Sarcomatoid Cancer of Penis in a 45 Year Old Male

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CASE PRESENTATION

A 42-year-old male patient presented to the outpatient department of our hospital with purulent discharge per urethra when voiding and a mass at the tip of the penis for the past 3 months. The patient had visited multiple practitioners of alternative medicine at his hometown before visiting our centre, but had no relief in his symptoms along with a progression in the size of the mass. There was no history of any surgical intervention or intervention on the penis in the past. The patient was sexually active and monogamous. He had no history of unsafe sexual contact or altered sexual practices. There was no family history of cancer. The patient was a nonsmoker, nonalcoholic, and did not indulge in any recreational drugs. On examination, the patient was well built with a BMI of 30.5 kg/m^2 and unremarkable cardiovascular, respiratory, and systemic examination. He was found to have an ulcerated fungating mass arising from the glans of the penis and replacing the distal one-third of his penis (Fig. 1). The prepuce was normal and uninvolved by the mass lesion. There was no significant lymphadenopathy in bilateral inguinal regions. Per rectal examination was normal. Suspecting it to be a case of penile cancer, the patient underwent a wedge biopsy of the lesion. The histopathology of the lesion revealed sarcomatoid carcinoma of the penis.

With these findings, the patient underwent partial penectomy for the lesion under penile block with a 1 cm margin and remnant penile stump of 2 cm. Histopathology of the resected specimen demonstrated the presence of polygonal to spindle shaped cells with prominent nucleoli and moderate amount of cytoplasm (Fig. 2A). The cells demonstrated brisk mitosis and immunohistochemistry of the tumor cells demonstrated immunopositivity for p63, high molecular weight cytokeratin and vimentin while negative for CD31 and pancytokeratin (Fig. 2B and C). Based on these markers, the tumor was characterized as sarcomatoid carcinoma. The margins of the resected tumor as well as the skin margin sent separately were free of tumor.

Postoperatively, the patient developed surgical site infection which was managed conservatively and resolved completely by postoperative day 40. The patient also underwent a fluorodeoxyglucose (FDG)-Positron Emission Tomography (PET) scan a part of staging work-up for the patient in this duration itself (around postoperative day 30). The PET scan revealed a faintly FDG-avid lesion measuring 1.4 × 1 cm at the penile stump with an SUVmax of 5.9 and no FDG avidity elsewhere in the body (Fig. 3A,B, and C). Clinically, there was no induration or appearance of a new mass at the penile stump or shaft and no significant lymphadenopathy. After consultation with nuclear medicine specialists as well as histopathologist, the FDG uptake was attributed to underlying inflammation to secondary to the surgical site infection and the patient was planned for follow-up a repeat PET scan after 1 month once the inflammation settles.

Although the repeat FDG-PET scan demonstrated a decrease in the avidity (SUVmax 3.7 vs 5.9) as well as size of the lesion (subcentimetric vs 1.4 × 1 cm; Fig. 3F), there were also omnious new findings, much to our dismay. Multiple pleural based and parenchymal nodules (SUVmax 9.2; largest 2.5 × 2.2 cm) were noted in this PET scan (Fig. 3D and E). The patient further underwent CT-guided needle aspiration from the pleural nodule which confirmed the diagnosis of metastatic sarcomatoid carcinoma. No new findings were noted at the penile stump and neither were any lymph nodes noted in the inguinal region at the time of this repeat PET scan as well.

It remains unanswered whether the FDG avid lesion noted in the first PET scan could have led to such a rapid recurrence or was it natural history of the disease per se which progressed so rapidly irrespective of the FDG avid nodule. Whether excision of the FDG avid penile lesion at the time of detection could have benefitted the patient still perplexes the authors. The patient is presently undergoing systemic chemotherapy (Paclitaxel, ifosfamide, and cisplatin) for metastatic sarcomatoid variant of penile cancer and has completed 3 cycles so far.

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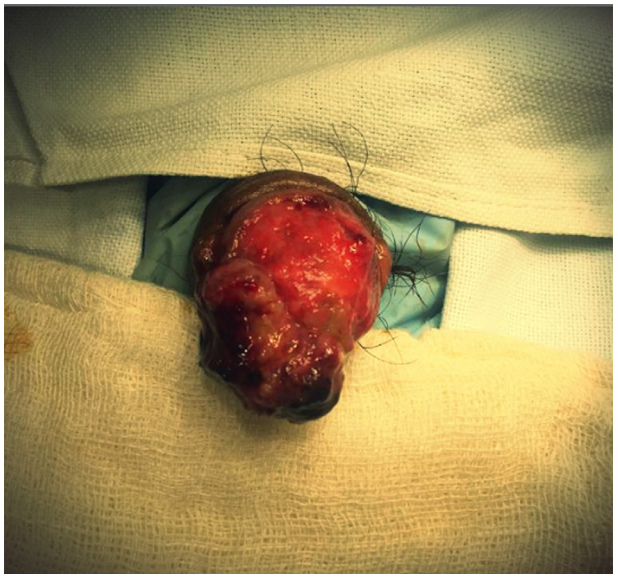

Figure 1. Fungating mass arising from the glans of the penis replacing the glans and distal thirds of the penis with relative sparing of the prepuce. (Color version available online).

DISCUSSION (BY DR KALPESH M PARMAR)

Penile carcinoma is a rare malignancy in men with an estimated incidence of less than 1 per 1,00,000 men. Squamous cell carcinoma (SCC) is the most common histologic variant of penile cancers. Sarcomatoid carcinoma is an extremely rare and aggressive variant of penile cancer comprising of only 1%-2% of all cancers.[1] Only 40 odd cases of sarcomatoid penile carcinoma have been reported worldwide till date.[1,2] Most of the patients have advanced disease at presentation with regional or distant metastasis in up to 90% patients with patients ranging in age from 28 to 81 years in a series of 15 patients by Velazquez et al.[3] Those presenting with localized disease also develop metastasis on follow-up within a brief span of up to 6 months despite aggressive surgical resection. Rarely have survivals more than 1 year been reported for patients with these aggressive tumors.[2] The most common site of origin is the glans penis; with lungs being the commonest site of metastasis as was the case in the index case as well.[1,3]

Apart from lymphatic, hematogenous and direct spread, another recently described mode of metastasis is "Satellitosis" that is unrecognized intracorporal penile metastasis.[4] This particular pattern is frequently encountered in patients with high-grade SCCs and sarcomatoid

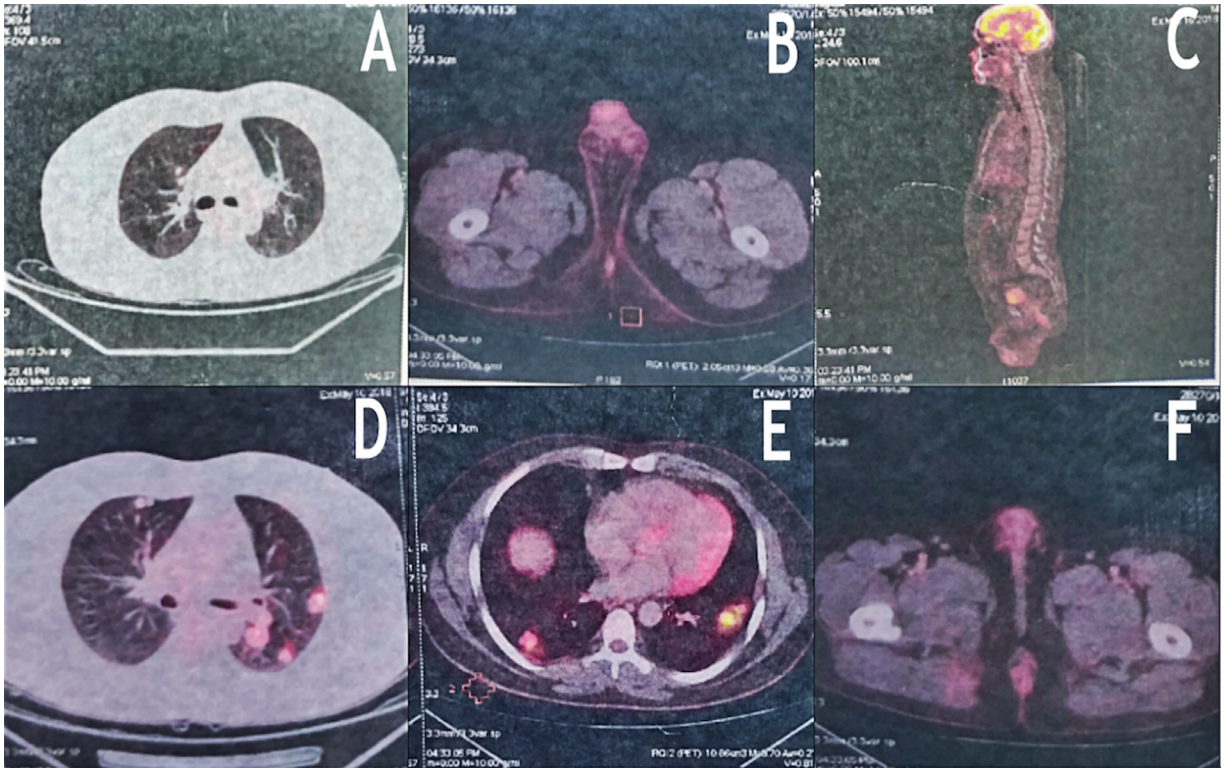

Figure 2. (**A**) Initial FDG PET/CT of the patient depicting no lung metastasis. (**B**) Initial FDG PET/CT showing faint uptake in the penile stump (SUVmax 5.9). (**C**)Sagittal sections depicting absence of FDG uptake anywhere else in the body. (**D**) and (**E**) Repeat PET/CT showing multiple lung metastasis. (**F**) Repeat FDG PET/CT showing faint FDG uptake in the penile stump (SUVmax 3.7) with no locoregional or lymphatic spread. (Color version available online).

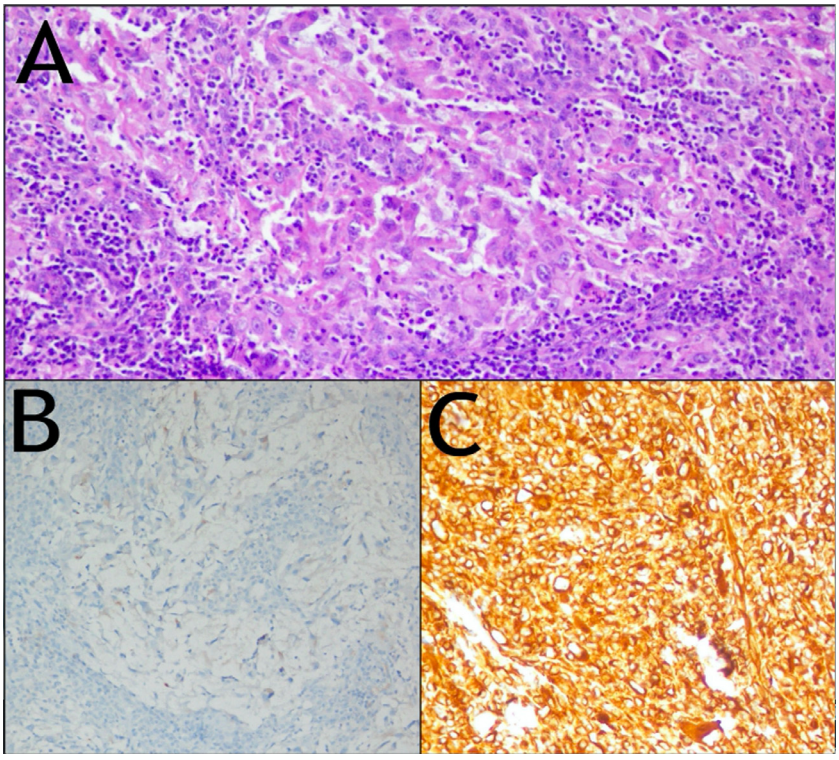

Figure 3. (**A**) High power field images demonstrating presence of multiple polygonal to spindle shaped cells with moderate amount of cytoplasm and eccentrically placed nuclei and prominent nucleoli. (**B**) IHC demonstrating p63 and high molecular weight cytokeratin positivity. (**C**) Tumor cells demonstrating diffuse positivity for vimentin. (Color version available online).

carcinomas as well. This modality of tumor progression might well explain the presence of rapid distant metastasis in the index case despite the presence of negative surgical margins. A point of importance is still the absence of palpable nodules on physical examination anytime during the course of evaluation in the patient.

Sarcomatoid carcinomas are high-grade tumors, predominantly composed of spindle cells. These are biphasic tumors with 2 components: carcinomatous component with predominant lymphatic spread and the sarcomatoid component with hematogenous spread, leading to both regional and distant metastases. These account for the aggressive nature and poor prognosis of the disease.[5] The epithelial component usually merges with imperceptibly with the spindle cell component.[3] The histopathological diagnosis of sarcomatoid carcinoma is clinched with the aid of immunohistochemistry and has become indispensable in differentiating it from other variants as well as close differentials like melanoma and sarcoma.

The spindle cells are diffusely positive for vimentin, p53 and p63, helping in arriving at the diagnosis of sarcomatoid carcinoma.[3,5] Melanomas are differentiated from sarcomatoid carcinoma on the basis of presence of melanin and intraepidermal melanocytic proliferation as well as S-100 and HMB45 positivity on immunohistochemistry. Sarcomas of the penis are often of vascular origin, located deep in the penile shaft commonly involving the corpora cavernosa which is a highly unlikely location for carcinomas. Sarcomatoid carcinomas are positive for vimentin but negative for markers of mesenchymal differentiation like actin, smooth muscle actin as which shall be positive in sarcomas.[3]

Contrast enhanced computed tomography of the abdomen, pelvis and thorax often suffice for staging of penile carcinoma.[6] PET/CT is also gaining acceptance rapidly across the globe for staging of penile cancers, albeit limited by high cost and restricted availability.[7] A recent study by Salazar et al demonstrated the role of 18-FDG PET/CT as a prognostic tool in penile cancers. In their study of 53 patients, tumor uptake (pSUVmax) of 16.6 and nodal uptake (nSUVmax) of 6.5 were established as predictors of poor prognosis in these patients, further strengthening the role of FDG-PET/CT in staging of penile carcinomas.[8] Aggressive tumors like high grade SCCs and sarcomatoid carcinomas may be better served by including PET/CT as a part of their staging work up, effectively prognosticating the patient as well.

Radical surgery with negative margins remains the treatment of choice for these dreadful tumors.[1] No effective chemotherapy options are yet available for sarcomatoid owing to the rarity of the disease as well as the high mortality associated with the tumor; sarcomatoid carcinomas being considered chemo-refractory by a lot of authorities across different organ systems.[9] The recent advent as well as benefit of epidermal growth factor receptor inhibitors and PD-1/PD-L1 immune checkpoint inhibitors

across genitourinary cancers and their trials in penile cancers may provide a much needed breakthrough in managing these aggressive tumors.[10]

SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.1016/j.urology.2018.11.027.

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