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ABOUT COVER

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Primary sigmoid squamous cell carcinoma with liver metastasis: A case report

Xin-Yang Li, Gen Teng, Xing Zhao, Cui-Min Zhu

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Abstract

BACKGROUND

The pathological type of simple squamous carcinoma in colorectal malignancies is rare. Simple squamous cell carcinoma of the colorectum occurs most frequently in the rectum. The clinicopathological features and biological behaviors of squamous colorectal carcinoma are unclear, and its prognosis may be worse than that of simple adenocarcinoma. Studies on squamous colorectal cancer are currently limited to case reports, and there is no standard treatment protocol. Therefore, more case reports are required to fully understand squamous colorectal cancer.

CASE SUMMARY

We reported the case of a 56-year-old woman who complained of constipation for 2 years. Colonoscopy revealed a sigmoid colon tumor, and the pathological result of colonoscopy was squamous carcinoma. After completing the relevant assessment, the patient was clinically diagnosed with cT4aN0M0, stage IIB, and surgery was performed. Based on postoperative pathological results, the patient was diagnosed with pT4bN0M0, stage IIC. Six cycles of adjuvant chemotherapy were administered after surgery. Liver metastasis and abdominal wall mass were found more than 1 mo after the end of the last chemotherapy session. Targeted local treatment was not performed because the liver had multiple metastases, but I¹²⁵ particle implantation of the abdominal wall mass was performed. Two cycles of first-line chemotherapy were administered after the surgery. The patient underwent 14 mo of treatment and eventually died from the tumor.

CONCLUSION

Squamous carcinoma of sigmoid colon is a rare tumor with unclear pathogenesis. Its clinicopathological diagnosis should be paid close attention.

Key Words: Colon malignancies; Sigmoid colon; Squamous carcinoma; Liver metastases; Case report

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Core Tip: Simple squamous cell carcinoma of colorectal cancer is very rare, especially when it occurs in the sigmoid colon. Squamous colon cancer appears to have a worse prognosis than adenocarcinoma and there are no standard treatment options. The case also had liver metastases, which may also have some impact on the prognosis. We need more reports to understand its prognosis and treatment.

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INTRODUCTION

Colorectal malignancies are among the most common malignancies worldwide[1], and their most common pathological type is adenocarcinoma[2], followed by adenosquamous carcinoma. Squamous carcinoma alone is rare, accounting for approximately 0.1 to 0.25 per 1000 of all colorectal cancers[3]. Squamous cell carcinoma (SCC) of the colon was first reported in the German literature published in 1919[4]. Ozuner *et al*[5] reported 11 cases of squamous carcinoma of the colon, of which eight were squamous carcinoma of the rectum, two were squamous carcinoma of the ascending colon, and only one was squamous carcinoma of the sigmoid colon. In 2019, researchers[6] compiled the Surveillance, Epidemiology, and End Results (SEER) database for the period 1998–2012 and analyzed its clinical staging and other characteristics. A total of 464 patients were diagnosed with squamous carcinoma of the colon, of which only 50 (10.8%) patients had squamous carcinoma of the colon. The pathogenesis of colonic squamous carcinoma is unclear, and its prognosis is worse than that of simple adenocarcinoma [7]. Most studies have been limited to case reports, and there are no standard treatment protocols.

Herein, we reported a case of primary SCC of the sigmoid colon with liver metastasis. This study aimed to analyze and study the characteristics of this case and summarize the clinical characteristics, pathological features, and treatment of squamous carcinoma of the colon to improve our understanding of such disease.

CASE PRESENTATION

Chief complaints

A 56-year-old woman presented to our gastrointestinal surgery clinic in March 2019 who complained of constipation for 2 years.

History of present illness

The patient complained of a history of constipation, with stools 3-5 d/once, requiring oral laxatives for 2 years.

History of past illness

The patient was previously physically fit.

Personal and family history

Personal and family histories were not exceptional.

Physical examination

The patient had no positive signs.

Laboratory examinations

Laboratory tests were unremarkable (Table 1).

Table 1 The laboratory examination before surgery

Project name	Result	Unit	Reference range
White blood cell count	17.08	10 ⁹ /L	3.5-9.5
Red blood cell count	4.00	10 ¹² /L	3.8-5.1
Hemoglobin	118	g/L	115-150
Platelet count	390	10 ⁹ /L	125-350
Alanine aminotransferase	18.8	U/L	0.00-50.00
Aspartate aminotransferase	14.54	U/L	0.00-40.00
Total bilirubin	10.96	μmol/L	3.00-22.00
Urea nitrogen	2.81	mmol/L	2.50-6.10
Creatinine	53.6	μmol/L	46.00-92.00

Imaging examinations

The patient underwent computed tomography examination, which confirmed the presence of an irregular soft tissue mass located in the left lower abdomen with unclear borders and nonuniform density (Figure 1A) and the absence of metastatic lesions in the liver (Figure 1B). Total colonoscopy was advised, which indicated the presence of an ulcerated mass with infiltrative growth in the colon approximately 30 cm from the anus (Figure 2). Pathological examination of the tissue obtained by colonoscopy revealed squamous carcinoma (Figure 3).

Pathologic evaluation

A biopsy was performed at colonoscopy, and histology showed squamous carcinoma.

FINAL DIAGNOSIS

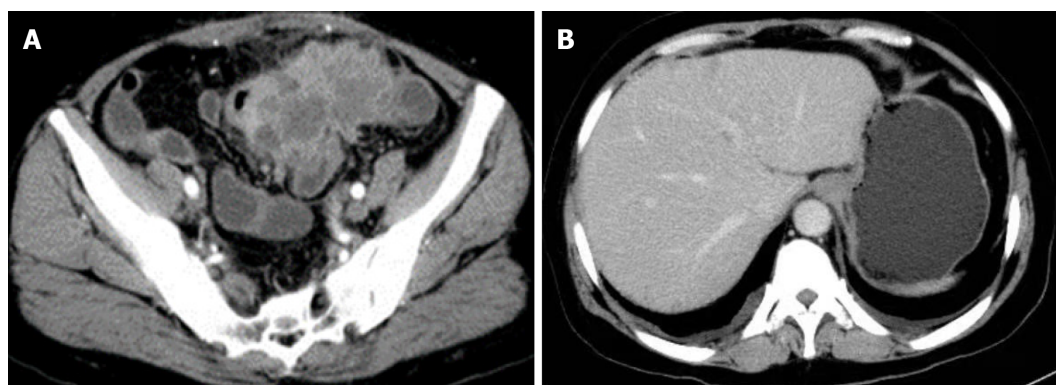
The patient underwent combined partial ileal and anterior peritoneal resection for sigmoid colon cancer on March 28, 2019. The sigmoid colon was incised 12 cm from the proximal edge and 6 cm from the distal edge of the tumor. Intraoperatively, the mass invaded the anterior peritoneum and ileum approximately 40 cm from the ileocecal region and was resected.

The specimen was embedded in paraffin and cut into 4-μm-thick sections. Hematoxylin and eosin staining was performed, and the sections were examined microscopically at the Pathology Department of the Affiliated Hospital of Chengde Medical College. Histologically, the tumor cells were arranged in irregular nest-like clusters, the tumor cells were ill-defined, the nucleoplasm ratio was disordered, the nuclei were large and densely stained, the polar direction disappeared, the nuclear membrane was clear, and the chromatin was concentrated, consistent with the diagnosis of intermediate-to-low differentiated squamous carcinoma (Figure 4A and B). The cancerous tissue had invaded the entire layer of the intestinal wall (Figure 5), and no residual cancer was observed on the upper and lower incision margins. Immunohistochemically, the cancer cells were negative for C-erbB-2, bcl-2, COX2, CDX2 (Figure 6A), PS2, and CK7. These cells were positive for MSH2, PMS2, MSH6, MLH1, P53, EGFR, P40 (Figure 6B), CK5/CK6 (Figure 6C), D2-40, CD34, and TOP2. The Ki-67 proliferation index was 70%.

Eight lymph nodes were examined, and no lymph node metastasis was observed on postoperative pathology. The results of the preoperative examination suggested no distant organ metastasis, such as liver, lung, or brain metastasis. Combining the above information on histopathological specimens, lymph nodes, and distant metastases, the stage of sigmoid squamous carcinoma was determined to be pT4bN0M0, stage IIC.

TREATMENT

The patient was diagnosed with early-stage colon cancer, and surgical treatment was preferred, without prior systematic treatment. After surgical treatment, the patient received six cycles of postoperative adjuvant chemotherapy.



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Figure 1 Preoperative computed tomography enhancement scan of the abdomen. A: An irregular soft tissue mass located in the left lower abdomen with unclear borders and nonuniform density; B: No metastatic lesions in the liver.



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Figure 2 Colonoscopy showing an ulcerated mass with infiltrative growth observed in the colon approximately 30 cm from the anus.

OUTCOME AND FOLLOW-UP

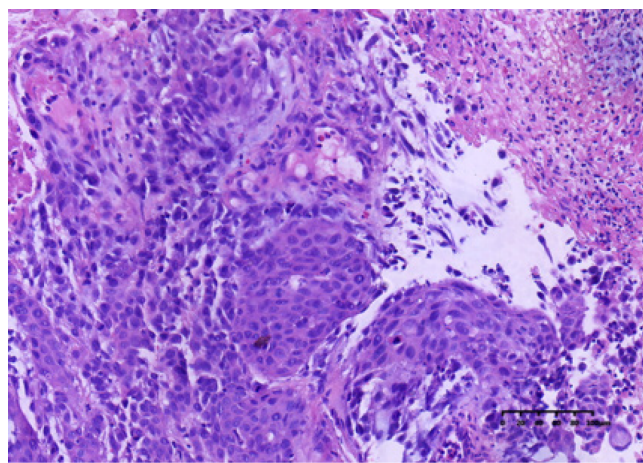
Postoperatively, the patient recovered well, without complications. Routine chemotherapy and regular follow-up were performed postoperatively. On November 10, 2019, multiple liver metastases (Figure 7A) and an anterior pelvic mass (Figure 7B) were observed. A liver biopsy was performed immediately after the discovery of liver metastases, and the pathological results showed that it was a metastatic SCC derived from the liver (Figure 8). Genetic testing revealed the presence of somatic mutations (Table 2). Unfortunately, the liver cannot be surgically removed because of multiple metastases. The patient did not undergo radiofrequency or ablation therapy. However, I¹²⁵ seed implantation was performed on the abdominal wall mass. After seed implantation, two cycles of first-line chemotherapy were administered. By May 2020, the patient had died of the tumor. The patient's overall survival rate was 14 mo.

DISCUSSION

SCC occurs most often in areas covered by squamous cells; therefore, it rarely occurs in organs without squamous cell coverage. The colon is not covered by squamous epithelium and is dominated by glandular epithelium. Therefore, SCC in the primary colon is significantly rare, with an incidence of approximately 0.025-0.1 per 1000 colon cancers[8]. Regarding the high incidence age of colorectal squamous carcinoma, Donato-Brown *et al*[6] reported that the average age for the entire cohort in the SEER database was 60.7 ± 13.7 years, and the median age of onset of colonic SCC was 55-60 years according to the literature[9-15]. SCC can occur in any part of the colorectum[5,16]; the majority of them are located in the rectum (93.4%), followed by the right hemicolon (3.4%), and SCC in the left hemicolon is extremely rare. The first reported SCC of the colon in China also occurred in the ascending colon[17].

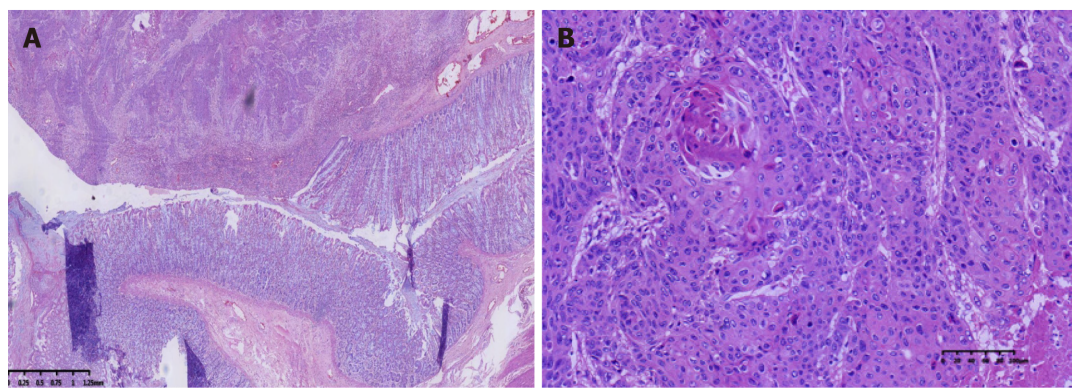
Table 2 The genetic testing report of liver metastases				
Gene name	Type of mutation	Exon number	Variant site	Mutation frequency
FBXW7	SNV	Exon11	p.S550R	2.21%
TP53	SNV	Exon7	p.S241Y	51.98%
KRAS	SNV	Exon2	p.G12D	55.95%
PTEN	SNV	Exon5	p.G127E	56.89%

SNV: Single nucleotide variation.



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Figure 3 Hematoxylin and eosin staining of tissue specimens taken for colonoscopy. Anisocytic tumor cells in a striated or scattered pattern (hematoxylin and eosin, 20 ×).

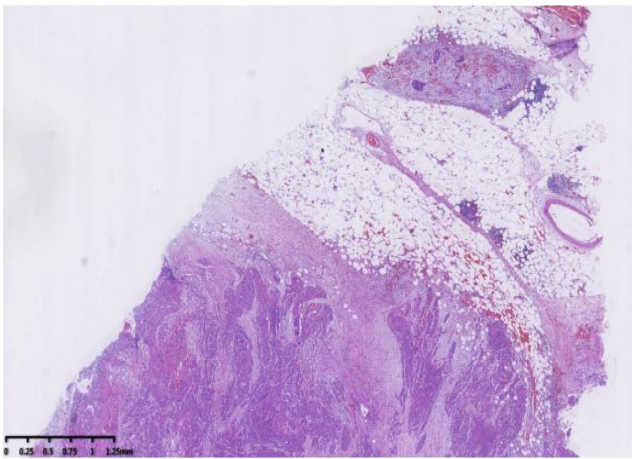


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Figure 4 Hematoxylin and eosin staining of tissue specimens taken for surgery. A: Normal structure and canceration of the sigmoid colon (hematoxylin and eosin, 2 ×); B: Postoperative pathological image (hematoxylin and eosin, 20 ×).

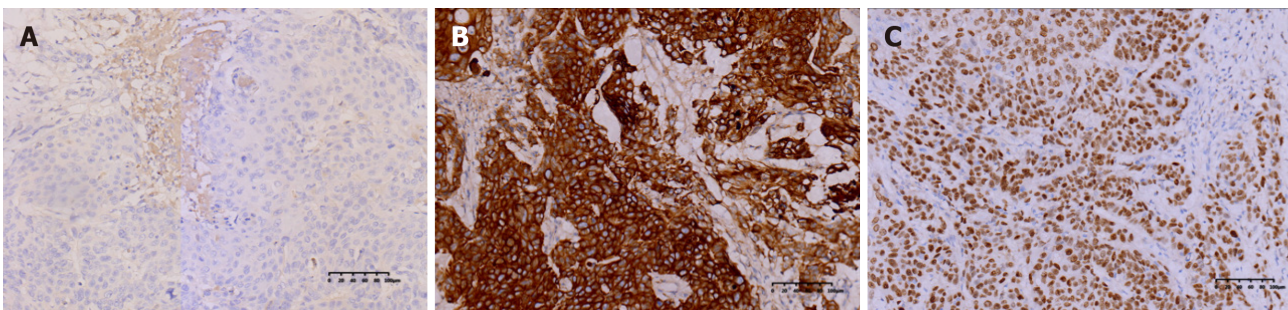
The clinical manifestations of patients with colorectal squamous carcinoma are similar to those of adenocarcinoma, mainly including abdominal pain, blood in the stool, and change in bowel habits, and a few may present with acute abdominal and intestinal obstructions[9]. We reported a case of simple squamous carcinoma of the sigmoid colon, the main clinical manifestation of which was chronic constipation without blood in the stool or abdominal pain.

The possible mechanisms of colonic squamous carcinoma pathogenesis are currently reported in the literature with the following possibilities. First, squamous metaplasia of the glandular epithelium is commonly caused by chronic inflammation due to radiation therapy[18], schistosomiasis infection[19], and inflammatory bowel disease[17], and squamous cell metaplasia is caused by continuous chronic stimulation of the glandular epithelium, which in turn leads to cell degeneration and carcinoma, as reported by Cheng *et al*[20] in a 51-year-old female patient with squamous colorectal cancer who had a



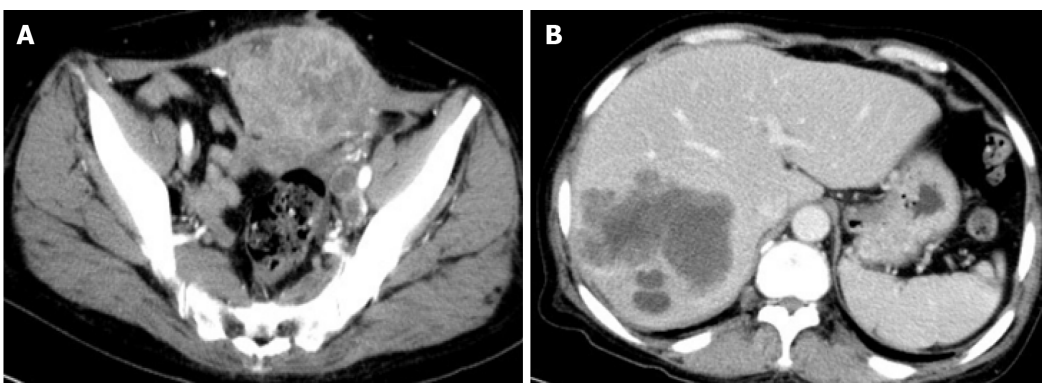
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Figure 5 The cancer tissue invades the full thickness of the intestinal wall (hematoxylin and eosin, 2 ×).



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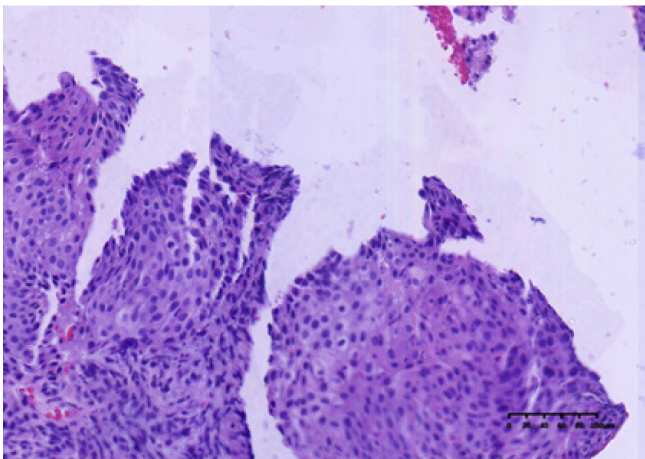
Figure 6 Immunohistochemical staining of CDX2, CK5/CK6, and P40. A: The cancer cells were negative for CDX2 [immunohistochemistry (IHC), 20 ×]; B: The cancer cells were positive for CK5/CK6 (IHC, 20 ×); C: The cancer cells were positive for P40 (IHC, 20 ×).



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Figure 7 Computed tomography enhancement scan of the abdomen 7 mo postoperatively. A: Irregular soft tissue mass and nodular shadow were observed in the anterior pelvis, with inhomogeneous enhancement, posterior downward extrusion of the bladder, and indistinct demarcation with the anterior peritoneum and muscles; B: Multiple nodules of variable sizes and mass-like hypointense shadow were observed in the liver.

history of ulcerative colitis for more than 10 years with a long history of hormonal therapy. Second is the pathological process of undifferentiated cell proliferation, squamous differentiation, and carcinogenesis. Comer *et al*[21] suggested that basal cells undergo proliferation and repair after colorectal epithelial damage, whereas repeated destructive effects cause basal cells to lose their normal differentiation ability and produce adenocarcinoma, squamous carcinoma, or adenosquamous carcinoma. Michelassi *et al*[22] proposed that SCC originates from undifferentiated basal cells after mucosal damage proliferation and malignant transformation. Third, adenoma or adenocarcinoma cells differentiate into squamous carcinoma, and squamous cells have been gradually recognized in colonic adenomas[23].



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Figure 8 Metastatic squamous cell carcinoma from the liver (hematoxylin and eosin, 20 ×).

Cramer *et al*[24] reported three cases of colonic adenomas in which multipotential reserve cells were found to differentiate into squamous epithelium, and primary colonic SCC may originate from squamous cell differentiation and carcinoma of cells within the adenoma. Fourth, considering ectopic ectodermal cell nest carcinoma, Gooneratne *et al*[25] reported a case of SCC of the sigmoid colon originating from a malignant teratoma of the ovary. Fifth, residual implantation of squamous cell epithelial cells is more common due to trauma and surgery[26].

The following conditions should be met to establish the diagnosis of colorectal SCC[27]: first, consistent with the pathological features of SCC without adenoid differentiation; second, ruling out the possibility of metastasis or direct invasion of other tissues or organs by SCC; third, ruling out the possibility of upward extension of SCC of the anal canal to the lower rectum; and fourth, absence of long-term persistent squamous cell epithelium-lined fistula in the intestinal canal where the tumor is located.

In this case, the tumor was 30 cm away from the anal verge, excluding cloacogenic embryologic nests as origins of the SCC. The patient had no specific past medical history, no evidence of SCC on imaging, and no colonic fistula formation. After three pathological examinations, both the primary lesion and liver metastases showed simple SCC on hematoxylin and eosin staining. Positive AE1/AE3 suggests an epithelial origin tumor; positive p40 and CK5/CK6 suggest SCC, negative CDX2 rules out the possibility of adenocarcinoma; and negative CGA and Syn rule out neuroendocrine origin. Immunohistochemistry was consistent with the pathology of primary SCC.

Commonly used treatments for colorectal cancer include surgery, radiotherapy, and chemotherapy. Owing to its extremely low incidence rate, there is no clear standard treatment plan for SCC. Some case reports have suggested chemoradiotherapy as the initial treatment and surgery as the treatment in case of poor chemotherapy effect or tumor recurrence because chemoradiotherapy can effectively control rectal squamous carcinoma well[28,29]. Zhao *et al*[13] reported a patient with ascending colon squamous carcinoma combined with rectal adenocarcinoma who received two cycles of neoadjuvant chemotherapy based on gemcitabine, combined with oxaliplatin and capecitabine, and experienced disease stabilization. Surgery was performed in this patient. The original regimen was continued for six cycles of chemotherapy after surgery, and progression-free survival exceeded 10 mo after treatment.

SCC of the colon is rare; the sigmoid colon is even rarer, and its treatment is mostly referred to as adenocarcinoma of the colon. We reported the case of a patient with squamous carcinoma of the sigmoid colon who developed liver metastases and pelvic metastases 7 mo after surgery and postoperative chemotherapy treatment, which showed poor sensitivity to conventional chemotherapy regimens for colorectal adenocarcinoma. Therefore, summarizing the case characteristics and treatment experience of patients with colonic squamous carcinoma and determining a more suitable chemotherapy regimen for colonic squamous carcinoma to improve the survival time of such patients are the main issues to be explored in the future.

CONCLUSION

Colon SCC, especially sigmoid colon SCC, is one of the rare lesions encountered by surgeons and pathologists. Due to its rarity, it is easily misdiagnosed. Here, we reported the case of a patient with sigmoid SCC at stage IIC (pT4bN0M0). Colon SCC appears to have a worse prognosis and no standard treatment options; therefore, determining the accurate diagnosis and appropriate management of SCC is

important.

FOOTNOTES

Author contributions: Li XY was responsible for follow-up of the patient, reviewed the literature and contributed to drafting the manuscript; Teng G was responsible for follow-up of the patient; Zhao X was the pathologist involved in the patient's diagnosis; Zhu CM was responsible for revision of the manuscript for important intellectual content, contributed to manuscript drafting and revision; all authors approved the final version of the paper prior to submission.

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