Case Report

Running Title: Adenosquamous Colonic Carcinoma

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Adenosquamous Carcinoma of the Colon: A Report of Two Cases and Literature Review

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Abstract

Colon cancer is one of the commonest tumours in the world. Although most colon cancer patients are colonized by adenocarcinoma, some other pathologies such as adenosquamous carcinoma are rarely encountered. We present two patients with right colon adenosquamous carcinoma. Both patients were males, and both suffered a node-positive disease. Furthermore, one of them developed recurrence 7 months after initial radical surgery, despite formal colon adjuvant chemotherapy given. In conclusion, the patients with adenosquamous colon cancer are a subgroup with a worse prognosis, and questionable response to the conventional chemotherapeutic regimens as FOLFOX (flourouracil, leucoverin, and oxaloplatin) and CAPEOX (capecitabine and oxaloplatin).

Keywords: Carcinoma, Adenosquamous, Colon Neoplasms

Introduction

Colorectal cancer is the third most commonly diagnosed cancer in the world and the second cause of cancer death.[1] The most common pathological subtype of colon cancer is adenocarcinoma.[2] In contrast, rare pathological subgroups of colon cancer include adenosquamous carcinoma, sarcomas, lymphomas, and neuroendocrine tumors. 3 With a reported incidence of 2 percent to 4 percent for lung cancer and 0.38 percent to 10 percent for pancreatic carcinoma, adenosquamous carcinoma has been shown to occur in a variety of organs,

including the lung, pancreas, and colon. The least incidence was documented in the colon comprising approximately 0.1% of colon cancer.[4] Due to scarce reports, there are no concise data about presentation, clinical outcomes, and management of these patients.[5] Hence, we report two cases of colonic adenosquamous carcinoma, their management, and prognosis.

Case Presentation

The case report was approved by the institutional review board of the faculty of medicine Mansoura University (IRB-MFM) with code number R 22.04.1690.

Case 1

A 56-year-old man smoker who had previously had stomach discomfort visited our hospital. His medical and surgical background were irrelevant. Abdominal ultrasonography and computed tomography were used to assess his complaint (CT). The CT indicated an exophytic heterogeneously enhancing mass including the hepatic flexure and the upper third of the ascending colon as well as enlarged pericolic lymph nodes (LNs), coupled with a well-defined lengthy segment of mural thickening accompanied with enlarged pericolic lymph nodes (Figure 1).The patient performed a colonoscopy that revealed a fungating cauliflower mass at the hepatic flexure which was biopsied to reveal moderately differentiated squamous cell carcinoma that was confirmed by diffuse cytoplasmic positivity to immune histochemical stain CK 5/6 (Figure 2). Carcinoembryonic antigen (CEA) level was 10.61 ng/ml, while cancer antigen 19-9 was 0.6 u/ml. The case was discussed at the multidisciplinary tumour board (MDT) of our hospital, and surgery was decided.

An upper midline laparotomy approach was selected to perform right hemicolectomy along with complete mesocolic excision followed by end-to-end ileo-transverse hand-sewn anastomosis after exclusion of any peritoneal or hepatic metastasis. The patient experienced a smooth postoperative course.

Post-operative pathological assessment revealed malignant tumoural proliferation formed of malignant epithelial cells reaching down to the subserosa. These were arranged both as glandular elements lined by cells showing pleomorphism, hyperchromasia, with a moderate degree of atypia with detected mucin component. They were admixed with sheets of malignant squamous cells, entrenched in the desmoplastic stroma, with limited keratin pearl production (Figure 3). Since there were discrete rather than arbitrary configurations of both the malignant squamous and malignant epithelial components, adenosquamous carcinoma (composite type) was determined to be the cause. Dissected surrounding LNs showed infiltration in 2 out of 40 LNs by the same tumour tissue (TNM staging: pT3N1M0). The patient was subjected to 8 cycles of CAPEOX regimen after which he was maintained on follow up till writing this report, 15 months from starting the active treatment.

Case 2

A forty-nine years-old male patient with the irrelevant medical history, had a right hemicolectomy for adenosquamous carcinoma of the ascending colon. The histopathological examination revealed adenosquamous carcinoma infiltrating down to the subserosal fat with detected lymphovascular emboli and no detected perineural invasion. The adenocarcinoma component was positive for CK7 and CDX2, while the squamous component was positive for p63. Nine out of the 29 LNs that were evaluated had adenocarcinoma component infiltration. In addition to the free appendix, both surgical margins were devoid of tumor tissue. Stage IIIC of the AJCC staging was pT3N2aM0. The patient had six rounds of the FOLFOX treatment as adjuvant

chemotherapy. Unfortunately, 7 months after the surgery, the patient suffered from right lumbar pain. A PET CT was requested and revealed a well-defined cystic mass measuring 5.2 x 4.5 cm in the right iliac fossa showing increased tracer uptake (SUV = 15). This mass was seen inseparable from the right psoas major muscle, entangling the right ureter leading to right-sided hydroureteronephrosis and abutting the external iliac vessels. The serum creatinine was mildly elevated 1.7 mg/dl (normal range 0.6-1.3 mg/dl), and serum CEA was elevated 7.29 ng/ml (normal range 0-4.7 ng/ml).

A CT-guided core needle biopsy was requested and revealed moderately differentiated adenocarcinoma focally positive for CK7 and CDX2, while CK20 was non-conclusive suggestive of a local recurrence of previous caecal adenosquamous carcinoma. In light of the patient's irresectable tumor, fast recurrence, and advanced primary illness, the MDT decided to provide the patient palliative treatment. They also spoke with urologists about inserting a nephrostomy tube for the hydroureteronephrosis and re-evaluating the patient's response. Unfortunately, follow-up on the patient was lost.

Discussion

The majority of colon carcinoma is adenocarcinoma, while adenosquamous carcinoma of the colon is considered exceedingly rare.[6] This rare entity comprises both adenocarcinoma and squamous cell carcinoma components with an increased tendency of metastasis and hence poorer prognosis.[7]

Though it is customary in >90% of colon cancer cases to express Ck20 & CDX2, and stain negative to CK20, it is accepted and reported that colon cancer can be positive for Ck7 in 10%-50% of cases according to Tuffaha et al.[8] This was the case in the second reported patient, where the tumour was CK7+ve.

Colonic adenosquamous carcinoma's pathophysiology is still poorly understood. In addition to squamous metaplasia as a result of persistent inflammation, squamous differentiation from pluripotent stem cells, and/or malignant squamous malignant transformation from unidentified basal cells were some of the possibilities put forward. Some authors hypothesized a connection between endometriosis, the human papilloma virus, and ulcerative colitis.[9, 10]

In their study, Nasseri et al., reported a female to male predominance in adenosquamous colonic carcinoma, unlike our report of two male patients. This pathology affected the caecum and ascending colon in more than 50% of their study patients which is consistent with the presentation pattern of our two reported patients. Furthermore, they found that 40% of adenosquamous colonic carcinoma patients presenting with stage IV disease.[11]

The mainstay of therapy for colonic adenosquamous carcinoma is surgical resection in the form of colectomy and mesenteric lymph node dissection. The recommended chemotherapeutic drug and the function of adjuvant chemotherapy are not yet standardized.[4] In our patients, right hemicolectomy with complete mesocolic excision was followed by adjuvant FOLFOX or CAPEOX protocol. Unfortunately, this was not effective, particularly in the second case who developed local recurrence 7 months after his primary surgery.

In their study, Frizelle et al. reported aggressive behaviour and a bad prognosis in colorectal adenosquamous carcinoma patients, especially those who presented with advanced disease stage.[12] The same results were stated by Masoomi et al., who highlighted the impact of advanced disease stage on the increased overall mortality.[3] Moreover, Nasseri et al. reported a

significant increased risk of death among adenosquamous colonic carcinoma patients who presented with adverse features as advanced disease stage, nodal metastasis and/or lymphovascular tumour emboli.[11] Both patients reported here had adverse features like advanced disease stage, nodal metastasis, and/or lymphovascular emboli.

Conclusion

In conclusion, adenosquamous carcinoma is a rare pathological subtype of colorectal cancer. Patients commonly present at the advanced disease stage. Surgical resection is the cornerstone in management since chemoradiation therapy is not standardized yet.

Informed Consent

Informed consent was obtained from all individual participants included in the study.

Conflict of Interest

None declared.

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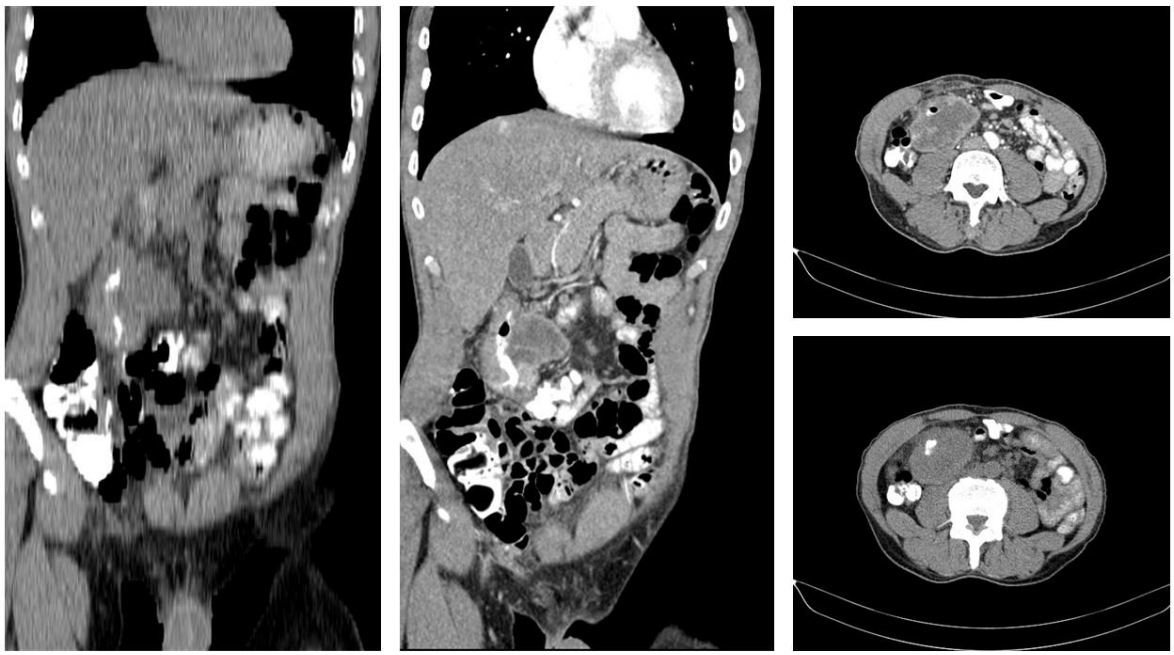

Figure 1. Sagittal and coronal sections of a post-contrast CT scan of the abdomen and pelvis showing a well-defined long segment of irregular circumferential wall thickening associated with significant luminal narrowing is seen involving the hepatic flexure as well as the related upper third of the ascending colon. It is associated with large extra-luminal exophytic heterogeneously enhanced mass extending posteromedial abutting related right psoas muscle.

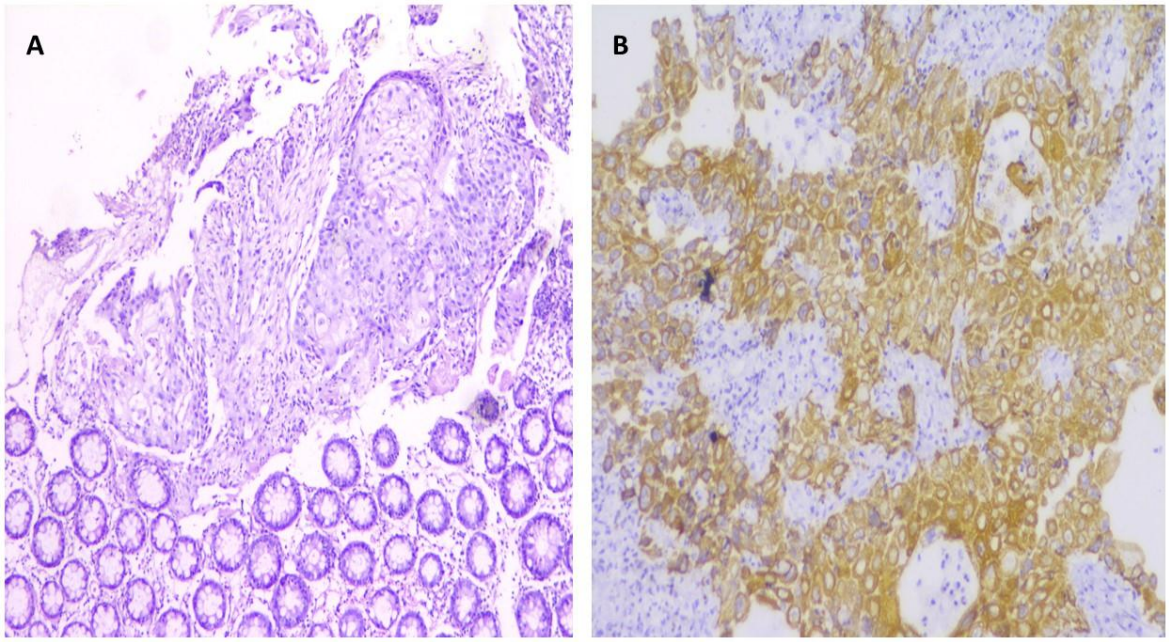

Figure 2. (A): Colonoscopic biopsy: the sheets of malignant squamous epithelial cells infiltrating lamina admixed with inflammatory infiltrate. These are lined by malignant pleomorphic squamous cells showing abundant eosinophilic cytoplasm and moderate atypia. Some cells show evident prickling (H & E, ×10). (B) Diffuse cytoplasmic positivity of tumour cells for CK5/6 (H & E, × 20).

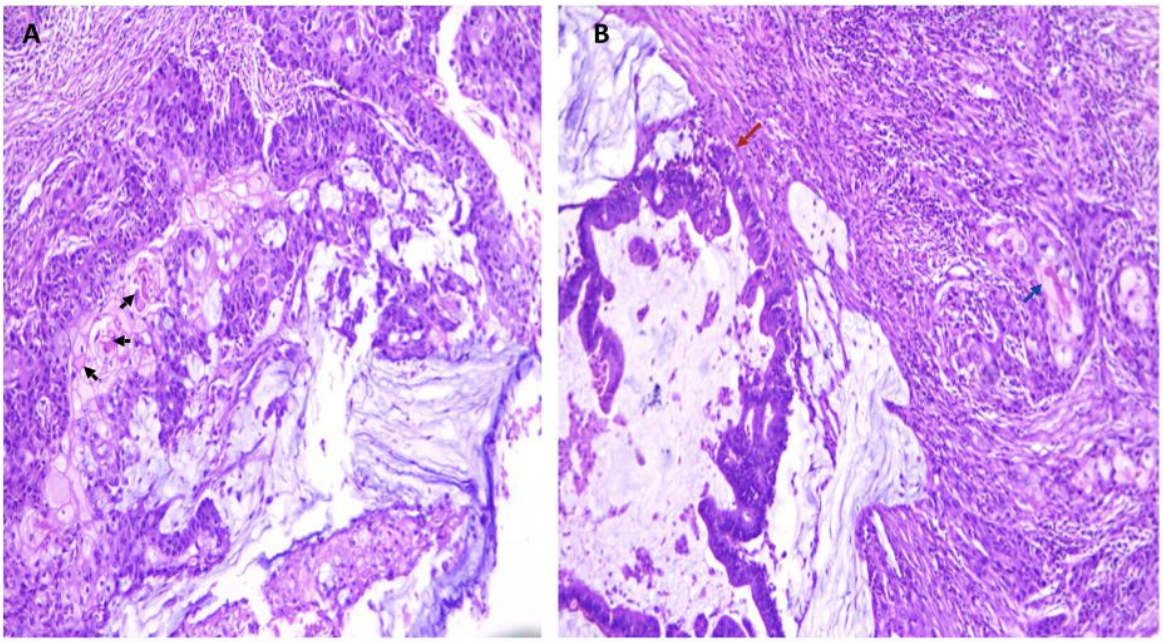

Figure 3. (A) The sheets of malignant squamous cells embedded in mucin pools and desmoplastic stroma (H & E, ×10). These are encased by sheets of malignant epithelial cells with minor glandular formation. Arrowhead shows poor keratin pearls. (B) Right; squamous morulas with surrounding desmoplasia, left; adjacent glands lined by malignant epithelial cells embedded in mucin pools (H & E, ×10).