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Case Report

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# SARCOMATOID SQUAMOUS CELL CARCINOMA OF UTERINE CERVIX: A CASE REPORT AND REVIEW OF THE LITERATURE

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## ABSTRACT

Sarcomatoid squamous cell carcinoma of uterine cervix represent a rare entity, few cases were reported in the literature till date. We report a case of a 61-year-old lady with FIGO III sarcomatoid carcinoma of uterine cervix referred to our oncology hospital. The patient was treated with concurrent chemo-radiotherapy and is disease free at 3 months follow-up. The literature is reviewed and the management is discussed in this paper.

**KEYWORDS:** Sarcomatoid carcinoma, Cervix, Radiation therapy.

## INTRODUCTION

Sarcomatoid squamous cell carcinoma (SSCC) of the uterine cervix, also known as spindle cell carcinoma of the uterine cervix is a rare malignancy with aggressive clinical behavior.[1] It differs from squamous cell carcinomas of the cervix in terms of having a poorer prognosis.[2] The tumor is usually diagnosed at an advanced stage at presentation and characterized by early recurrence following treatment.[1] SSCC is a rare variant of infiltrating squamous cell carcinoma. The diagnosis is generally based on histological, immunohistochemical and ultrastructural charteristics.[1] About 20 cases have been reported in the literature.[1,3] Because of the rarity of the disease, no standard diagnosis and treatment approach are available.[4] it is usually managed like squamous carcinoma of the cervix.

## CASE

A 61-year-old postmenopausal lady presented in our oncology hospital, with 1 year history of abnormal vaginal bleeding and foul smelling discharge, she also complained of pain in the lower abdomen. The patient did not have a history of previous irradiation. On pelvic examination, she was found to have a large ulceroproliferative growth replacing the cervix, and infiltrating vaginal posterior wall extending down to the lower third of the vagina, with no evidence of parametria involvement. An incisional biopsy was performed, histopathological examination revealed a tumour composed of poorly differentiated squamous cell carcinoma blended imperceptibly with spindled cells, these tumour cells had moderate nuclear pleomorphism with vesicular eosinophilic cytoplasm (fig 1: a,b). There were frequent mitoses (12 per 10 high-power fields) and focal tumor necrosis. There was no evidence of any glandular differentiation. A diagnosis of malignant tumour suggestive of sarcomatoid squamous cell carcinoma was suggested. No microbiological testing for HPV was done.

Immunophenotyping revealed strong positive staining for pan-cytokeratin AE1/AE3 on both the epithelial and the spindle cell components (fig 1: c), focally positive staining for CK5/6. Some cells were positive for p63 and desmine (fig 1: d), but negative for S-100 and CD34. Based on histopathologic findings and immunoprofile, the diagnosis of poorly differentiated squamous cell carcinoma, with sarcomatoid differentiation was approved.

MRI of the pelvis revealed a large heterogeneous mass of the cervix attached to vaginal wall (45x48, 8x53, 6mm) (fig 2,3) extending inferiorly to involve the totality of the vagina (fig 2) with no significant regional lymph nodes. Chest CT scan and bone scan were negative.

The patient was clinically identified as having International Federation of Gynecology and Obstetrics (FIGO) stage IIIA disease. She received radiotherapy, which consisted of an external-beam radiation therapy to the whole pelvis (including gross tumor volume (GTV), cervix, entire uterus, external, internal iliac and presacral lymph nodes), with a dose of 46 Gy in 23 fractions over 6 weeks and weekly cisplatin chemotherapy of 40 mg/m$^2$. The MRI and clinical examination one week

after the end of chemoradiation showed a residual mass of the vagina (32×25) extending down beyond the middle third vagina. patient juged not suitable for brachytherapie. An additional dose was delivred by external beam-therapy to the residual mass up to 66 GY in 10 fractions concurent with weekly cisplatin chemotherapy. The patient is disease free at 3 months follow-up on clinical examination.

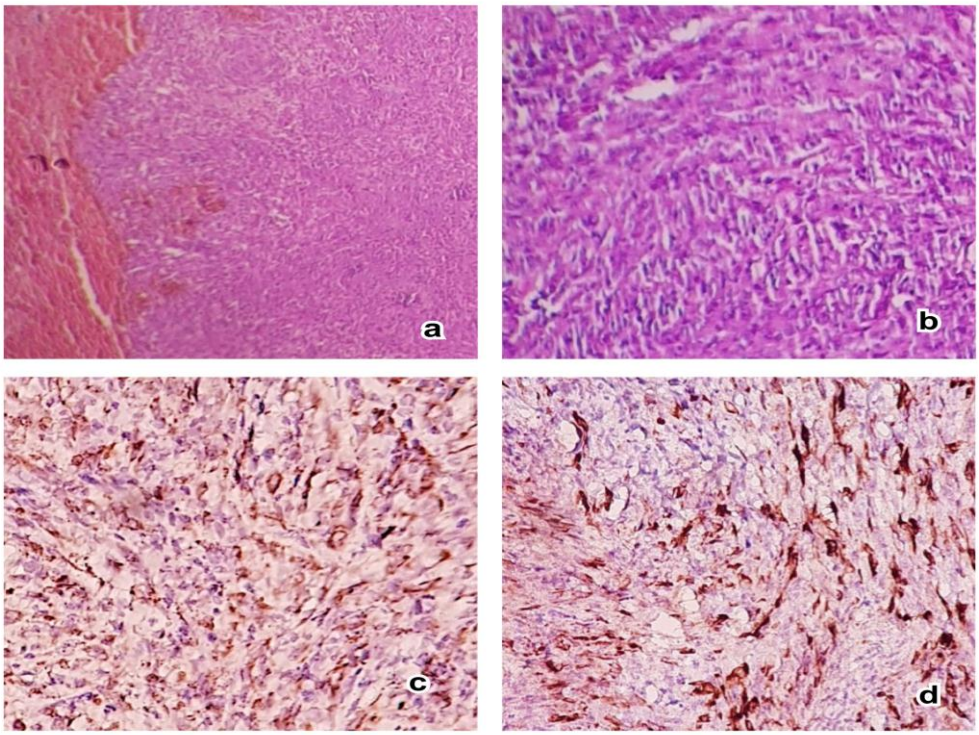


**Figure 1: Histological findings of the tumor. a) The tumor consists of squamous cell carcinoma with spindle cell component (H&E, 4 x10). b) The sarcomatous element shows spindle cell sarcoma with hypercellularity and nuclear atypia. (H&E, 40x10). c) Membranous staining of both epithelial and spindle cell components with cytokeratin marker (AE1/AE3) (40x10). d) cytoplasmique desmine staining (40x10).**

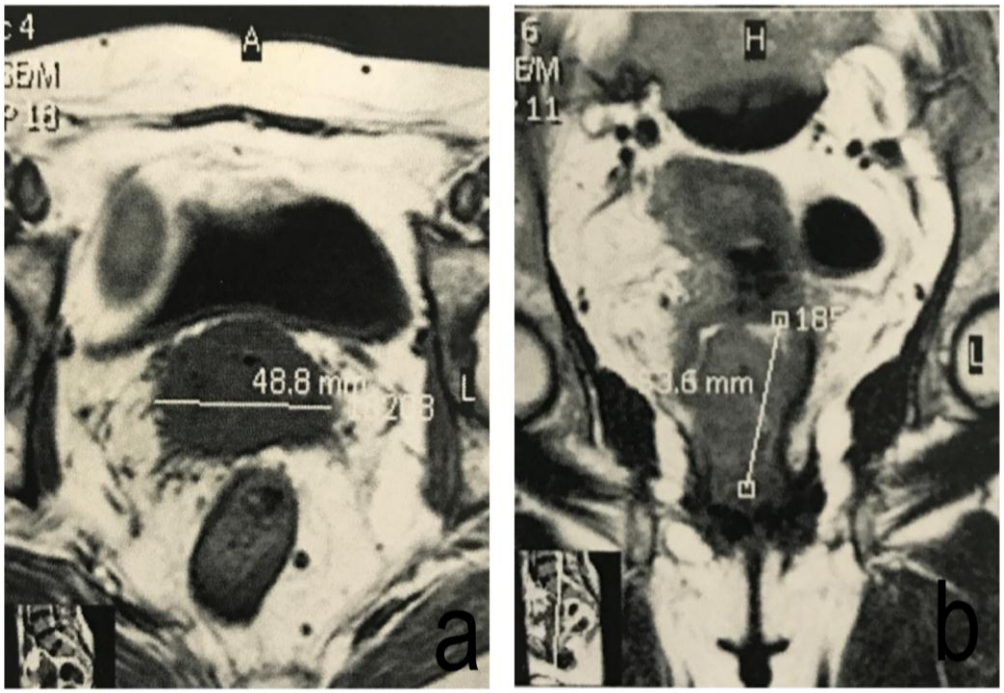


**Figure 2: Axial (a) and coronal (b) T2W magnetic resonance imaging showing hyperintense mass replacing utering cervix infiltrating the vaginal fornices and extending to lower third of the vagina (stage III A).**

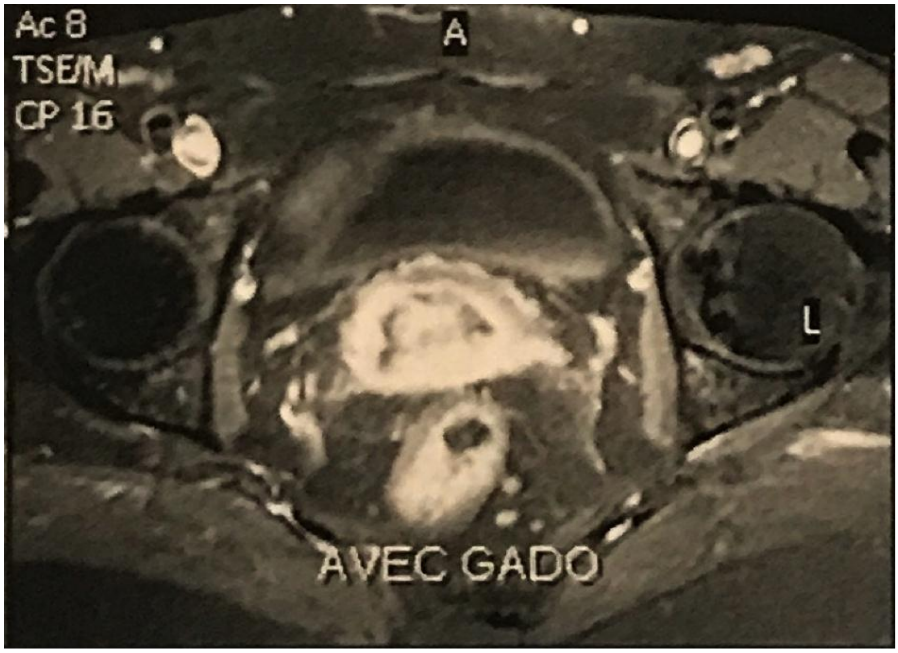


**Figure 3: Axial T1 fat-suppressed post-gadolinium magnetic resonance imaging showing homogeneous enhancement of the cervical mass.**

## DISCUSSION

Cervical cancer is the fourth most common cancer in women in the world.[5] squamous cell carcinoma accounts for over 85% of cervical cancer pathology, other histological types, such as adenocarcinoma, carcinosarcoma, lymphoma, and sarcoma, account for the rest.[6] SSCC is a rare histological variant of squamous cell carcinoma, more common in the head and neck, lung and urinary bladder.[1,6,9,10] It's a very rare pathological entity in female genital tract and even more rare in the cervix.[2] Rarity of this diagnosis makes it difficult to draw firm conclusions from limited data.[1] SSCC of the female genital tract tend to occur in older women who are postmenopausal, usually at an advanced stage at presentation.[5] The pathogenesis is uncertain but HPV has been widely accepted as the etiologic agent in the development.[7,8]

In an English literature search for cervical SSCC, only 20 cases were reported. The largest case series reported till date was published by *Brown et al*, it includes 9 patients. All patients had a complete response to initial therapy, regardless of treatment modality.[1]

Five patients subsequently experienced disease recurrence with a median disease-free interval of 4.9 months (range, 2–9.5 months). The patterns of recurrence were variable, and patients were treated with second-line therapy, however no patient with recurrent disease responded to second-line treatment. Survival from time of recurrence was 8 months in the 1 patient in whom the date of death is available. Survival data on the other 4 patients is not available.[1]

Four patients remain disease-free at 5, 22, 40, and 42 months following completion of therapy. The latter shared several characteristics, most importantly, each had limited disease at diagnosis, treated with radiation therapy.[1]

*Pang LC* reported two case of SSCC stage IB treated with Hysterectomy, lymphadenectomy, radiotherapy and chemotherapy. The first patient didn't respond, she died after 2 month of follow-up, the second remains disease-free at 13 months following. However, she died after 14 months of her primary diagnosis.[3]

*Nageeti and Jastania* reported a case of SSCC stage IIIB, treated with radiotherapy and chemotherapy. However, she didn't respond to the treatment and presented with multiple metastasis on follow-up after radiotherapy. She died after 6 months of her primary diagnosis.[4]

The pathologic diagnosis of SSCC is based on histologic and immunohistochemical findings. Cytomorphologic and histopathologic criteria reveals a biphasic pattern. SSCC are composed of a well to moderately differentiated squamous cell carcinoma, which is usually easily recognisable on the tumour surface coexistent with an underlying spindle cell (stromal/mesenchymal) component.[11,12,13] Rarely, cartilaginous or osseous differentiation may occur.[11] and osteoclast-like giant cells may be present.[3] Sarcomatoid carcinomas and carcinosarcomas, are considered synonymous by some authors and distinct entities by others. The latter consider that in sarcomatoid carcinoma, the epithelial component merges imperceptibly with the spindle cell component, whereas in carcinosarcoma, the epithelial component stands out against a sarcomatoid/spindle cell component.[2,11] Sarcomatoid carcinoma represents an entirely epithelial tumour with sarcomatoid features, but no malignant mesenchymal component, moreover, the

carcinomatous component of carcinosarcoma is usually adenomatous or undifferentiated type.[11]

Heterogeneity of SSCC generates a spectrum of differential diagnostic including other tumors with biphasic pattern. especially carcinosarcoma/malignant mixed Mullerian tumor (MMMT), synovial sarcoma, and leiomyosarcoma. However immunostaining pattern (wide diffuse immunoreactivity of the sarcomatoid component for both epithelial markers, CK 5/6 and AE1/AE3) and morphologic analysis makes a strong argument for a sarcomatoid squamous cell carcinoma.[12] In some reports few tumors coexpressed the mesenchymal marker vimentin.[1,2,12] Amelanotic melanoma may also be considered in the differential diagnosis, but negative melanoma markers (S100, MART-1, and HMB45) allows to rule out this entity.[12] In our case S100 was negative.

The histogenesis of SSCC is controversial. Histological, immunohistochemical, ultrastructural and molecular biological evidence from various reports support the theory of divergent differentiation (metaplasia) in these tumours, as the mesenchymal component develops from the epithelial component which support a monoclonal epithelial basis for the development of SCC.[14,15]

Because of the rarity of the disease, no standard diagnostic and treatment approach are available at the moment.[4] It is difficult to draw conclusions from limited data, the patients have been treated according to the treatment guidelines set out for squamous cell carcinoma of the cervix.[16] In the previous reports free interval is short after initial therapy, with rapid development of local and distant recurrence. Second-line therapy is ineffective.[1,3,4] Radiation therapy may be preferred because adequate margins of resection are diffcult to achieve.[16] In *brown* study the patients who did well were all treated with radiation therapy, and patients treated with surgery relapsed, however the outcomes seems likely related to the disease process and extent of tumor present, rather than the treatment modality. All patients treated with surgery had spread of tumor beyond what could be removed by surgery alone, or had such aggressive disease that postoperative radiation therapy was given in addition to surgery. Patients who remain free of disease had limited disease at diagnosis, and were all treated with radiation therapy at early stage disease. This may explain the pattern of recurrence in this study.[1] It is therefore not appropriate to conclude that surgical therapy is not indicated in this disease, or that radiation therapy is superior to surgery, but more data are necessary to make specific treatment recommendations.[1] Our patiente had complete initial response wish joins the litterature finding but the follow-up is short. Patients with advanced clinical stage at presentation and those who have recurrence invariably succumb to this malignancy.[16]

## CONCLUSION

Sarcomatoid squamous cell carcinoma of the cervix seems to have a more aggressive behavior than squamous cell carcinomas. The tumor is characterized by early relapse after initial therapy and failure to respond to second-line therapy. Primary treatment with radiation in the early stage of the disease offers an effective form of therapy, however patients with advanced disease at presentation or recurrence succumb to their disease. Reporting such cases might help clinicians to understand this entity of cervical cancer. It seem reasonable that aggressive approach at the initial presentation treatments should be considered, meanwhile Optimal treatment modalities still remain to be defined for this tumor.

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