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CASE REPORT

Squamous Cell Carcinoma of the Rectum

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ABSTRACT

Squamous cell carcinoma of the rectum is a rare malignancy. Although some patients may become amenable to surgical resection after initial treatment, most may require second line chemotherapy. Combined versus sequential chemotherapy and radiation therapy is the standard of care for patients with widely metastatic unrespectable disease. Although regimens with mitomycin, 5FU or cisplatin have been used in the past, our recommendation is for enrollment in the National Cancer Institute MATCH trial for molecular profiling of the tumor and identification of any targeted therapy options.

Introduction

Squamous cell carcinoma (SCC) of the rectum is a rare malignancy with less than 150 cases reported in the literature. Here we report a case of a widely metastatic SCC of the rectum in a patient presenting with sciatica. Rectal SCC is a diagnosis of exclusion and we made it after extensive work-up which included examination under general anesthesia, pathologic confirmation and multiple biopsies. Specifically, we excluded SCC of other more common sites such as anus and cervix. Work up and treatment options available for this rare entity is included.

Case Report

58 years old white female presented with lumbar pain radiating to the right leg. She had a 15 pounds weight loss, rectal bleeding, weakness and fatigue. She had muscle loss, anterior rectal mass and numerous nodules on her posterior vaginal wall. Ten months prior to this presentation patient had a Computed Tomography (CT) of the abdomen and pelvis, which was negative for any pathology. Iron deficiency anemia was present.

CT of the abdomen and pelvis showed a 7.2 cm right sided sacral mass with extension into S1-S2 neural foramina with direct bone invasion of the sacrum (pictures). The rectal tumor had sacral and posterior vaginal wall invasion (pictures). Four metastatic tumors were found in the liver and 2 lesions in the spleen that were highly suggestive of metastatic foci.

Under anesthesia, a gynecologist performed a cystoscopy and curettage of the cervix, which confirmed the absence of primary cervical or bladder tumor. The histologic sections of the cervical curettage showed detached fragments of

benign squamous epithelium. No viral cytopathic effect was appreciated. No evidence of malignancy was identified.

A colonoscopy with rigid sigmoidoscopy found no evidence of any anal primary tumor. Pathology of the rectal mass showed underlying nests of moderately differentiated SCC. Focally the SCC was present at the mucosal surface. Areas of keratinization were also noted. Immunostains show that the carcinoma was positive for CK5/6, P63 and P16. Immunostaining for CD31 showed staining around some of the rounded nests consistent with lymph vascular invasion. A stain for D240 was non-contributory. Human Papilloma Virus (HPV) was negative.

The patient's symptoms rapidly progressed during her work-up. The bilateral paresis of lower extremity was treated with emergent chemo-radiation. Chemotherapy with regimen classically described for SCC of the anus (2 cycles of mitomycin and 5-FU) was given along with daily radiation for 6 weeks. After completion of treatment, patient's paresis improved with the ability to stand and ambulate with a three-sided walker. The pain caused by the sacral bone invasion has been resolved. She is receiving bisphosphonates for bone metastasis (Figure 1).

It is not clear at this time if she will be a candidate for surgical resection due to the volume and number of sites of metastatic disease. We are currently evaluating response and referring her for MATCH (Molecular analysis for therapy Choice) trial to National Cancer Institute.

Discussion

SCC of the rectum is a rare tumor first described in 1919. It is estimated to be present in 0.1 to 0.5 per 100,000 cases of colorectal carcinoma. It has a higher female to male ratio. It behaves more aggressively than adenocarcinoma but may be responsive to neoadjuvant chemo/radiation [1].

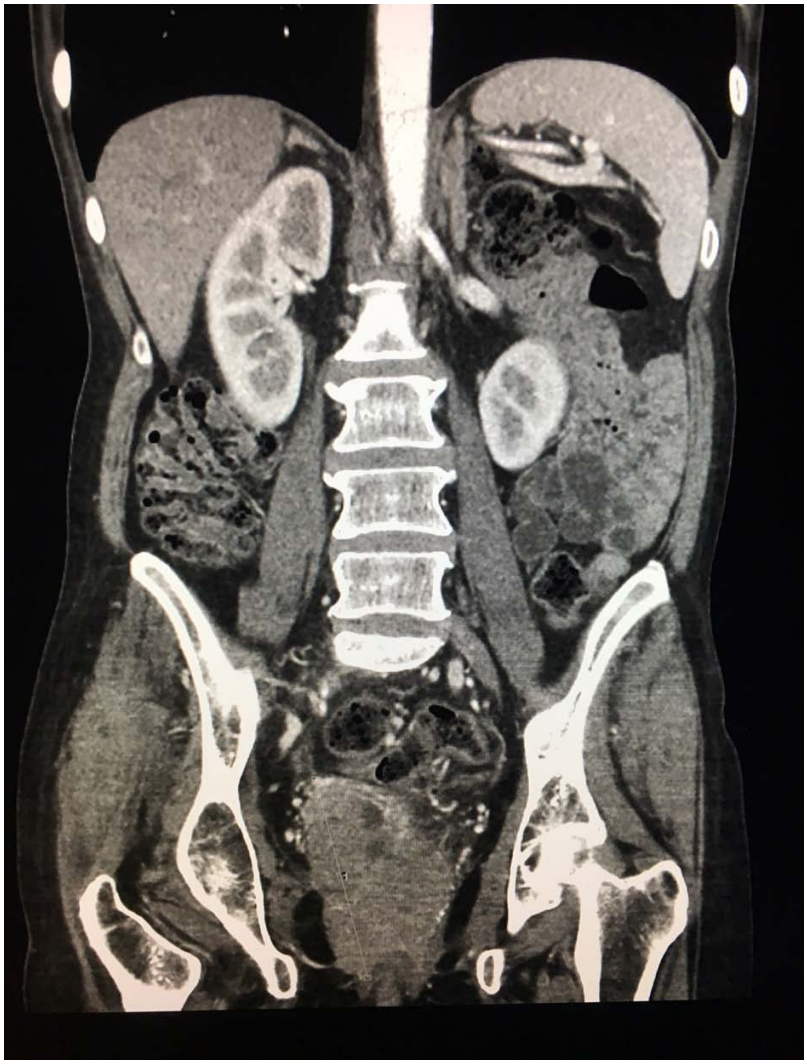
It is important to differentiate between primary sites of SCC to rule out other areas as the source. SCC of the cervix as well as metastatic rectal cancer is treated with Vascular Endothelial Growth Factors (VEGF) inhibitors. We do not know of any VEGF inhibitors for rectal squamous cell carcinoma. Rectal carcinoma is not usually associated with HPV positivity and our patient was also HPV negative. Classically HPV positive tumors have responded better than HPV negative tumors to chemo radiation [2].

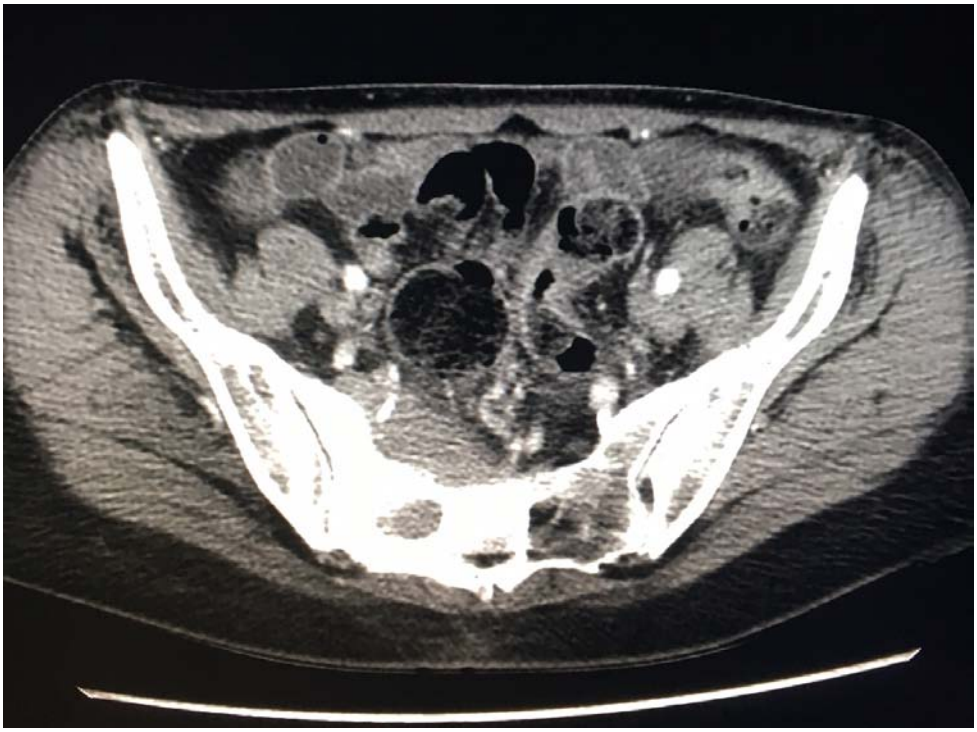
There have been case reports of tumor regression allowing for primary surgical resection after neoadjuvant chemo radiation therapy. Chemotherapy options include those traditionally associated with treatment of SCC of the anus and cervix.

There is no literature regarding maintenance chemotherapy for persistent metastatic disease. It is not clear whether mitomycin plus 5-FU could be used as a salvage second line regimen if cisplatin based regimen was used initially or the other way around. Mitomycin has been used in ocular, bladder and head/neck SCC. It acts by rapidly killing growing cells.

P16 and P63 are cell cycle regulatory proteins. A high level of p63 expression in SCC may participate in the survival advantage by forming a transcription repressor complex. Cisplatin based therapy uses this pathway to increase his tone acetylating and enhance apoptosis. P16 has been found in colorectal cancer, head and neck squalors tumors, melanocytic tumors and neuroendocrine tumors. It is a tumor suppressor gene, which can be methylated and becomes inactive, which can lead to possible role as a proto-oncogene. Mediation of P53, transcriptional regression may enhance survival in SCC. The co-expression of p63 and CK5/6 has been described in lung SCC. Studies have shown this co-expression is not only a diagnostic indicator, but also a good prognosis factor.

National cancer institute (NCI) MATCH trial (Molecular analysis for therapy Choice) is a precision trial that assigns patients to receive treatment based on the genetic changes found in their tumors through genomic sequencing and other tests. Currently there are 18 treatment arms that are enrolling patients whose tumors have a specific genetic change that are picked up during routine genomic cancer profiling. Patients with advanced solid tumors, lymphomas or myeloma may be eligible for MATCH, if they fail the standard treatment





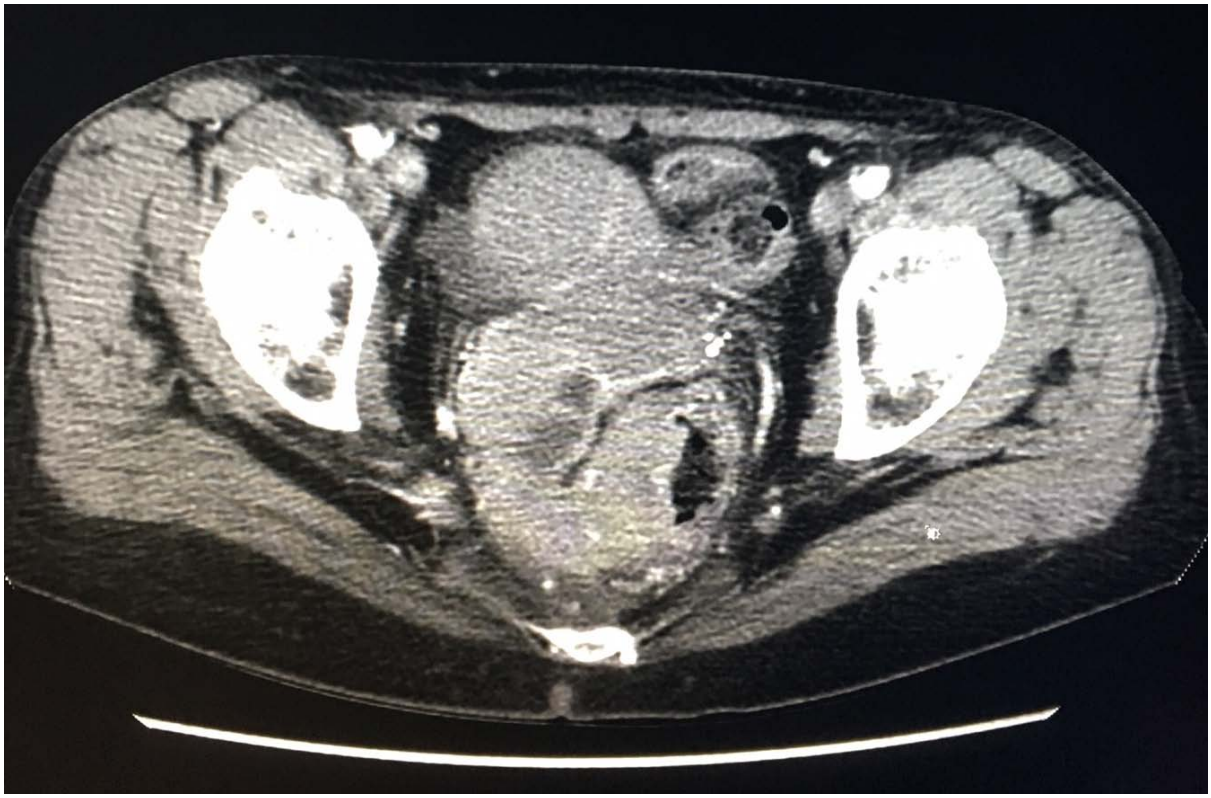


Figure 1: Scans of the tumor and its relation to other organs in Coronal and sagital views.

or have a rare form of disease. The drugs used in the arms are either approved by Food and Drug Administration for another cancer or are still in trials with some shown effectiveness [3,4]. A rare case such as ours is a typical candidate for MATCH and was referred therefore.

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