PS100, CD34, CD45, CD20, CD3, CD117, OCT4, SALL4, TdT, and BCL2 (Fig 5). The proliferative index assessed by Ki-67 was approximately 80%.

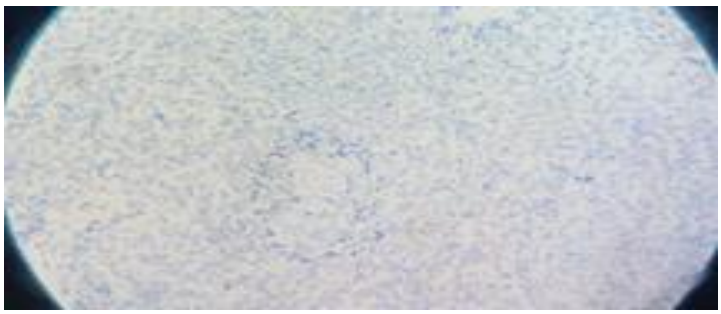

Figure 3: Immunohistochemical staining showing diffuse cytoplasmic positivity for vimentin

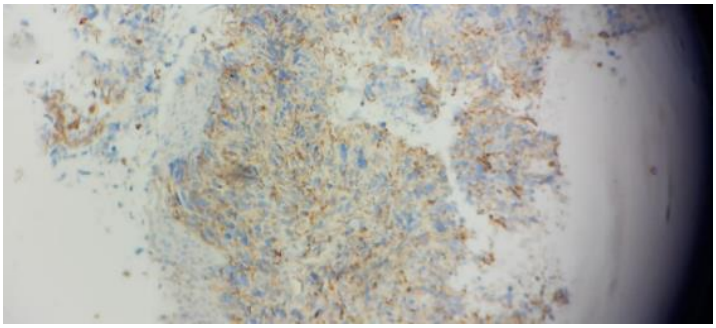

Figure 4: Immunohistochemical staining showing negativity of antibodys

The overall morphologic features and immunophenotypic profile supported the diagnosis of a high-grade undifferentiated vaginal sarcoma, while excluding differential diagnoses such as rhabdomyosarcoma, leiomyosarcoma, synovial sarcoma, lymphoma, germ cell tumors, and melanocytic neoplasms.

The case was discussed at the multidisciplinary consultation meeting, and the decision was to initiate chemotherapy and then reassess the possibility of surgery depending on the evolution. The patient received six cycles of VAC (vincristine, actinomycin D, and cyclophosphamide).

After chemotherapy, the patient spontaneously expelled two necrotic tumor masses (Fig.5). A subsequent MRI showed no evidence of tumor response. The case was again discussed at the multidisciplinary consultation meeting with the gynecology team, and given the lack of radiological response, the decision was to proceed with concomitant radiotherapy and chemotherapy.

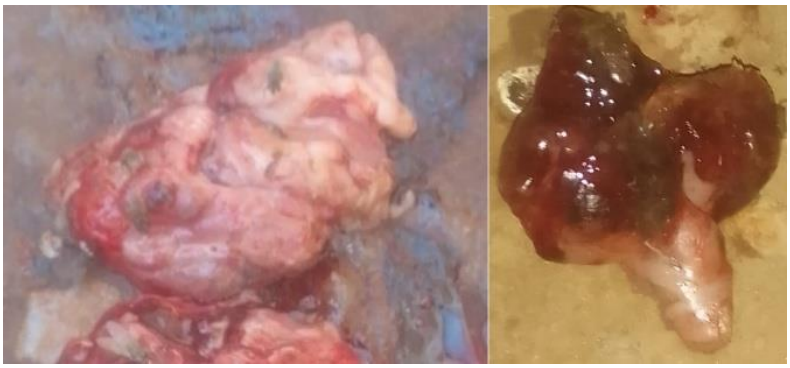

Figure 5: Gross appearance of expelled tumor fragments showing irregular, friable tissue with necrotic and hemorrhagic areas

The patient received a total dose of 70 Gy, delivered with the 3D conformal radiotherapy (3D-CRT) technique, in daily fractions of 2 Gy per session, concomitant with chemotherapy. The treatment was well tolerated and resulted in a significant clinical improvement.

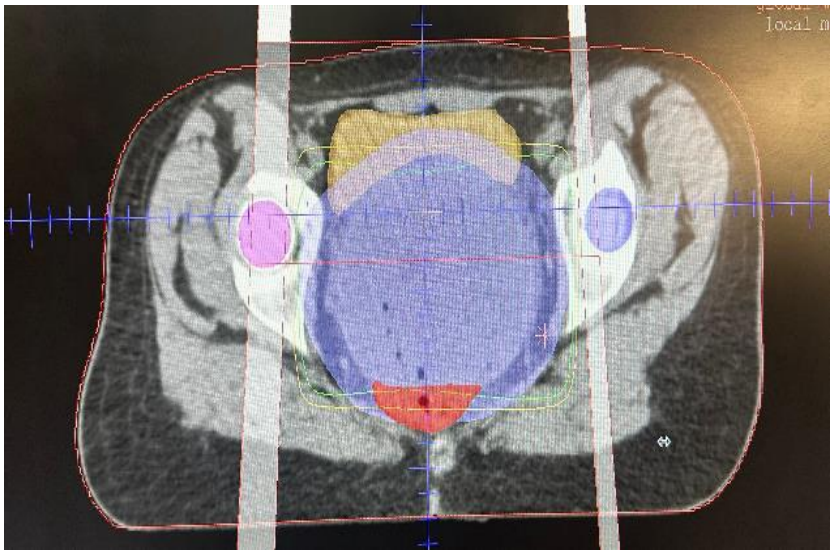

Figure 6: Axial CT slice of radiotherapy planning showing the contoured planning target volume (PTV, blue) and organs at risk: bladder (yellow), rectum (red), and femoral heads (purple). The isodose curves demonstrate appropriate coverage of the tumor

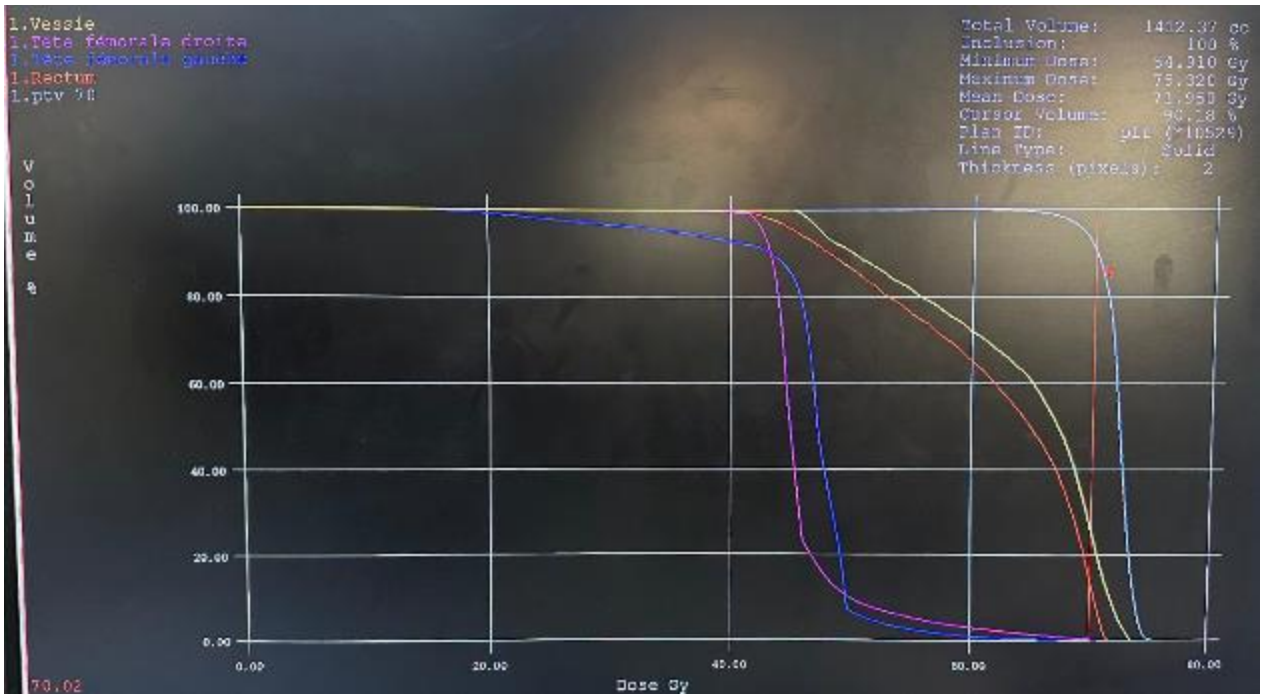

Figure 7: Dose-volume histogram (DVH) of the 3D conformal radiotherapy plan showing adequate coverage of the target volume (PTV 70) with acceptable sparing of organs at risk, including bladder, rectum, and femoral heads

DISCUSSION

Primary malignant lesions of the vagina are uncommon, and vaginal sarcomas are even rarer [5]; fewer cases have been documented in the literature, mostly as isolated case reports or s mall institutional series. The largest series to date include a 15-patient cohort reported by Yuan *et al.,* [11], an earlier 15-case series from Memorial Sloan Kettering by Curtin *et al.,* [12] an 8-case series from China by Wang *et al.,* [13]

Our report adds to the limited literature on primary undifferentiated vaginal sarcoma, which remains one of the rarest histological subtypes of vaginal sarcomas. In the study by Wang *et al.,* conducted at Sun Yat-Sen University Cancer Center, only one case of undifferentiated sarcoma was identified among eight patients with primary vaginal sarcoma over a 15-year period [13] Vaginal sarcoma can occur at any age from pre-birth to post-menopause [12-14].

Patients with vaginal sarcomas are usually younger than those with squamous cell carcinoma or adenocarcinoma. They often have larger tumors, but with less regional extension and lymph node positivity [10] Our 19-year-old patient corresponds to these same features described in the literature.

The mechanism of genesis of soft tissue sarcomas remains unknown, some of the contributing factors are known, and others are suspected. The exact role of any one factor is difficult to determine because of the rarity of sarcomas and the long latency period between exposure to that factor and the occurrence of the tumor.[15] Previous pelvic irradiation and certain genetic syndromes such as neurofibromatosis and Li-Fraumeni are the most clearly recognized risk factors.

Vaginal sarcomas remain asymptomatic for a long time [16]. Indeed, they are generally diagnosed at the stage of a mass (sensation of intravaginal mass), a sensation of pelvic discomfort, and/or genital bleeding frequently after coitus or vaginal douching may also present with dyspareunia, or pain in the perineum or pelvis [4, 8] more rarely at the time of leucorrhoea or urinary signs or even revealing metastases [16,17]

Clinical examination gives important information about the tumor, such as its size, location, extension, lymph node status, and the patient's general condition. However, these findings are not specific, so further investigations are always needed to make the diagnosis. Several studies on vaginal sarcomas have shown that clinical evaluation alone is not enough to clearly identify these rare tumors. Ghezelayagh *et al.,* [10] reported that first clinical signs are often ambiguous. Wang *et al.,* [13] and Curtin *et al.,* [12] also confirmed that diagnosis cannot be based only on physical examination.

Imaging, although not specific for vaginal sarcoma, is crucial for management: it helps confirm diagnostic suspicion, assess operability, guide biopsy, orient therapeutic strategy, monitor treatment response, and ensure follow-up. Still, the definitive diagnosis relies exclusively on histopathology, as no imaging modality can reliably distinguish benign from malignant lesions.

Pelvic ultrasound with Doppler has no specific pattern for sarcomas, but features such as size >3 cm, heterogeneous echotexture, necrotic areas, and intralesional vascularization suggest malignancy [18]. Thoracic and abdominopelvic CT scans are mainly useful for staging and pre-therapeutic assessment, though they are less sensitive for diagnosis [19]. Pelvic MRI is considered the reference imaging modality for vaginal sarcomas, as it best evaluates local extension. Typically, sarcomas appear as large vaginal masses with intermediate to high signal on T2, low signal on T1, and heterogeneous contrast enhancement with necrotic areas, features that strongly support a sarcomatous origin [20]

The diagnosis is made with a targeted biopsy of the lesion, accompanied by a clinical to rule out primary tumors onthe cervix or vulva [4]. In general, sarcomas are a very heterogeneous group histologically, and different types have been described [21] there are various types of vaginal sarcoma. Leiomyosarcoma is the most common histology, comprising approximately two-thirds of vaginal sarcoma cases [12,14,17]

The histological identification of spindle-shaped cells with cigar-shaped nuclei can suggest sarcoma, but this alone is often insufficient. Immunohistochemistry is therefore essential for confirming the diagnosis and plays a central role in classifying vaginal sarcomas through specific antigenic markers [22].

Undifferentiated sarcoma is considered a diagnosis of exclusion among soft tissue sarcomas. Histologically, it is characterized by a highly malignant proliferation with atypical nuclei, brisk mitotic activity, and frequent necrosis, but without any morphologic features allowing assignment to a defined sarcoma subtype. On immunohistochemistry, undifferentiated sarcoma typically expresses vimentin, confirming its mesenchymal origin, while lacking more specific lineage markers such as desmin or myogenin (muscle), S100 (neural), CD34 (vascular), or cytokeratins (epithelial) [23].

Sarcomas are classified into 3 FNCLCC histopronostic grades according to three histological parameters [22] tumor differentiation, mitotic index, proportion of necrosis. Given the rarity of this disease, the therapeutic strategy for vaginal sarcoma is not consensual [13].

The management of patients, especially young ones, is a real challenge given first the rarity of these tumors which also led to the paucity of information regarding the clinical features, secondly, we have the poor prognosis of these tumors and the impact of treatment on sexual function and fertility.

To sum up, due to all the factors mentionned above, there is no standard of treatment in the literature and management should be undertaken by clinicians experienced in these particular malignancies [8] Treatments have traditionally included radiotherapy and/or surgery in selected cases [24].

Surgery is the main treatment for primary vaginal sarcoma, especially for patients with early stage (localized disease) where complete resection with tumor-free margins can be achieved [5,13]

Radical surgery is associated with the best prognosis. although some patients are only diagnosed

with sarcoma after a simple initial excision. Overall. Patients initially treated with surgery show a 5-year survival rate of approximately 57% [9]. However , there is no consensus on the optimal surgical method, but pelvic exenteration remains a therapeutic option in selected cases, particularly in stage III–IV or recurrent disease [9], with an acceptable rate of complications, especially digestive and urinary, and postoperative mortality [25] but ultimately management should continue on a case by-case.

The role of adjuvant radiotherapy and chemotherapy is not clearly defined in vaginal sarcomas, primarily due to the limited number of case reports and series,

In our case, the tumor was unresectable and the patient was treated with exclusive radiotherapy, receiving a total dose of 70 Gy with 3D conformal technique, in daily fractions of 2 Gy. The treatment was well tolerated and resulted in a significant clinical improvement.

Although there are no established guidelines for undifferentiated vaginal sarcoma, therapeutic strategies are often extrapolated from more common vaginal malignancies.

In squamous cell carcinoma of the vagina, Treatments have traditionally included radiotherapy and/or surgery in selected cases [24] Because of the anatomic proximity of the bladder and rectum, however, appropriate surgical margins are difficult to achieve and combinations of external beam radiotherapy (EBT) and brachytherapy (BT) have been the mainstay of treatment [26] previous studies of EBT and BT have reported favorable local control and overall survival for early stage disease, but poor results for advanced stages[14,24,26]

Frank reported 71% pelvic disease control in stage III–IV cases among which 66% were treated with EBT alone (without BT) and attributed this to more complete and homogeneous dose coverage in advanced cases [27]. Intensity modulated radiation therapy (IMRT) may be useful to deliver homogeneous doses to such irregular volumes [27].

External radiotherapy or brachytherapy or a combination of the two are used either as adjuvant therapy or neoadjuvant therapy in locally advanced disease. Adjuvant radiotherapy improves the local control rate without impacting on overall survival [12].

By analogy, this body of evidence supports the use of exclusive radiotherapy in rare histologies such as undifferentiated sarcoma of the vagina, particularly when surgery is not feasible or would result in unacceptable morbidity. Modern advances including IMRT and MRI-guided techniques may further improve tumor coverage and minimize toxicity in this challenging setting.

Given sarcoma's relative rarity, the precise doses of radiotherapy to achieve local control in microscopic and gross residual disease categories are not well known. However, Raney *et al.,* usually propose to use a dose of 55 Gy for microscopic or recurrent disease after surgical removal, and somewhat higher, about 60 Gy, in the presence of visible residual tumour [28].

The literature on chemotherapy in vaginal sarcoma is still poor and its effect is uncertain [12,17,29] but it is often reserved for unresectable locally advanced tumors and metastatic forms with the aim of reducing the tumour volume, thus facilitating surgical resection. Ngan et al. reported that neither chemotherapy nor radiotherapy was particularly useful in late or recurrent disease based on their own limited experience [29]. Hensley recommended chemotherapy for persistent and recurrent disease [30]. Wang *et al.,* announced that the effect of chemotherapy for early stage patients could not be evaluated. Chemotherapy also made little impact in patients with stage IV disease and recurrent disease [13].

Vaginal sarcomas carry a poor prognosis, with lower survival rates, in fact, The 5-year survival of vaginal sarcoma ranges from 35% to 70% [12], and a high risk of both local and metastatic relapse[31]. The patients with isolated recurrences may benefit from cytoreductive surgery with complete resection. Same as uterine sarcomas, resection of pulmonary metastases can also improve survival and maintain quality of life in selected cases [32].

The unfavourable prognostic factors, described in several studies, include a tumour size more than 5 cm, tumour localization in a non-extremity site, primary treatment outside a referral centre, a patient age of more than 25 years, the presence of tumour necrosis areas and bone invasion and the presence of a particular SYT-SSX translocation (SYTSSX1) [33]. However, the strongest prognostic factor associated with local recurrence, metastases and tumour-related death in a multivariate analysis is the presence and the amount of poorly differentiated areas within the tumour.

Our case highlights several limitations. First, the extreme rarity of vaginal sarcoma makes it difficult to draw firm conclusions or establish standardized treatment strategies. Second, there is no consensus regarding optimal management, and therapeutic decisions remain heterogeneous. While surgery is generally regarded as the cornerstone of treatment for vaginal sarcoma, our patient did not benefit from this approach: despite neoadjuvant chemotherapy, the tumor remained unresectable due to its extent and unfavorable localization, obliging us to proceed directly with definitive radiotherapy. Finally, surgical procedures for vaginal sarcomas are technically challenging and further complicate interpretation. These considerations

underscore the need for cautious analysis of individual cases and highlight the importance of larger prospective studies to validate treatment approaches.

CONCLUSION

Primary vaginal sarcomas are aggressive neoplasms with diverse clinical presentations. Among them, undifferentiated sarcoma represents an exceptionally rare and highly aggressive subtype, with no standardized therapeutic guidelines available. Surgery remains the mainstay of treatment when feasible, but in locally advanced unresectable cases or when surgery would be excessively mutilating, exclusive radiotherapy can serve as an effective alternative. Prognosis is generally poor due to high recurrence rates, Treatment options should be individualized and tailored to each patient's condition, and systematic reporting of such rare cases is essential to improve understanding and guide future therapeutic strategies.

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