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Neoadjuvant chemotherapy in uterine carcinosarcoma: A case report of a complete remission of the epithelial component and successful surgical management

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Abstract
Introduction and importance: Uterine carcinosarcomas are rare tumors that account for less than 5% of all uterine malignancies. Surgery remains the mainstay of treatment for early-stage disease, and there is no consensus on a standard regimen of chemotherapy.
Case presentation: We report the case of a 22-year-old woman who presented with vaginal bleeding. An initial excision revealed a benign lesion. Nine months later, she presented with the same symptoms. Examination under general anesthesia revealed a friable mass filling the vaginal cavity, originating from the cervix, while the vaginal walls and parametrium were intact. Pelvic MRI showed a solid-cystic mass in the uterine cavity. Histopathology confirmed a sarcomatous component with rhabdomyoblastic differentiation. A multidisciplinary team recommended neoadjuvant chemotherapy, resulting in tumor shrinkage from 100 mm to 25 × 48 mm. The patient subsequently underwent an interadnexal hysterectomy, pelvic dissection, lombo-aortic lymph node sampling, and ovarian transposition. The postoperative course was uneventful. She received adjuvant chemotherapy, followed by concomitant chemoradiotherapy. Follow-up was conducted quarterly, and as of her last clinical and radiological assessment in March 2025, there was no evidence of recurrence.
Clinical discussion: Uterine carcinosarcomas are aggressive tumors with both carcinomatous and sarcomatous components. MRI is essential for diagnosis and staging. Neoadjuvant chemotherapy may reduce tumor burden, but sarcomatous elements often show limited response.
Conclusion: Chemotherapy can contribute to tumor control but may be less effective on the sarcomatous component.

Keywords: Carcinosarcoma, rhabdomyosarcoma, neoadjuvant, chemotherapy, uterine

Introduction
Uterine carcinosarcomas, or malignant mixed Müllerian tumors, constitute a minority (less than 5%) of cancers of the uterus but are notorious for their adverse clinical prognosis [1].
They are composed of two distinct components; carcinomatous (epithelial) and sarcomatous (mesenchymal); which create a complex therapeutic challenge. While operative resection is still the mainstay of treatment for early-stage disease, the adjuvant and neoadjuvant chemotherapy role is undefined, and optimal regimens remain a matter of debate [2].
Literature shows that while certain chemotherapeutic agents (typically platinum-based or anthracycline regimens) may be effective in producing a response, particularly in the epithelial component, the sarcomatous component may be less responsive [3, 4].
This differential response has significant implications for treatment plannig and prognosis. In this report, we describe the case of a young woman with cervical carcinosarcoma who experienced resolution of the epithelial component after neoadjuvant chemotherapy.

Case Report
A 22-year-old Caucasian female patient, single, with no significant family history. She has a history of hypothyroidism. The patient reports no sexual activity. Regarding lifestyle habits, she denies any use of alcohol, tobacco, or recreational drugs.
The patient first presented to the emergency department with vaginal bleeding. The clinical examination revealed a polyp protruding through the cervix. Histopathological study was benign, revealing an endometrial polyp composed of endometrial mucosa centered around a

fibrovascular core, containing dilated glands lined by a regular pseudostratified epithelium.

Nine months later, the patient reconsulted with the same symptoms and examination revealed tumor debris in the vagina. An examination under general anesthesia was therefore necessary.

On examination under general anesthesia, a friable crumb-like mass was detected in the vaginal cavity that originated from the cervix and the rest of the examination revealed that the parameters were supple and that the vagina was free of abnormalities. A follow-up pelvic MRI was then conducted, which identified a solid-cystic mass in the uterine cavity that was almost entirely solid in nature and measured approximately 10 × 9.5 × 13.5 cm.

The mass appeared to originate from the cervix and extended to the level of the inferior third of the vagina. While there was considerable mass effect on nearby structures, specifically the sigmoid colon and bladder, there were no imaging indications of direct invasion and the myometrial tissue had a normal signal pattern.

The tumor showed intermediate T2 signal intensity and diffusion restriction.

The MRI showed also a left external iliac lymphadenopathy measuring 38*26mm, rightexternal iliac one measuring 17*10mm and right primitive iliac one measuring 20*13mm (Figure 1).

A PET-scan revealed an hypermetabolism in the cervix associated with a second focus in the uterine fundus (Figure 2).

A targeted biopsy of the tumor was performed. Pathologically, there was a sarcomatous element with rhabdomyoblastic differentiation (Figure 3).

Differential diagnoses included botryoid rhabdomyosarcoma or the mesenchymal component of a mixed Müllerian neoplasm (adenosarcoma or carcinosarcoma). It should be emphasized, however, that no malignant epithelial element could be detected despite the existence of foci of chondroid metaplasia.

An immunohistochemistry study was performed to identify the lesion more definitively. Desmin was focally positive in the tumor cells, which was consistent with muscle differentiation (Figure 4).

Myogenin, MyoD, cytokeratin (CK), estrogen receptor (ER), progesterone receptor (PR), and other markers stain negatively, which is compatible with a diagnosis of a predominantly sarcomatous process.

The patient presented with a multidisciplinary tumor board, and neoadjuvant chemotherapy has been decided upon, taking into account the advanced local presentation and the necessity of reducing the tumor burden prior to surgical resection. Two cycles of ifosfamide with doxorubicin were administered to the patient, and the treatment course concluded on 17 August 2022.

One month following the end of chemotherapy a pelvic MRI was performed revealing a partial response. The overall tumor size decreased significantly-from the initial maximal diameter of 100 mm to a dimension of approximately 25 × 48 mm.

The tumor showed intermediate T2 signal intensity, hypointense on T1, and no diffusion restriction.

An impressive increase in pelvic lymphadenopathy size was also observed, with the largest node measuring 44 × 34 mm.

Because the response to chemotherapy was unclear, the remedy was to proceed with surgery.

The patient underwent an inter-adnexal hysterectomy and extensive pelvic dissection, lombo-aortic node sampling, and ovarian transposition for the preservation of endocrine function (figure 3).

The surgical procedure was performed under general anesthesia via laparotomy. The procedure took two hours and proceeded without any complications. Intraoperatively, a lomboaortic Redon drain and two pelvic Redon drains were placed; these drains were removed on day 5 after surgery.

The patient was hospitalized for 6 days after surgery and then discharged.

The histopathological examination of the definitive surgical specimen showed a cervix involved by residual tumor with a sarcomatous component, likely consistent with a carcinosarcoma. Surgical margins were free of tumor, and no intravascular tumor emboli were observed.

Pelvic lymphadenectomy revealed one positive lymph node, while the lomboaortic lymphadenectomy showed negative lymph nodes.

Our multidisciplinary team decided to administer adjuvant chemotherapy consisting of 4 cycles of Adriamycin (doxorubicin) and cisplatin, followed by concomitant chemoradiotherapy based on cisplatin.

She received pelvic and pelvic nodal irradiation with a total dose of 50.8 Gy.

The treatment was completed in September 2023.

A pelvic MRI performed in November 2023 showed no locoregional recurrence. Subsequently, she was followed up quarterly without evidence of recurrence.

Her last consultation was in March 2025, with a normal clinical examination and pelvic MRI showing no signs of recurrence.

Discussion

Uterine carcinosarcomas, or malignant mixed Müllerian tumors (MMMTs), are rare, aggressive biphasic tumors with both carcinomatous and sarcomatous components [5].

Imaging, primarily magnetic resonance imaging (MRI), plays an initial role in assessing and treating uterine carcinosarcomas. MRI is preferable since it results in extremely high soft tissue contrast and multiplanar capabilities that are exceptional and serve to accurately depict the morphology as well as the extent of the tumor. In our case, pelvic MRI demonstrated a huge, heterogeneous solid-cystic mass of 10 × 9.5 × 13.5 cm in size that originated from the cervix and extended into the lower third of the vagina. Interestingly, the study demonstrated a mass effect on adjacent structures such as the sigmoid colon and bladder, without direct invasion, and with normal myometrial signal intensity.

These imaging features are consistent with those described in the literature in which uterine carcinosarcomas are seen as tumors that are prone to heterogeneous signal intensities due to necrosis, hemorrhage, and admixed tissue components [6].

Additionally, MRI was very useful for initial staging and 89 surgical planning, particularly for delineating the extent of the tumor and assessing local invasion. The subsequent appearance of pelvic lymphadenopathy and its increase in size following chemotherapy illustrated the value of MRI in evaluating the response to treatment and in detecting residual or progressing disease [7].

Since they are rare, no treatment modality has been proven

definitively optimal and management is most frequently extrapolated from experience with high-grade endometrial cancers and soft tissue sarcomas.

Surgery remains the cornerstone of treatment for early stage disease. However, multimodal therapy radiotherapy and systemic chemotherapy is often employed in advanced or recurrent cases [8].

In particular, neoadjuvant chemotherapy has been investigated as a means of reducing tumors before surgery. Regimens with drugs such as doxorubicin and ifosfamide have been used with the goal of achieving tumor reduction and enabling complete surgical resection [9].

One of the hindrances in the treatment of uterine carcinosarcomas is the differential chemosensitivity between sarcomatous and epithelial components of the tumor. Many studies have shown that the epithelial component is more sensitive to conventional chemotherapy, whereas the sarcomatous component is generally resistant [10].

This is what occurred in our case: after a considerable reduction in the sum of the tumor size following neoadjuvant chemotherapy, residual and even growing pelvic lymphadenopathy was detected by imaging, reflecting a poor response in the sarcomatous compartment.

The comparative paucity of effects of chemotherapy on the sarcomatous component is a recurring theme in the literature. Gershenson (2008) noted that the poor chemosensitivity of the sarcomatous component is most likely one of the contributing factors to the overall dismal prognosis of MMMTs. Similarly, McCluggage (2002) noted the inherent aggressiveness of these tumors due to their biphasic histology and advocated more research into more effective, targeted treatments.

Our case highlights the importance of individualized, multidisciplinary treatment for uterine carcinosarcomas, addressing their heterogeneous nature. Combining new targeted drugs with established chemotherapy may improve outcomes, especially against the resistant sarcomatous component. While neoadjuvant chemotherapy can reduce the epithelial part, sarcomatous resistance remains a challenge. Large studies are needed to define standardized protocols. The patient's recurrence-free survival after treatment shows the potential success of multimodal approaches and ongoing research into more effective therapies is crucial for this complex malignancy.

Conclusion

This case report emphasized that while neoadjuvant chemotherapy is able to decrease the tumor load of the epithelial component of cervical carcinosarcoma optimally, it may have a suboptimal impact on the sarcomatous component. Therefore, radical resection remains the cornerstone of treatment for these tumors. An individualized multimodal treatment modality with newer targeted agents is necessary to further improve the prognosis of patients suffering from this malignant condition.

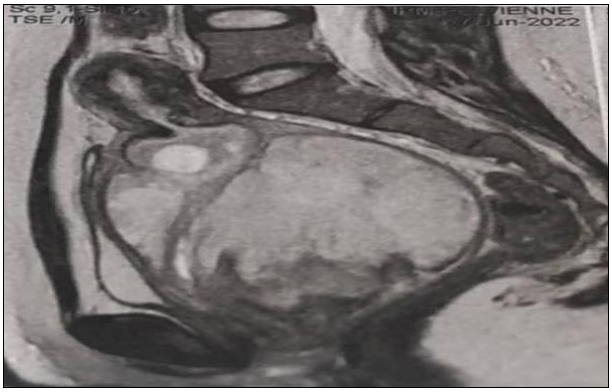


Fig 1: MRI showing a solid-cystic mass in the uterine cavity

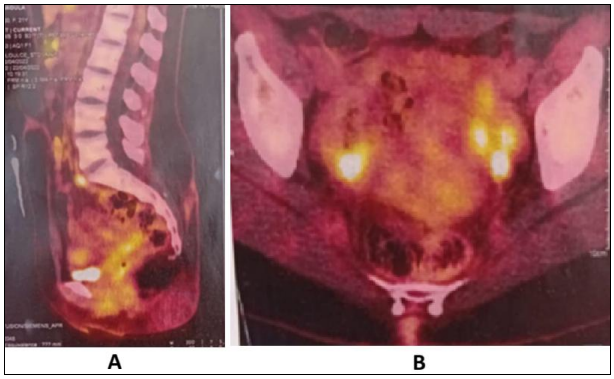
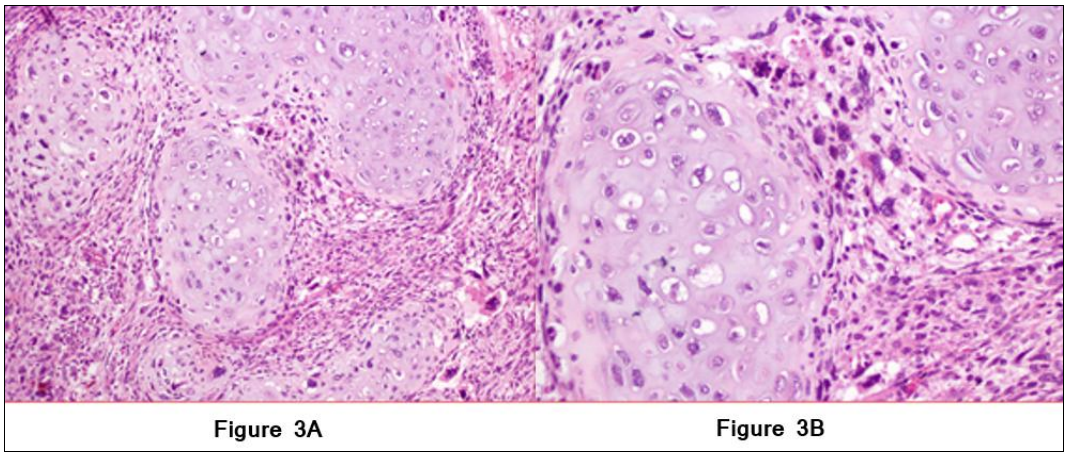


Fig 2: PET-scan showing hypermetabolism located in the cervix associated with a second focus in the uterine fundus; A: Axial slice B: sagittal slice



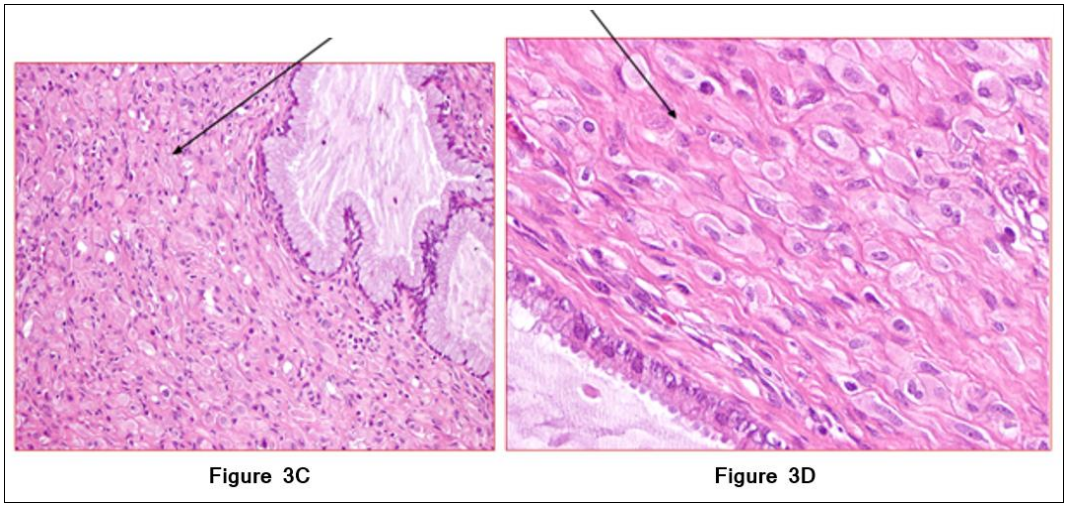


Fig 3: Microscopic histological study of a sarcomatous element with rhabdomyoblastic differentiation. A, B: mesenchymal heterologous components represented by chondrosarcomatous components. C, D: Rhabdomyosarcomatous components, the arrows showing numerous well differentiated rhabdomyoblasts with eosinophilic, focally striated cytoplasm

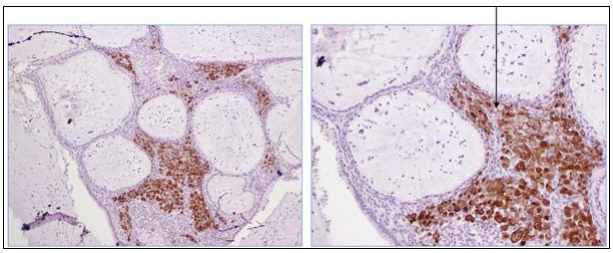


Fig 4: Desmin focal positivilty by immunochemistry study

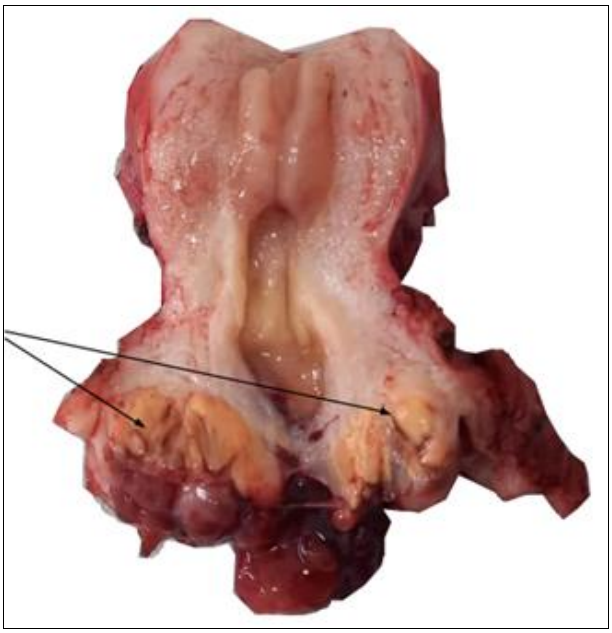


Fig 5: Sectioned Hysterectomy specimen, the arrow showing the tumor limited to the cervix which was entirely

Abbreviations

- **CK:** Cytokeratin
- **ER:** Estrogen receptor
- **PR:** Progesterone receptor
- **MRI:** Magnetic resonance imaging
- **MMMTs:** Malignant mixed Müllerian tumors

Acknowledgments

Not applicable.

Conflict of Interest

Not available.

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Not available.

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