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Carcinosarcoma of the uterus and its monoclonal behavior – a case report with review of literature from rural India

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ABSTRACT

Introduction and aim. Carcinosarcoma of the uterus is a rare and aggressive monoclonal tumor composed of both epithelial and mesenchymal components. It is associated with poor prognosis and shows a marked tendency for early metastasis and recurrence, posing a significant challenge in gynecological oncology. This study aimed to identify the precise clinicopathological features of uterine carcinosarcoma that may facilitate accurate diagnosis and, ultimately, timely patient management.

Description of the case. A 53-year-old nulliparous woman presented with vaginal bleeding and an abdominal mass. Clinically, the case was initially diagnosed as leiomyoma uteri. The patient underwent hysterectomy, and the specimen was submitted for histopathological examination. Histopathology suggested a malignant mixed Müllerian tumor (homologous type). Immunohistochemistry was performed to confirm the diagnosis and to exclude differentials such as endometrial carcinoma. The tumor was positive for cytokeratin, vimentin, cyclin D1, and CD10, while negative for p53 in both components. The coexistence of epithelial and mesenchymal elements of common embryonic origin, together with the absence of p53 expression, confirmed the monoclonal nature of the tumor.

Conclusion. Accurate diagnosis of uterine carcinosarcoma requires the combined use of clinical evaluation, histopathology, and immunohistochemistry, which are essential for guiding optimal therapeutic interventions and determining prognosis.

Keywords. carcinosarcoma, corpus uterus, hysterectomy, immunohistochemistry, mixed Mullerian tumor

Introduction

Malignant mixed Müllerian tumor is also defined as carcinosarcoma, which means a tumor with a combination of both carcinoma and sarcoma simultaneously. It is an extremely uncommon malignant tumor of the uterine corpus, leading to scanty contribution to gynecological malignancies.¹ The frequent mutations

are TP53, PTEN, PIK3CA, PPP2RIA, FBXW7, and KRAS. Regarding the origin of carcinosarcoma, the primitive Müllerian duct develops from the mesenchyme of the urogenital ridge and the lining of the coelomic epithelium. These ducts undergo differentiation into the body of the uterus, fallopian tubes, and cervix. This analogy gives rise to myometrial smooth muscle, endometrial stroma, and endometrial glands. So, the mixed Müllerian tumor consists of both elements.² These tumors are common in the uterus because epithelial and mesenchymal components both arise from the common embryonic origin.³ It is commonly seen in women of the postmenopausal age group but has also been reported in younger women.⁴ This tumor has bilateral components. On the basis of components, it is bifurcated into two subtypes and is called homologous when sarcomatous components are composed of fibrous or smooth muscle tissue, such as fibrosarcoma, endometrial stromal tumors, or leiomyosarcomas. Similarly, it is named heterologous when the sarcomatous components are composed of cartilage, skeletal muscle, and bone, therefore rhabdomyosarcoma, chondrosarcoma, osteosarcoma, and liposarcoma.¹ In both types, the carcinomatous component is mainly composed of endometrioid, serous, or clear cell type adenocarcinoma.

Aim

The aim of this study was to identify the diagnostic significance of histopathology and immunohistochemistry in uterine carcinosarcoma with homologous elements.

Description of the case

A 53-year-old nulliparous postmenopausal woman presented with abdominal pain, bleeding per vaginam, and an abdominal mass. There was no history of tamoxifen use or pelvic radiation therapy.

Ultrasonography revealed an intramural tumor mass that did not extend beyond the uterus. Clinically and radiologically, it was diagnosed as a fibroid uterus. Therefore, a hysterectomy with bilateral salpingo-oophorectomy was performed, and the surgically resected specimen was sent in 10% formal saline to the Department of Pathology for histopathological examination. The uterus with bilateral adnexa measured 7×9×10 cm grossly (Fig. 1).



Fig. 1. Gross section of hysterectomy specimen showing endometrium and myometrium, the endometrium and myometrium were replaced by tumor mass, the tumor was grey/white in color, fragile with hemorrhagic and necrotic areas

After macroscopic examination, the specimen was sectioned, processed, and embedded in paraffin. Subsequently, 4 μ m sections were prepared and stained with hematoxylin and eosin (H&E).

On histopathological examination, the endometrium and myometrium were replaced by glandular components showing marked atypical features. This was accompanied by a cellular stroma exhibiting pronounced pleomorphism and frequent mitoses. These findings were suggestive of a malignant mixed Müllerian tumor (homologous type). The cervix, ovaries, and fallopian tubes were free of invasion.

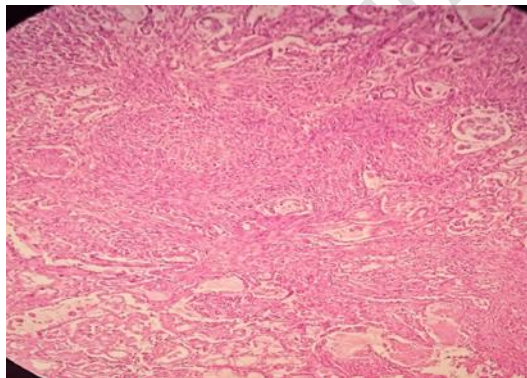


Fig. 2. H&E stained section of carcinosarcoma showing both epithelial and mesenchymal components (200x)

Immunohistochemistry was performed to confirm the diagnosis, to determine the nature of the tumor, and to exclude differential diagnoses. The procedure included tissue preparation, deparaffinization with

rehydration, antigen retrieval, blocking, antibody incubation, detection, counterstaining, mounting, and visualization. The antibodies applied were cyclin D1, cytokeratin, vimentin, CD10, and p53. Cytokeratin (Fig. 3), vimentin (Fig. 4), and cyclin D1 (Fig. 5) were strongly positive, whereas CD10 was weakly positive (Fig. 6) and p53 was negative in both components (Fig. 7).

Endometrial carcinomas usually show positive immunoexpression for cytokeratin AE1/AE3, cyclin D1, and p53, while being negative for vimentin and often negative for CD10.

Based on histomorphology and immunohistochemistry, the diagnosis of carcinosarcoma of the uterine corpus (homologous variant) was established.

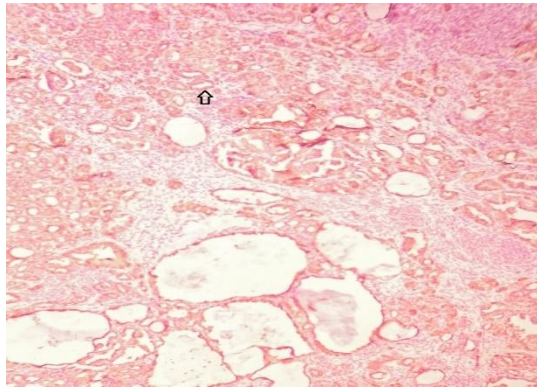


Fig. 3. Strong immunopositivity of cytokeratin AE1/AE3 in the epithelial component of carcinosarcoma (200×)

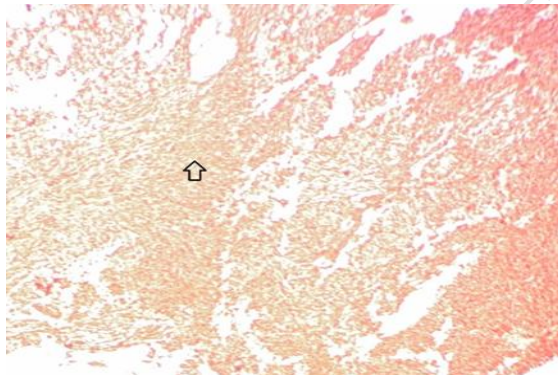


Fig. 4. Strong immunopositivity of vimentin in the sarcomatous component of carcinosarcoma (200×)

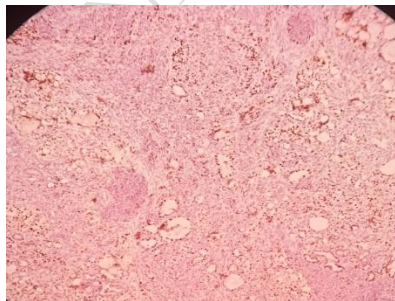


Fig. 5. Section of carcinosarcoma (100×) showing cyclin D1 positivity in epithelial components

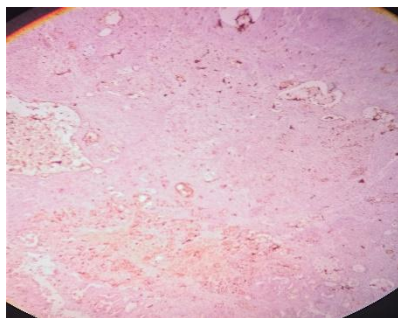


Fig. 6. Section of carcinosarcoma showing CD10 focal positivity in mesenchymal components (100×)

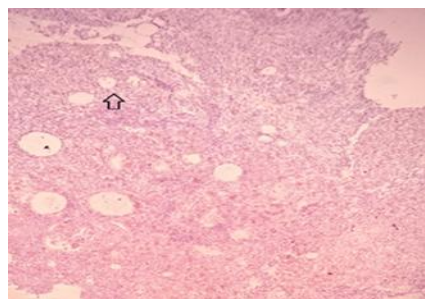


Fig. 7. Section of carcinosarcoma showing p53 immunonegativity in both components (100×)

Discussion

Mixed Müllerian tumors are classified by the WHO as carcinosarcomas, consisting of both carcinomatous and sarcomatous components. The first case was reported by Gerhardt in 1989 and later confirmed by Meyer.⁵ The majority of patients diagnosed with carcinosarcoma are in the 5th decade of life. In the present study, the patient was a 53-year-old nulliparous woman.

The locations of mixed Müllerian tumors include the uterine corpus, other parts of the uterus, and extragenital sites. The most common site is the uterine body (corpus uteri), which was also the case in this study. Clinical symptoms include pain, bleeding per vaginam, and the passage of necrotic debris or material.⁶ In this case, the patient presented with pain, abdominal mass/growth, and postmenopausal bleeding. There was no history of tamoxifen use or pelvic radiation therapy.

Regarding histogenesis, four theories have been proposed:

- A) Collision theory – both elements originate separately and later collide.
- B) Combination theory – both components arise from the same stem cell, which later undergoes divergent differentiation.
- C) Composition theory – the spindle cell element represents a pseudosarcomatous reaction to carcinoma.
- D) Conversion theory – the sarcomatous elements develop from the carcinomatous elements via a metaplastic process.⁷

On gross examination, the tumor may present as a polypoid, fleshy, bulky, and fragile growth, with necrosis and hemorrhage being common findings. In the present case, similar features were observed (Fig. 1).

Mixed Müllerian tumors are classified into two subtypes: homologous and heterologous.⁸ The tumor is considered homologous when the sarcomatous component consists of nonspecific malignant stroma, while it is termed heterologous if the sarcomatous component contains tissues not native to the uterus, such as cartilage. The most frequent glandular component is adenocarcinoma, while the most common mesodermal component is undifferentiated sarcoma in homologous tumors and rhabdomyosarcoma in heterologous tumors.⁹ The present case was diagnosed as a homologous carcinosarcoma of the uterine corpus. Immunohistochemical markers cytokeratin AE1/AE3, vimentin, CD10, cyclin D1, and p53 were applied to confirm the diagnosis.

Ahmed reported that cytokeratin, cyclin D1, and CD10 are significant immunomarkers in determining carcinosarcoma.⁹ Cyclin D1, a member of the cyclin family of cell cycle regulators, is involved in tumorigenesis when mutated, and its immunohistochemical expression is useful for prognostic evaluation.^{9,10} Vimentin is a cytoplasmic intermediate filament characteristic of cells of mesenchymal origin.¹¹ CD10 is an antibody that identifies neprilysin, useful in the diagnosis of female genital tract tumors, particularly endometrial stromal neoplasms.^{9,11-13}

Mutation in the p53 tumor suppressor gene represents a common genetic alteration in human tumors. The altered mutant protein has a much longer half-life and can be detected by immunohistochemistry.^{11,12,14}

Among the immunomarkers applied, AE1/AE3 cytokeratin, vimentin, and cyclin D1 were strongly positive, whereas CD10 was weakly positive. p53 was analyzed and found to be negative in both components. Several studies have shown homogeneous p53 staining in both components of uterine sarcomas. p53 immunostaining usually yields similar results in both components – it may be positive or negative in both – which supports the hypothesis of a common origin of the two components (Tab. 1).^{11,12,14}

Table 1. Comparison of immunohistochemical characteristics of carcinosarcoma reported by different researchers

S no.	Authors	Epithelial elements	Sarcoma elements	Cytokeratin	p53	Vimentin	CD10	Cyclin D1
1	Adachi Y et al. ¹¹	serous adenocarcinoma	homologous	positive (epith)	positive (both)	positive (sarcoma)	positive (sarcoma)	-
2	Al Dallal HA et al. ¹²	endometroid ca	heterologous	positive (epith)	positive (both)	-	negative (both)	
3	Dragusin A et al. ¹³	endometroid ca	homologous	positive (epith)		positive (sarcoma)	positive	positive

4	Kord A et al. ¹⁴	endometroid ca	homologous	positive (epith)	positive (both)	positive (sarcoma)		-
5	Current study	endometroid ca with serous ca	homologous	positive (epith)	negative (both)	positive (sarcoma)	positive (sarcoma)	positive (epith)

Carcinosarcoma is a rare malignant neoplasm. If a postmenopausal woman presents with bleeding per vaginam, the possibility of malignant mixed Müllerian tumor should be considered. Histopathology together with immunohistochemistry is essential to establish the correct diagnosis, which is also crucial for optimal therapeutic interventions and prognosis. Our findings further support the most widely accepted histogenesis theory, which suggests that carcinosarcoma originates through transdifferentiation of uterine carcinoma into sarcoma.

Conclusion

Carcinosarcoma of the uterus is a rare and aggressive neoplasm that primarily affects postmenopausal women. Early diagnosis is pivotal for effective management. Histopathological examination combined with immunohistochemistry is essential to exclude differential diagnoses and to confirm the tumor variant; therefore, these investigations should be performed in every case of carcinosarcoma.

Declarations

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Author contributions

Conceptualization, S.D.; Methodology, S.D.; Software, S.D.; Validation, S.D.; Formal Analysis, S.D.; Investigation, S.D.; Resources, S.D.; Data Curation, S.D.; Writing – Original Draft Preparation, S.D.; Writing – Review & Editing, S.D.; Visualization, S.D.; Supervision, S.D.; Project Administration, S.D.; Funding Acquisition, S.D.

Conflicts of interest

The author have no conflict of interest to declare.

Data availability

The data that support the findings of this study are available from the author.

Ethics approval

Not required for a case report but ethical clearance on histopathology evaluation of hysterectomies specimens was already taken (reference no.30/UPUMS/Dean/ 2017-18).

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