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Case Report
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Complete Pathologic Response after Chemo-Radiation for a Rare Entity: Squamous Cell Carcinoma of the Recto-Vaginal Septum

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Abstract

Introduction: Squamous Cell Carcinoma (SCC) is a frequent pathology in pelvic cancers, especially those of the uterine cervix and anal canal and can be associated with HPV infection. Some tumor localizations are extremely rare, such as SCC of the recto vaginal septum. To our knowledge this would be the third reported case of this entity.

Case Report: A 67-year-old, G2P2 female presented with impending large bowel obstruction. The CT showed a 7 cm mass anterior to the rectosigmoid colon, 8 cm from the anal verge, in close approximation to the uterus. Cervical exam and rectal mucosa on endoscopy were normal. Several deep endoscopic biopsies of the mass showed invasive squamous cell carcinoma, p16 positive. Treatment consisted of pelvic radiation therapy 45 Gy in 25 fractions, with subsequent reduced field boosts to the mass achieving a final dose of 65 Gy with concurrent cisplatinum at a dose of 40 mg/m^2 weekly. Surgery was performed 6.5 months after completion of treatment. Pathology report showed no evidence of residual disease.

Conclusion: Because of the rarity of this entity there is a lack of evidence to guide management. Follow up imaging with MRI and PET CT may be difficult to interpret. Definitive treatment with chemo radiation may be a viable option given the complete pathologic response in this case.

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Case Presentation

A 67-year-old, G2P2, retired female school teacher, presented with impending large bowel obstruction. She had a 3-month history of lower abdominal discomfort, bloating and a 2-month history of inability to have a bowel movement, but she was able to pass small-caliber pellets with no evidence of bleeding.

There had been no vaginal bleeding or discharge and Pap smears were normal up to 2017. Her family physician diagnosed diverticulitis, started antibiotics empirically, and ordered a CT scan of the abdomen and pelvis. The CT demonstrated of a 7 cm mass arising anterior to the rectosigmoid colon, 8 cm from the anal verge, in close approximation to the uterus. Prominent left iliac nodes were noted, up to 1.2 cm in diameter.

She was referred to a surgical oncologist and underwent a colonoscopy. The mass was encountered 8 cm to 10 cm from the anal verge, slightly to the left of midline. The overlying mucosa was completely normal in appearance. The scope was navigated past the mass and the remainder of the colon was normal apart from diverticulosis. Several endoscopic biopsies of the mass showed invasive squamous cell carcinoma, p16 positive.

She subsequently was referred to a gynecologist. The exocervix was normal on examination. A Pap smear and endometrial biopsy were taken and were normal. On bimanual pelvirectal exam, the recto vaginal septum was thin and smooth and the mass was palpable at the tip of the examining finger. Origin in the high cervical stroma could not be ruled out.

At this point the differential diagnosis included a stage 3B cervical cancer, primary tumour of the rectovaginal septum, or primary squamous cancer of the rectum.

Pelvic MRI (Figure 1a, 1b) identified the mass arising behind the cervix and anterior to the

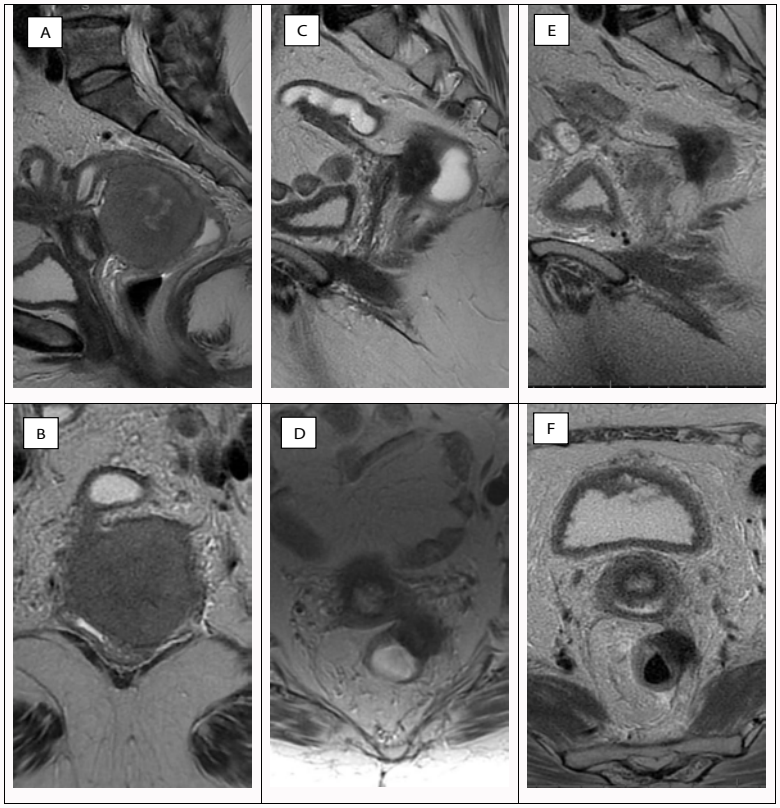

Figure 1: Pelvic MRI T2: Upper panel shows sagittal images. Lower panel corresponding axial images.
A/B: Baseline; C/D: Immediately post-treatment completion; E/F: 5 months after treatment.

lower rectum and confirmed the proximal left internal iliac lymph node. FDG PET scan (Figure 2a, 2b) showed the highly FDG-avid 6 cm mass with SUVmax of 30, centered just anterior to the low anterior rectal wall abutting the posterior margin of the cervix. The cervix itself did not have any uptake. There was a 1.4 cm left internal iliac lymph node with SUVmax of 19.8. There was no other evidence of any lymphadenopathy or metastatic disease.

Squamous cell carcinoma antigen was elevated at 11 ug/L.

She was then referred to radiation oncology for assessment and management. As she had significant rectal obstruction, a diverting colostomy was performed prior to initiating treatment. Although the site of origin was still uncertain, the p16 positive squamous pathology suggested that the best course of action would be definitive radiation with concurrent cisplatin as per primary cervical cancer management. Both GI and gynecology multidisciplinary tumor boards concurred.

Radiation therapy consisted of 45 Gy in 25 fractions to the pelvis, with an integrated boost to 52.5 Gy to the involved left iliac lymph node. A Volumetric Modulated Arc Technique (VMAT) was used. Concurrent cisplatinum was administered at a dose of 40 mg/m^2 weekly. Since brachytherapy was not an option as it would be for a cervical primary, a VMAT boost was planned for a dose of 10 Gy in 5 fractions to the residual primary mass. Replanning for an additional final phase of 10 Gy in 5 fractions allowed for further volume reduction as primary tumor mass had shrunk from 105 cc to 17 cc during the course of treatment. This brought the tumor dose to 65 Gy with concurrent platinum for the first 45 Gy. Treatment duration was 7.5 weeks (52 days).

An MRI on the final day of treatment (Figure 1c, 1d) showed marked decrease in size measuring 3.2 cm × 2.5 cm seemingly arising from the anterior wall of the rectum. The adenopathy was resolved. Her case was presented again at multidisciplinary conference as to whether surgical clearance was indicated given the residual disease. There was no clear consensus.

Squamous cell carcinoma antigen had decreased from 11 ug/L to 1.6 ug/L after treatment.

Two months after treatment she was well with overall functional status ECOG 0. On examination, there was no evidence of any residual mass between the cervix and the rectum, and the rectal space was quite clear. MRI and PET-CT (Figure 2c, 2d) at 3 months after treatment showed further interval reduction in the residual tumor with significant decrease in FDG activity to SUVmax 6.8. The pelvic lymphadenopathy had resolved. Her case was presented at the multidisciplinary conference again, and the recommendation was to give her additional time to reevaluate response.

Two and a half months later (5.5 months from treatment) FDG PET-CT (Figure 2e, 2f) showed a persistent exophytic mass on the anterior left rectum abutting the lower cervical segment measuring 2.4 cm with a SUVmax of 8.3, and apparent involvement of the posterior lower cervical segment with a SUVmax of 9.6. There was also a new left external iliac lymph node measuring 0.9 cm with an SUVmax of 3.6. MRI (Figure 1e, 1f) 4 days later showed further interval size reduction, with the residual now measuring 2.5 cm, with no evidence of adenopathy.

Given the suspicion of residual disease in a location not easily accessible to ongoing surveillance or assessment, such as colposcopy or biopsy, it was decided the safest and most definitive course

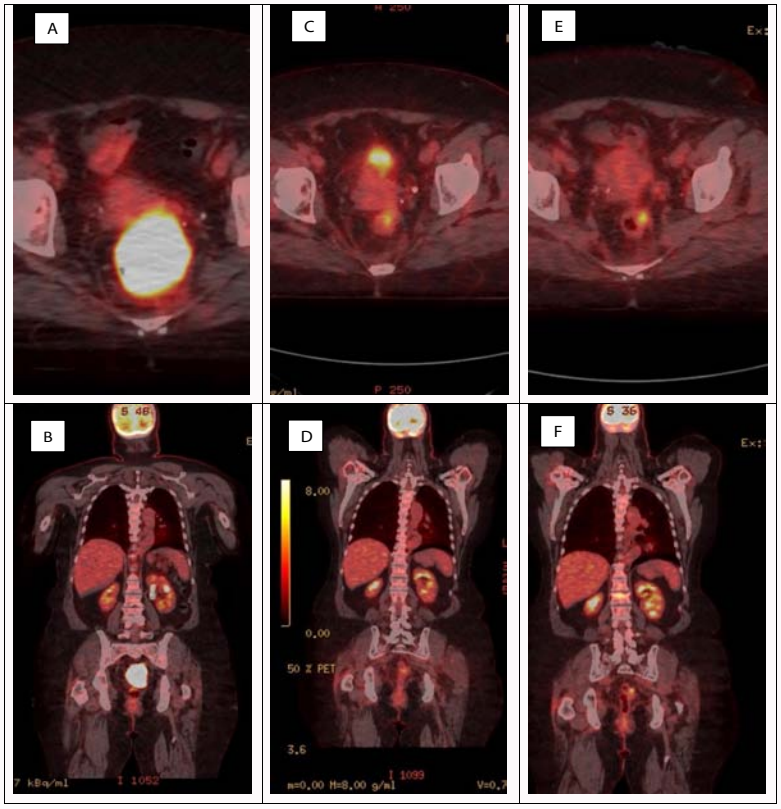

Figure 2: FDG PET-CT: Upper panel shows axial images. Lower panel corresponding coronal images.
A/B: Baseline; C/D: 3 months post treatment; E/F: 5 months post treatment.

of management would be a low anterior resection with en bloc hysterectomy, bilateral salpingo-oophorectomy and diverting loop ileostomy.

Surgery was performed 6.5 months after completion of treatment. Pathology report showed no evidence of residual disease. The "rectal mass" was comprised of foamy histiocytes and fibrosis extending from submucosa into pericolic fat, mild crypt architectural distortion and overlying mucosa with no dysplasia or malignancy. Thirty-two lymph nodes were removed and all were negative for carcinoma. Endocervical glandular epithelium showed atypia in keeping with radiation, but no cervical squamous epithelium was present.

She recovered well from surgery and underwent closure of the loop ileostomy 10 months after treatment. Given her complete pathologic response, no further adjuvant treatment is indicated. She will continue follow ups with SCC tumor marker, physical examination and periodic cross sectional imaging surveillance. SCC antigen remains normal at 1.1 ug/L.

Discussion

Squamous Cell Carcinoma (SCC) is a well described malignancy in pelvic cancers, especially those of the uterine cervix and anal canal associated with HPV infection [1,2]. Standard treatment for these entities varies from local resection to definitive treatment with concurrent chemo-radiation [3].

Some tumor localizations are extremely rare, such as SCC of the recto vaginal septum. To our knowledge this would be the third reported case of this entity [4]. The rectovaginal septum is a layer of connective tissue that separates the anterior wall of the rectum from the posterior wall of the vagina [5]. Tumors that arise from this location are mostly from endometriosis foci, and can undergo malignant transformation in about 1% of cases [6]. Other non-endometriosis tumors have been reported, such as Gastrointestinal Stromal Tumor (GISTs), adenocarcinoma, sarcomas or metastases from other sites [5].

Primary squamous cell carcinoma of rectum is also an extremely rare entity, accounting for 0.3% of all histological subtypes in this location, with an incidence of 1.9 to 3.5 per million population [7]. Even though there is a strong association of Human Papilloma Virus (HPV) with anal squamous cell carcinoma, there is not enough evidence to support its correlation with primary rectal squamous cell carcinoma [7].

Symptoms vary in relation to the size of the tumor and degree of infiltration. Although about half of rectovaginal septum tumors remain asymptomatic, the most common symptoms include urinary retention, vaginal pressure, pelvic pain, and bleeding [4,5]. Our patient also experienced bowel obstruction requiring bowel diversion.

Extension from a gynecological or anal carcinoma should be ruled out. In addition, metastases to the rectum from other organs, or a fistulous tract involving the rectal area, can both masquerade as rectal carcinoma [7].

Physical examination and direct observation with colposcopy and/or colonoscopy are extremely important. Changes in the mucosa of the cervix, anal canal or rectum can indicate a possible tumor etiology. In our case, the mucosa of the uterine cervix, the anal canal and rectum appeared completely normal, making the diagnosis of a rectovaginal septum SCC more likely.

Complementary imaging is also important to assess local and systemic extension. Transvaginal ultrasound is useful and can be complemented with an MRI [4,7]. PET–CT is also useful to determine systemic extension. There is no consensus as to the gold standard in investigation of this entity.

Serum SCC-antigen (SCCag) as a tumor marker for diagnosis and follow up lacks supporting evidence [7], but may be useful to follow treatment response and screen for recurrence. Because of the rarity of this presentation and lack of evidence to guide management, there is not a definitive consensus on the optimal management. Patient involvement and preferences may be considered in the decision-making. Although the literature seems to favor a primary surgical approach, chemo radiation is clearly an alternative option in these radiosensitive tumors [6].

Follow up imaging with MRI and PET-CT are both useful, although interpretations of findings can be challenging, as we have seen in this case [4,6]. The optimal frequency of imaging is unknown. If residual disease is suspected on imaging, biopsy may be difficult and surgery may be the only option.

Conclusion

Primary SCC of the recto vaginal septum is an extremely rare entity. Definitive treatment with chemo radiation may be a viable option given the complete pathologic response in this case. Interpretation of response on imaging can be challenging.

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