Primary Squamous Cell Carcinoma of the Small Intestine: Pathogenesis and Clinical Features

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Relative to the length and surface area of the gastrointestinal tract, malignant tumors of the small intestine are remarkably rare, with a global incidence of <1 per 100,000 population.[1] Among the forty different histological subtypes of small intestinal cancers, primary squamous cell carcinoma (SCC) is exceptionally rare with only occasional case reports in literature. The present study reported a case of primary SCC of the small intestine and reviewed all cases reported in English literature to provide a systematic overview of this rare disease.

A 49-year-old male doctor presented with abdominal distension, anorexia, and weight loss of 5 kg for 1 month. Laboratory examinations revealed slight anemia with hemoglobin of 116 g/L (normal 120–160 g/L), and positive fecal occult blood. Tumor markers were not significant. Enhanced computed tomography (CT) revealed markedly thickened intestinal wall from the third portion of the duodenum to the proximal jejunum, with the mesenteric side forming a mass which measured 5.1 cm × 5.8 cm × 3.8 cm. However, the lumen of the affected small intestine was preserved, and the nearby superior mesenteric vessels were suppressed anterior without signs of invasion [Figure 1a-1d].

A transretroperitoneal duodenal biopsy was performed. Histopathological examination revealed nests of dysplastic squamous carcinoma with keratinization [Figure 1e]. Immunohistochemical analysis showed that the tumor cells were positive for D2-40, p40, and p63, and negative for hematopoietic progenitor cell antigen CD34, cytokeratin (CK) 7, and CK20. To exclude possible metastasis from primary malignancies of other organs, positron emission tomography (PET)/CT was undertaken, which did not show any increased fluorodeoxyglucose (FDG) uptake other than in the mass of the duodenum and proximal jejunum with a maximum standard uptake value of up to 20.5 [Figure 1f].

The patient was diagnosed with primary SCC of the small intestine. Due to the size and location of the tumor, radical resection was considered impossible. Therefore, palliative chemotherapy combined with radiotherapy was recommended. Unfortunately, the patient refused the regimen and was lost to follow-up.

Primary SCC of the small intestine is an extremely rare malignant tumor. As far as we know, the first case of primary SCC of the small intestine was reported in 1981 by Adair and Trowell,[2] who described a 65-year-old man with SCC arising in a duplication of the small intestine. To date, there are 22 patients reported in English literature with primary SCC of the small intestine confirmed either by surgery or by biopsy, including the case reported in the present study.

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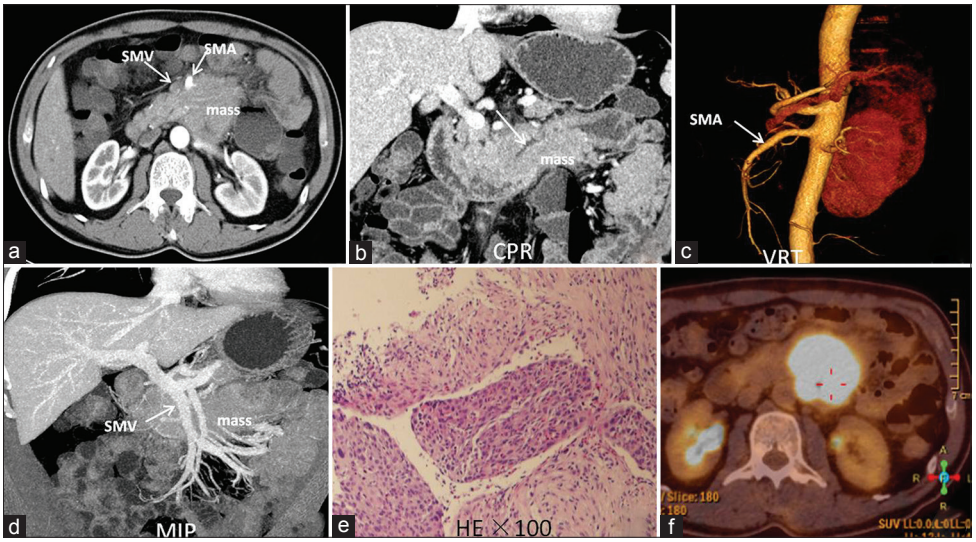

Figure 1: Primary squamous cell carcinoma of the small intestine. Axial CT image of arterial phase (a) and CPR of portal phase (b) revealed markedly thickened intestinal wall from the third portion of the duodenum to the proximal jejunum forming a mass-like lesion. The lumen was preserved (arrow in b). VRT (c) and MIP (d) showed that the SMA and SMV adjacent to the tumor were suppressed and not invaded. Nests of dysplastic squamous carcinoma with keratinization were seen within fibrous tissue, stained with H and E, ×100 (e). PET/CT (f) illustrated that the lesion surrounding the duodenum and proximal jejunum had highly active FDG uptake with an SUVmax of up to 20.5. CT: Computed tomography; PET: Positron emission tomography; CPR: Curved planar reconstruction; MIP: Maximum intensity projection; SMA: Superior mesenteric artery; SMV: Superior mesenteric vein; VRT: Volume rendering tomography.

Of the 22 patients, the male:female ratio was 1:1.4, and the median age was 61 years (28–80 years). The tumors were located in the duodenum, jejunum, ileum, duplication, and diverticula of the small intestine, with the duodenum the most affected portion (63.6%, 14/22), especially the second portion of the duodenum (50.0%, 11/22). Most symptoms were chronic and nonspecific depending on the site of the tumor while acute gastrointestinal bleeding and perforation were also present. Sixteen patients received radical surgery; chemotherapy was given to four patients and radiotherapy to three patients. Of the 11 patients with follow-up results, 6 (54.5%) died.

The pathogenesis of primary SCC of the intestine is unclear as the small intestine is normally devoid of squamous cells. There are four possible mechanisms: (1) malignant transformation of heterotopic squamous epithelium. A patient with primary SCC in the duplication supports this theory.[2] (2) Pluripotent stem cells differentiate to malignant squamous cells. This was supported by an interesting case reported by Barnhill *et al*.[3] where the same tumor in the duodenum was composed of adenocarcinoma, malignant squamous cells, and neuroendocrine elements. (3) Squamous metaplasia due to chronic mucosal damage undergoes malignant change. The pathology of the tumor described by Friedman *et al*.[4] showed pronounced chronic reactive inflammation adjacent to the tumor, and squamous metaplasia was also noted. (4) Adenocarcinoma transformed into adenosquamous carcinoma and eventually to SCC. According to the histological results, the specimens from all 22 patients did not show components of adenocarcinoma or adenosquamous carcinoma; therefore, this proposed mechanism seems less likely.

To diagnose primary SCC, metastasis must be excluded. However, it is quite difficult to differentiate between the two, both grossly and microscopically. Medical history is the first important clue. A history of SCC in other organs may indicate metastasis, especially diffuse metastases in other parts. Nevertheless, a history of malignancy does not necessarily mean that the lesion in the small intestine is metastatic when the primary malignancy is at an early stage, and the time interval is long. Second, in histological examinations, most metastatic tumors are located submucosal while the mucosa is involved in most primary SCCs. However, this is not reliable, as metastases may involve the mucosa, while the mucosa may be intact in primary SCC. In addition, the fact that metastatic SCCs do not reflect their primary tissue expression profile makes immunohistochemistry less helpful. Third, PET/CT is a useful tool for differentiating the two conditions. Our case underwent FDG-PET/CT scanning which showed no other sites with positive FDG uptake, supporting the diagnosis of primary SCC.

Imaging plays an important role in primary SCC of the small intestine in terms of locating, staging, and helping surgeons to determine whether the tumor is resectable. Upper gastrointestinal series may show indirect signs of the mass, including compression, constriction, filling defect, and an intraluminal niche.[4] The tumors, adjacent organs, vessels, and lymph nodes are clearly observed on enhanced CT. Nowadays, multidetector spiral CT can generate thin slice images with a slice thickness of 1 mm, and enable multiple reconstructions, such as multiplanar reconstruction, three-dimensional reconstruction, and CT angiography. Magnetic resonance imaging was only used in one case,[5] which showed a hypointense signal both on

T1- and T2-weighted images. The tumor showed slight enhancement on postgadolinium examination.

In conclusion, we reported a case of primary small intestinal SCC. A better understanding of the pathogenesis and clinical features of this disease would be helpful in optimizing early diagnosis and treatment of this tumor.

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Conflicts of interest

There are no conflicts of interest.

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