Solitary penile lesion, a peculiar presentation of colorectal cancer recurrence metastasis

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Introduction

- According to the World Health Organization (WHO), colorectal cancer (CRC) is the second leading cause of cancer related deaths noted in 2020.[1]
- Colorectal tumors at a genetic level have intratumor heterogeneity and can have genesis through many distinctive pathways:
  - Genetic adenoma-carcinoma sequence model: the predominant feature of this pathway is chromosomal instability, responsible for 70-75% of CRC where an aggregation of mutation in genes such as *APC*, *KRAS*, and *TP53* leads the epithelium to undergo a cascade of changes from aberrant crypt foci, low grade dysplasia, high grade dysplasia eventually resulting in adenocarcinoma.
  - The serrated pathway, the sessile serrated adenoma/polyp serve as the precursor for the serrated pathway which harbors *BRAF* oncogene activating mutations and CpG island methylator phenotype and results in 20%-30% of CRC.
  - The microsatellite instability pathway, commonly resulting from the germline mutation of DNA mismatch repair gene deficiency known to cause hereditary nonpolyposis CRC resulting in 2%-4% of all CRC. [2]
- Surgery and chemotherapy have served as the first-line treatments, however, despite these measures, prognosis still remains poor in those with metastatic disease, with less than 20% survival greater than 5-years.[3]
- The common sites of metastasis are the liver, lungs, and peritoneum however the spread to male external genital organs has rarely been reported.

Case Report

A 60-year-old male with past medical history significant for psoriasis and colorectal cancer successfully responsive to chemoradiation presented to his primary care physician with a painful red lesion on the glans penis. He denied any bleeding, discharge, dysuria or difficulty urinating at the time. However, he admitted to throbbing pain and pruritis at the lesion.

- Various interventions ranging from antibiotics, antifungals, to topical steroids were administered without improvement
- Rising carcinoembryonic antigen (CEA) level was noted
- Given the increase of minimal residual disease markers, restaging via computed tomography (CT) was obtained and scattered bilateral pulmonary nodules were noted and no evidence of active intra-abdominal disease.
- Given that there is no were improvement of the initial 1 cm diameter lesion, he was ultimately referred to urology (Figure 1)
- At which a 6 cm erythematous, raised mass involving the prepuce and glans penis with a 2 cm indurated base was found.
- Biopsy of the lesion demonstrated metastatic colorectal adenocarcinoma with abundant areas of infiltrative tumor cells filling the corpora cavernosa and corpora spongiosum (Figure 2)
- The patient underwent partial penectomy and treatment was followed by eight cycles of capecitabine plus irinotecan therapy.
- Thereafter, he was placed on capecitabine monotherapy.

Figure

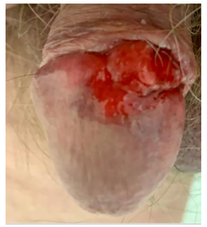

Figure 1: A 1.5 cm erythematous, raised mass in prepuce involving glans and a 2.0 cm indurated base with no phimosis or balanitis xerotica obliterans changes

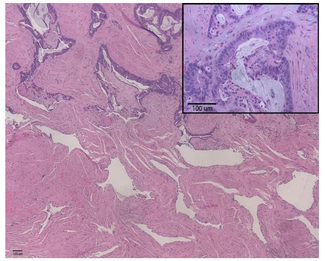

Figure 2: Low-power magnification of H&E sections of the penile biopsy shows the vascular corporal regions of the penis which are expanded by atypical glandular structures. Higher power (Top right inset) shows these glandular regions to be malignant with hyperchromasia, and cribriform growth with typical “dirty necrosis” of colorectal adenocarcinoma.

Discussion

Initial differential of a solitary penile lesion is broad and can include:

- Infectious etiologies- pseudoepitheliomatous hyperplasia and nodule formation secondary to candidiasis, and other benign conditions such as condyloma acuminatum
- Malignant lesions-HPV induced squamous cell carcinoma (SCC)
- Non-HPV induced SCC, commonly is seen arising in the setting of chronic injury or inflammation (e.g., in the setting of lichen sclerosus/balanitis xerotica obliterans)

Metastatic tumors to the penis are extremely rare; only 300 cases have been reported in the literature.[4]

Secondary tumors in the penis often are from the genitourinary organs within the pelvis, this commonly includes: bladder (33%), prostate (30%), colon (17%) and kidney (7%) [5]

To our knowledge less than 15 singular case reports of metastasis from colorectal cancers to the penis exist in literature.[5-18]

In the case of CRC, hematogenous dissemination via the portal circulation creates the greatest threat given the high vascular nature of the of liver it is no surprise that liver is the most common site of metastasis of CRC.[19]

Discussion

The rich vascularity in conjunction with being an end organ, the singular cases of metastatic spread to the penis have made this phenomenon a clinical paradox.

The five most accepted school of thoughts are:

- retrograde venous route
- retrograde lymphatic route
- arterial spread
- direct extension
- implantation and secondary to instrumentation[19]

Literature supports that regardless of the site of origin, secondary malignancy to the penis results in a poor outcome.[3]

Radiation, chemotherapy, and surgery serves as palliative pillars without any definite verdict for cure or overall survival benefit

In our case, it is reasonable to conclude that the lesion could be cancerous and given the highly vascular nature of the organ, could represent cutaneous metastasis and a harbinger of recurrence, particularly in the setting of primary sites within the rectal, sigmoid, or descending colon.

Conclusion

Metastasis of CRC present most commonly to highly vascular areas such as the liver; cutaneous metastasis to the penis specifically is uncommon. Our case showcases a novel presentation of metastatic colorectal cancer, and stands as a reminder to the consideration of metastasis to highly vascular areas, which is not restricted to the liver, but are also seen in this rare presentation to the penis.

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