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Case Report

Esophageal Squamous Cell Carcinoma, Revisit as Rectal Mass!

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Abstract

Background: SCC of the gastrointestinal tract is a rare malignancy; it usually involves the esophagus or the anal canal. Its occurrence in the rectum has an incidence rate of 0.1 - 0.25% per 1,000 cases [1]. Around 90% of cases of rectal cancers are adenocarcinomas; the remaining 10% consist of sarcomas and lymphoid tumors, which present similarly to rectal adenocarcinoma.

Metastatic involvement of the colon is a rare occurrence and is extremely rare from primary extra-abdominal tumors. To this date, there are three case reports from Asia published in English literature describing colonic metastasis from primary esophageal SCC [2-4].

Case Presentation: We describe a 73-year-old gentleman, with a heavy cigarette smoking history, whom was recently found to have a primary esophageal SCC; for which a combined management approach by chemotherapy and irradiation was used and resulted in a complete resolution. Approximately two years later he presented with constipation and tenesmus a rectal mass was found and the detailed morphological and immunophenotypic features of this mass were identical to his initial primary esophageal SCC. The patient is currently under chemotherapy for this newly developed metastatic disease.

Conclusion: Squamous cell carcinoma of the rectum is a rare disease and likewise, metastatic esophageal SCC to the rectum is an extremely exceptional finding; therefore the close multi-disciplinary approach, including the proper comparative histo-morphological assessment between the two remote lesions have helped to overcome this clinically unexpected scenario and proceeded with the most proper management approach.

Keywords: *Squamous Cell Carcinoma; Rectum; Rectal Mass*

Background

SCC of the gastrointestinal tract is a rare malignancy; it usually involves the esophagus or the anal canal. Its occurrence in the rectum has an incidence rate of 0.1 - 0.25% per 1,000 cases [1].

Case Presentation

A 73-year-old gentleman, known case of multiple co-morbidities, and esophageal cancer which was diagnosed in 2018 and treated in Germany.

He first presented to the Gastroenterology Clinic for a complaint of dysphagia for 2 months and an Esophagogastroduodenoscopy was done subsequently which revealed an ulcerated mass on the mid-esophagus (2 - 3 cm) with partial narrowing of the esophagus at around 30 cm from the incisura and 10 cm above the GE junction.

Gastroscopy findings

Mid esophageal ulcerated mass (2 - 3 cm) lesion with partial narrowing of the esophagus at around 30 cm from the incisora and 10 cm above the GE junction.

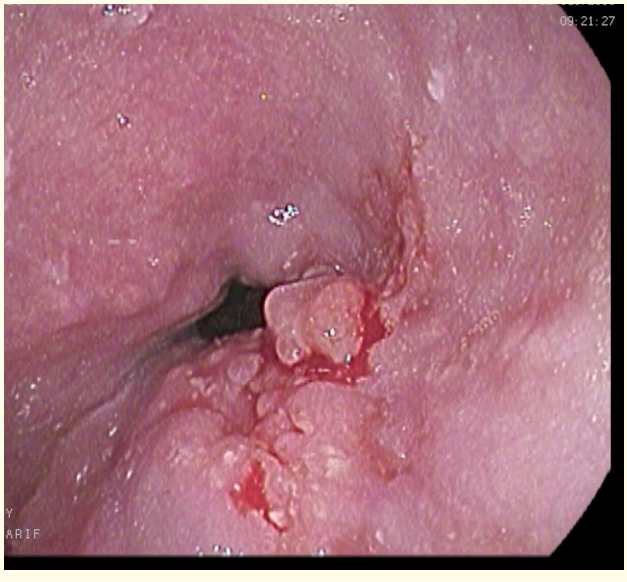

Figure A

Biopsies were taken and results showed moderately differentiated Squamous Cell Carcinoma; Grade II, cT2N1M0.

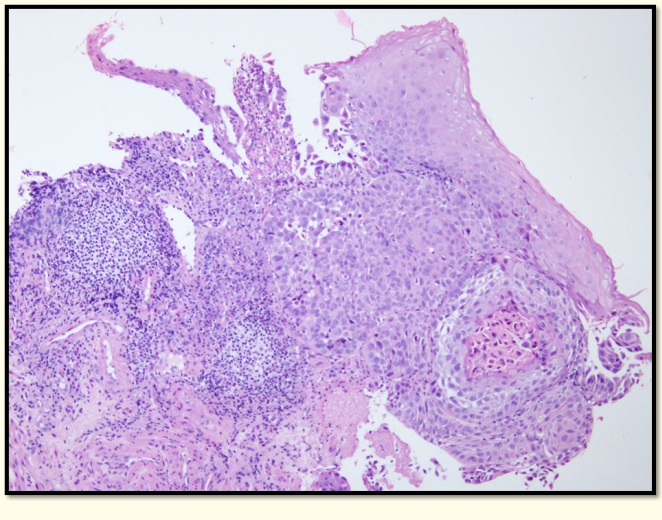

Figure 1: *Initial esophageal biopsy: Subepithelial morules of well differentiated squamous cell carcinoma and associated dysplasia.[H&E stained - HPF].*

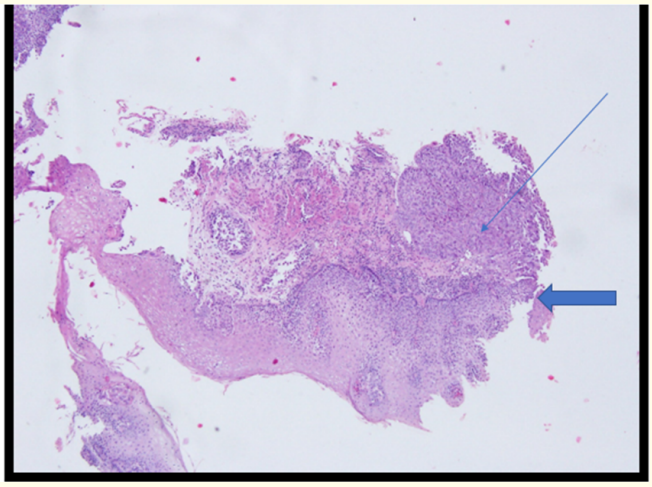

Figure 2: *Initial esophageal biopsy: Invasive squamous cell carcinoma (thin arrow) and associated overlying dysplasia (thick arrow) [H&E stained - LPF].*

Staging PET Scan done showed hypermetabolic esophageal lesion at the lower third of the esophagus (marked by arrows), in addition to FDG avid two celiac lymph nodes likely metastatic, as well as few bilateral subcentimetric pulmonary nodules and Focal FDG activity at the right adrenal of equivocal nature.

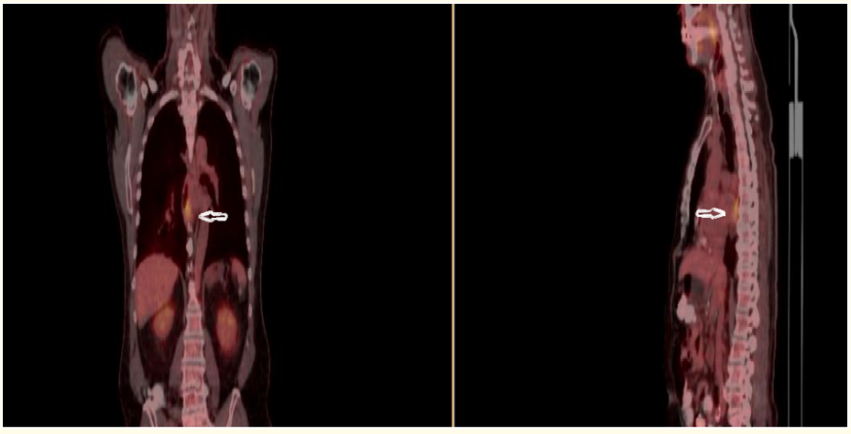

Figure B

He received radio-chemotherapy (Carboplatin/Paclitaxel) in Germany. He also received external beam radiation therapy with curative intent, to the esophagus, dose of 50.4 Gy in 28 fractions; followed by gross tumor boost to a dose of 9 Gy and 3.6 Gy to the celiac lymph-adenopathy. As well as chemotherapy, weekly paclitaxel and carboplatin.

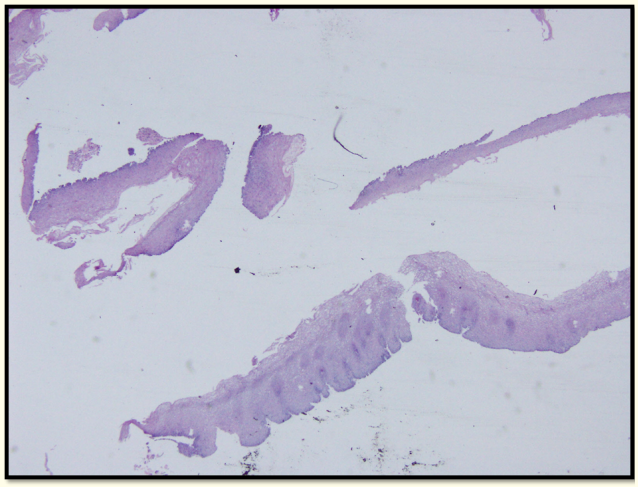

Figure 3: *Esophageal biopsy post neoadjuvant therapy: No residual in-situ or invasive malignancy [H&E stained - LPF].*

Re-staging PET/CT showed: total metabolic resolution in the primary esophageal cancer, partial metabolic regression in the previously noted celiac nodal lesions, newly developed mesenteric nodular deposit adherent to anterior part of gastric pylorus, total resolution in the previously noted FDG activity opposite right adrenal/porta-caval lymph node. Also seen heterogenous FDG activity over enlarged prostate & anterior rectal wall (marked by arrows), highly suspicious of neoplastic involvement for further evaluation. And the few sub-centimeteric pulmonary nodules deemed to be stable non FDG avid over a long-time-interval favoring their benign nature. Otherwise, the rest of the scanned body is keeping free.

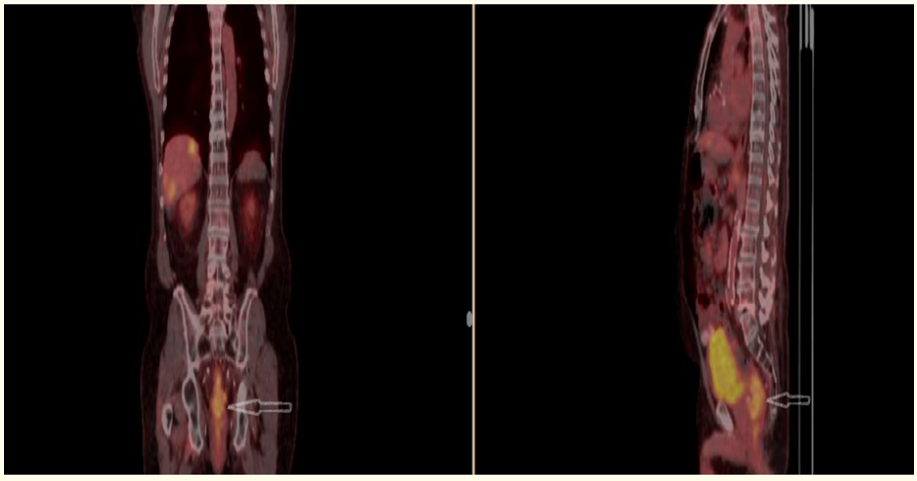

Figure C

And so, MRI Pelvis was done which showed lower rectum anterior wall invasive mass lesion with direct extension beyond the rectal wall, being inseparable from the right seminal vesicle and the posterosuperior aspect of the prostate (Marked by red arrows).

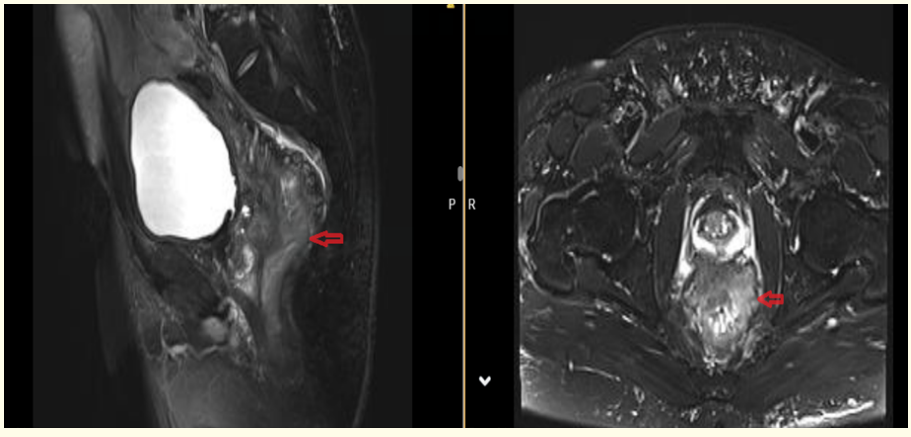

Figure D

Subsequently, gastroscopy and colonoscopy were done. While gastroscopy showed no evidence of disease in the esophagus; the colonoscopy revealed a large partially obstructing lower rectal mass with wall invasion, extending from 8 cm to 15 cm from the anal verge. Biopsy from the rectal mass was suggestive of Squamous cell Carcinoma Moderately differentiated; to determine whether it is primary or metastatic which was later found to be metastatic.

Colonoscopy finding: Large partially obstructing lower rectal mass with wall invasion, extending from 8 cm to 15 cm from the anal verge.

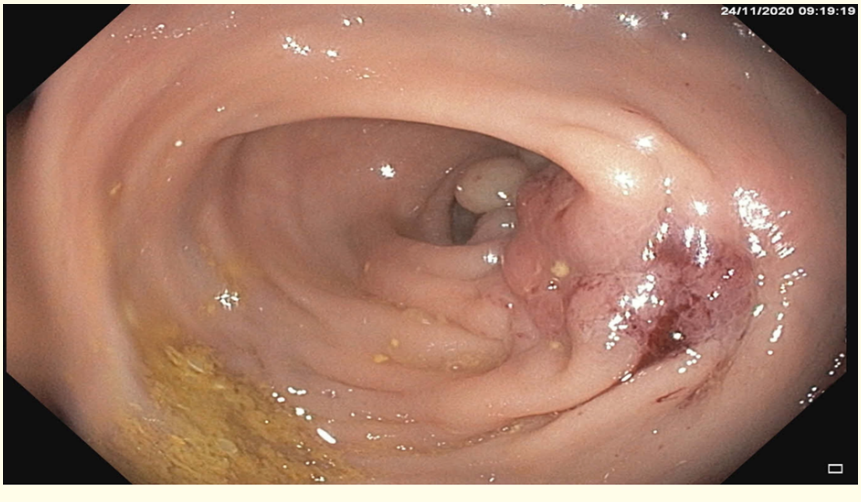

Figure E

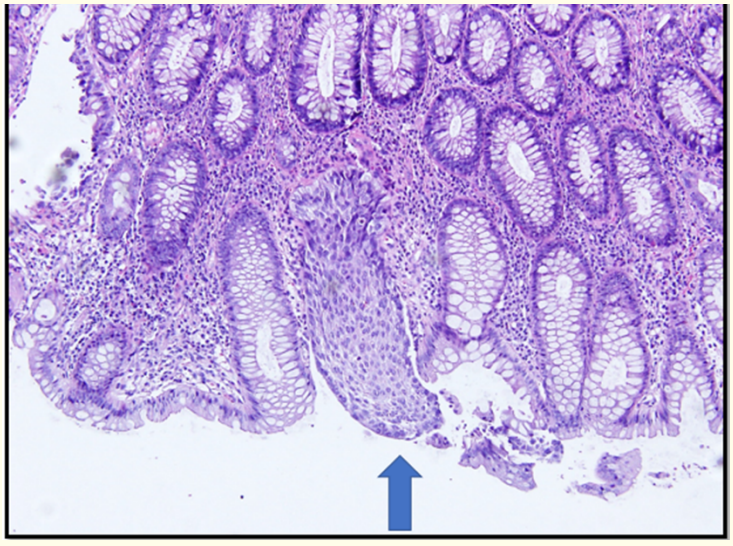

Figure 4: *Rectal biopsy: Island of squamous cells (thick arrow) within a normal glandular rectal mucosa. No adjacent squamous epithelium [H&E stained - HPF].*

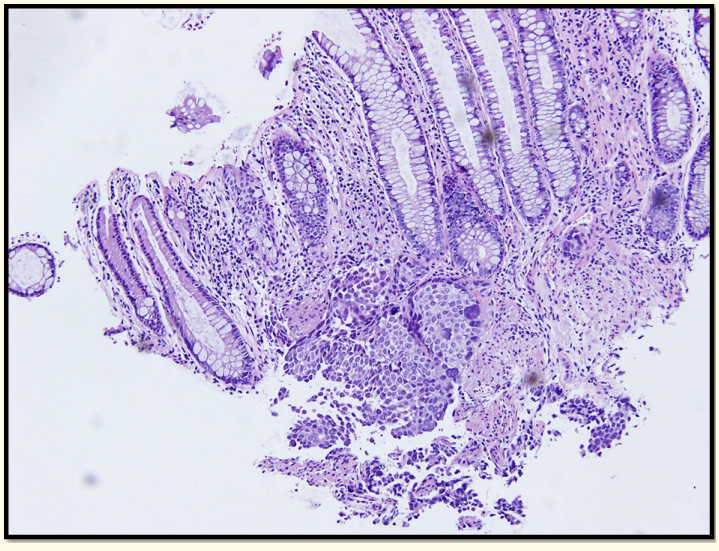

Figure 5: *Rectal Biopsy: Well defined Island of squamous cells within a normal glandular rectal mucosa abutting the location of superficial lymphatics. No adjacent squamous epithelium [H&E stained - HPF].*

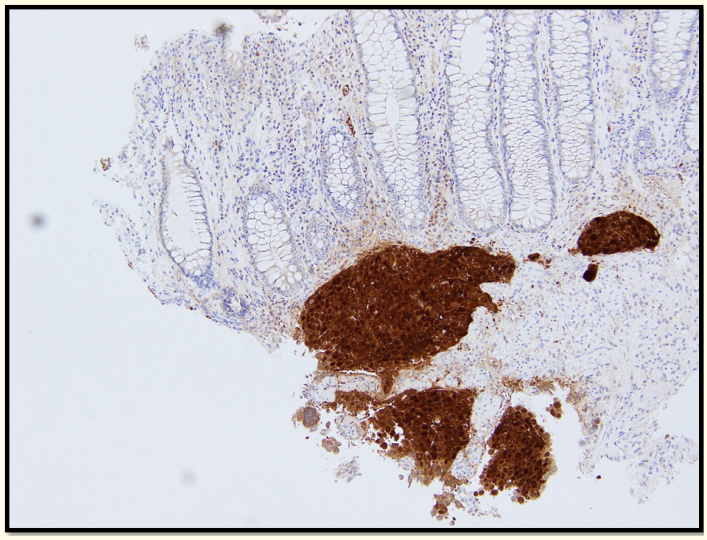

Figure 6: *Rectal Biopsy: Squamous cell islands with diffuse p16 nuclear & cytoplasmic immunoreactivity staining[IHC P16 stained - HPF].*

A follow-up PET revealed positive perigastric lymph node with which endoscopic ultrasound-guided FNAC for cytopathic verification revealed it to be positive for metastatic carcinoma. The patient received radiotherapy to the rectal deposit (20 Gy 5 fractions). Another PET/CT demonstrated stable celiac lymph nodes, with a stable, nodular mesenteric lesion adherent to the gastric pylorus (1.9 x 1.4 cm); and a newly developed segment VI hepatic lesion measuring 1.6 cm; as well as two newly developed FDG avid left para- colic gutter nodular lesions (1.1 cm and 0.9 cm). The proposed plan at the time was to request PD-L1 and MMR immunohistochemistry; revealing that PDL-1 tumor proportion score to be 10-20%; and pMMR respectively. The proposed plan was to look for the HPV status on the pathology of the anal canal and to begin pembrolizumab.

Discussion

Primary esophageal squamous cell carcinoma rarely metastasizes to the rectum or to the lower GI tract, compared to synchronous or metachronous malignancies of different locations within the GI Tract. There have been reported cases of metastasis from malignant ovarian tumor [5] and lung tumors [6], most cases were diagnosed based on clinical and histopathological criteria, while others didn't include any immunological comparison between the primary disease and the metastatic lesion. In our patient, based on the negative post-neoadjuvant follow-up esophageal biopsies and the biopsy of the new rectal mass favored lymphovascular metastasis rather than a second primary squamous cell lesion. The initial esophageal mass biopsies and the rectal mass biopsies were tested for HPV-p16, PD-L1 expression score and mismatch repair genes, which revealed identical results by morphology and immunoreactivity [7]. However, the PET scan findings of a positive intra-thoracic nodal disease, without inguinal or intra-pelvic nodal disease, substantiated the pathology findings of a post neoadjuvant systemic disease with a metastatic rectal deposit/mass for which the patient has been managed accordingly.

The first SCC case was recorded in 1919 in a 65-year-old male by Schmidtmann [8,9]. Age ranges from 39 to 93, with an average age of 63 years. It shows a predilection in females (57% vs 42%), most cases present as early stage localized (stage II), or regional (Stage III). The strongest association is that of proctitis, generally secondary to ulcerative colitis. Other risk factors in literature include a past

history of radiotherapy for other pelvic malignancies, asbestos exposure, and colonic duplication also have been associated (but not of rectal origin), HPV, parasitic infections schistosomiasis in 2 cases, and one case of amoebiasis. HPV has a strong association to SCC of other regions including the anus, cervix, head and neck; but its role in the pathogenesis of rectal SCC has not been clear yet. Audeu., *et al*. used immunohistochemistry to examine 20 squamous lesions without evidence of HPV. Nahas and Frizelle., *et al*. used in situ hybridization technique, again without evidence of HPV DNA. However, when Sotlar., *et al*, Kong., *et al*, Matsuda., *et al*. and Jaworski., *et al*. all identified HPV when utilizing PCR. This may indicate that the sensitivity of the test has masked its detection. Another postulated etiology arose from the finding of squamous differentiation within colorectal adenomas; William., *et al*. found separate villous adenoma containing both invasive squamous and adenocarcinoma.

Pathogenesis

Underlying etiology remains unclear. The theory of chronic inflammation leading to squamous metaplasia and subsequent carcinoma is one of the most prominent theories. This concept is based on the fact that irritation and inflammation can lead to a change in the epithelial lining, inducing metaplasia. Pluripotent mucosal stem cells are capable of multidirectional differentiation. Keratin profiles vary among epithelia but remain constant in neoplastic transformation Rectal SCC and adenocarcinoma stain for cytokeratin CAM5.2, which suggests a common cellular origin for rectal cancer subtypes, which leads to the idea that the rectum's mucosal lining contains a common pluripotent endodermal stem cell, which under certain condition undergoes squamous metaplasia to better withstand the injury of the inciting cause.

Clinical presentation

Patients with rectal SCC present similarly to patients with adenocarcinoma, with the most common symptom being rectal bleeding, followed by altered bowel habits, abdominal pain, and weight loss, over a period of weeks to months. Many rectal SCCs are an extension of an anal or gynecological carcinoma, therefore proper diagnosis is important. Certain criteria have been established for the diagnosis of primary SCC. In 1979, Williams., *et al*. [10] established diagnostic criteria, which include: 1) primary SCC from distant sites must be excluded; 2) the bowel tumor must not have a squamous lined fistulous tract; 3) the tumor cannot be a proximal extension of SCC of the anus, and 4) the tumor must be histologically confirmed [11].

The definitive diagnosis of rectal SCC is confirmed by performing a complete colonoscopy with biopsies of any abnormalities. Endoscopically, Rectal SCC can be demonstrated in different appearances depending on the stage, polyp, plaque, ulcerated lesion, or an obstructing mass. Immunohistochemistry may be used to aid in characterizing the lesion when the diagnosis remains unclear histologically, especially in poorly differentiated tumors.

Staging

Staging accurately is important to dictate prognosis and guide treatment. It involves primary tumor evaluation and assessment of regional and metastatic disease. MRI (for T3/4 tumors and local nodal involvement) and Endoscopic Ultrasound (depth of tumor invasion) both have a role for loco-regional evaluation. MRI has become an increasingly useful tool for both structural pretreatment staging, and more importantly to determine the response of the tumor after treatment to guide for operative intervention.

In order to exclude metastatic disease, computed tomography of the chest, abdomen and pelvis should be routinely carried out. PET CT and PET MRI allow exclusion of non-rectal primary SCC that has metastasized to the rectum and defines the extent of primary diseases and nodal involvement, in addition to it being able to assess response by comparing pre- and post-treatment scans.

Treatment

The treatment of rectal SCC has traditionally been surgical; however, recently treatment approaches have been shifted towards definitive chemotherapy in view of its response and encouraging results. Classically for most rectal squamous cell carcinomas, either anterior resection or abdominoperineal resections have been performed. The choice of the procedure is dependent upon several factors, including the location and depth of the tumor; with the trend towards anterior resection being more favorable which is likely reflected toward sphincter preservation. Moreover, the use of a stoma is an option for patients presenting with an obstructing tumor.

Chemoradiation

Following the validation of Nigro's protocol (5-FU-based chemotherapy concurrently with radiation and addition of either mitomycin or porfiromycin) in multiple randomised controlled trials, it has now become the accepted standard treatment for anal SCC.; with surgery being consigned to a salvage role [12,13]. In light of this development, there has been an increasing trend for the use of chemoradiation either as definitive treatment or in conjunction with surgical resections. Targeted therapy such as epidermal growth factor and vascular endothelial growth factor receptor inhibitors did not provide any additional benefit to chemotherapy [14,15]. One case report reported successful treatment of primary esophageal SCC with colonic metastasis by chemoradiotherapy followed by chemotherapy with S-1 and cisplatin. One early-phase study showed promising activity with PD-1 inhibitor immunotherapy and may eventually change the treatment options for metastatic esophageal squamous cell carcinoma [16].

Conclusion

Squamous cell carcinoma of the rectum is a rare disease and likewise, metastatic esophageal SCC to the rectum is an extremely exceptional finding; therefore the close multi-disciplinary approach, including the proper comparative histomorphological assessment between the two remote lesions have helped to overcome this clinically unexpected scenario and proceeded with the most proper management approach.

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