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CASE REPORT

Cytomegalovirus-associated gastric ulcer: A side effect of steroid injections for pyloric stenosis

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Abstract

The local injection of triamcinolone acetonide (TA) is effective in preventing pyloric stenosis and deformity following large endoscopic submucosal dissection (ESD). However, because of its long-acting nature, TA can induce long-term local immunosuppression and subsequent adverse events. We report a case of a cytomegalovirus (CMV) ulcer that formed only at the TA local injection site. A 68-year-old man underwent ESD to treat early gastric cancer that formed over the pylorus. The lesion extended to the duodenum, and an artificial ulcer covered more than two-thirds of the circumference of the pylorus. To prevent pyloric stenosis, TA was locally injected into the ulcer floor. On day 12, a deeper ulcer 10 mm in diameter was discovered in the center of the post-ESD ulcer. Biopsies revealed large cells with intranuclear inclusion bodies, which stained positive for the anti-CMV antibody. Local TA injections are useful, however, CMV ulcer might occur as adverse events.

Key words: Pyloric stenosis; Local triamcinolone acetonide injection; Local immunosuppression; Cytomegalovirus-associated ulcer; Adverse events

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INTRODUCTION

Endoscopic submucosal dissection (ESD) for early gastric cancer was developed to resect larger lesions *en bloc*[1-4]. ESD has an advantage over endoscopic mucosal resection in that it enables *en bloc* tumor removal[5-8]. However, ESD creates a large artificial ulcer that can lead to gastric stenosis[9]. In recent years, the local injection of triamcinolone acetonide (TA) has reportedly prevented post-ESD esophageal stricture, pyloric stenosis, and deformity following large ESDs because TA promotes the formation of granulation tissue at an early stage in the healing process, which leads to gastric mucosa regeneration[10-12]. However, because of its long-acting nature, TA can induce long-term local immunosuppression and can cause subsequent adverse events. We report a case of cytomegalovirus (CMV) ulcer formation that occurred only at the local TA injection site. This is the first case report of a side effect of local TA injection after treatment of an ESD ulcer floor in a non-compromised host.

CASE REPORT

A 68-year-old man underwent ESD to treat early-stage gastric cancer that was located over the pylorus (Figure

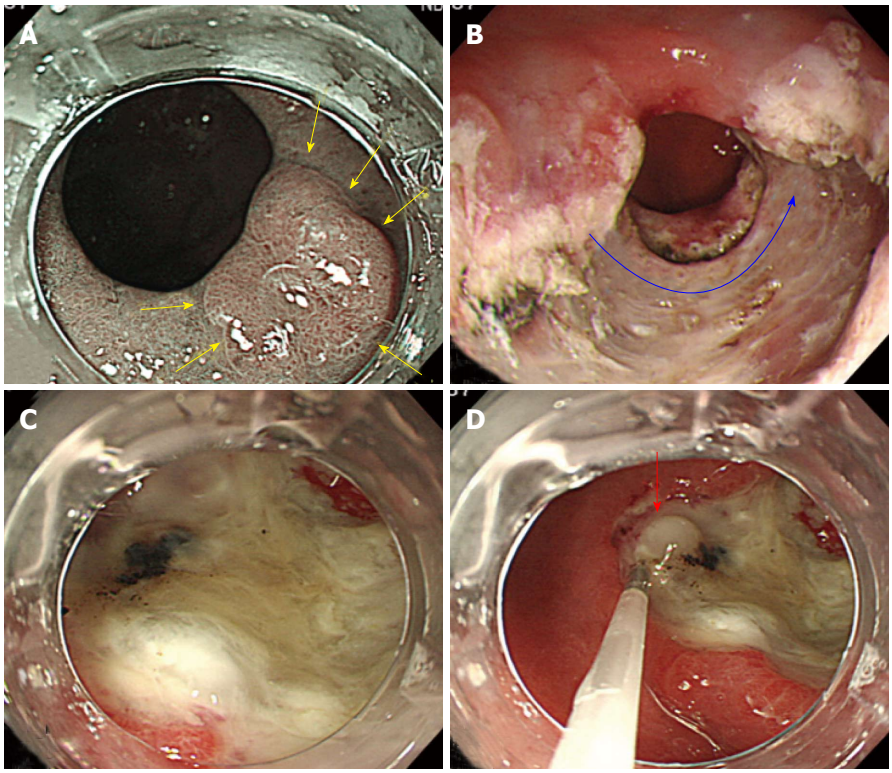

Figure 1 Endoscopic findings of tumor, post-endoscopic submucosal dissection ulcer and triamcinolone acetonide injection. A: An narrow band imaging endoscopic image reveals a flat, early gastric cancer lesion extending over the gastric outlet to the pylorus (yellow arrows); B: A post-endoscopic submucosal dissection artificial ulcer covering two-thirds of the circumference of the pylorus (blue curved arrow); C: The ulcer floor covered by a thick layer of white moss; D: Triamcinolone acetonide (2 mL) was injected locally at each site (red arrow).

1A). The lesion partially extended to the duodenum, and an artificial ulcer that formed after dissection covered over two-thirds of the pylorus circumference (Figure 1B). As routine pre-ESD examination, we conducted serology test, electrocardiogram, respiratory function test, abdominal ultrasound examination and computed tomography. These results indicated no underlying disease. To prevent pyloric stenosis, TA was locally injected into the ulcer, which was covered with white moss (Figure 1C) in 5-mm intervals [0.2 mL (2 mg)] at each site, on postoperative day 5 (Figure 1D). On day 12, abundant granulation tissue had formed over the ulcer, but another deeper ulcer approximately 10 mm in diameter was discovered centered in the post-ESD ulcer (Figure 2A). Biopsies that were conducted from the margin of the deeper ulcer revealed large cells with intranuclear inclusion bodies (Figure 2C) that stained positive for anti-CMV antibody staining (Figure 2D). As the patient wasn't a compromised host and had no other underlying disease, we thought the CMV activity of the ulcer floor was limited and focal. The CMV ulcer was occurred under focal immunosuppressive condition by TA. We considered after TA effect would subside about for 14 d, the CMV activity would decrease and the ulcer healed. We conducted frequent follow up endoscopy at POD12, 20 and 30, and confirmed negative conversion of CMV by serology test and histopathological examination. The deeper ulcer improved gradually (Figure 2B), and on day 20, the biopsies were negative for anti-CMV antibody staining. The post-ESD artificial ulcer healed without any pylorus stricture.

DISCUSSION

Some clinical studies have recommended administration of oral prednisolone[10] and local TA injection into post-ESD artificial ulcers[11] in order to prevent severe esophageal stenosis. The beneficial effects of this procedure were introduced at the Conference of Japan Gastroenterological Endoscopy in April 2009, and some clinical trials reported on the efficacy of local TA injections and oral prednisolone administration. After these reports, we reported that local TA injection into the floor of a post-ESD artificial gastric ulcer promotes the formation of granulation tissue in an early stage of the healing process, which leads to regenerated gastric mucosa without mucosal convergence or gastric deformity[12]. As our previous report, we conducted local steroid injection into post-ESD artificial ulcers to 21 patients and analyzed them according to the protocol, there were no complications. So, this case was the first case of CMV-associated ulcer development related to the side effects of local steroid injection following ESD. Pharmacologically, TA modulates the wound-healing process for post-ESD ulcers by suppressing inflammatory cell infiltration and fibrosis. This wound healing is caused by decreasing the procollagen-proline dioxygenase or prolyl hydroxylase levels. Decreasing the levels of these enzymes reduces the tissue

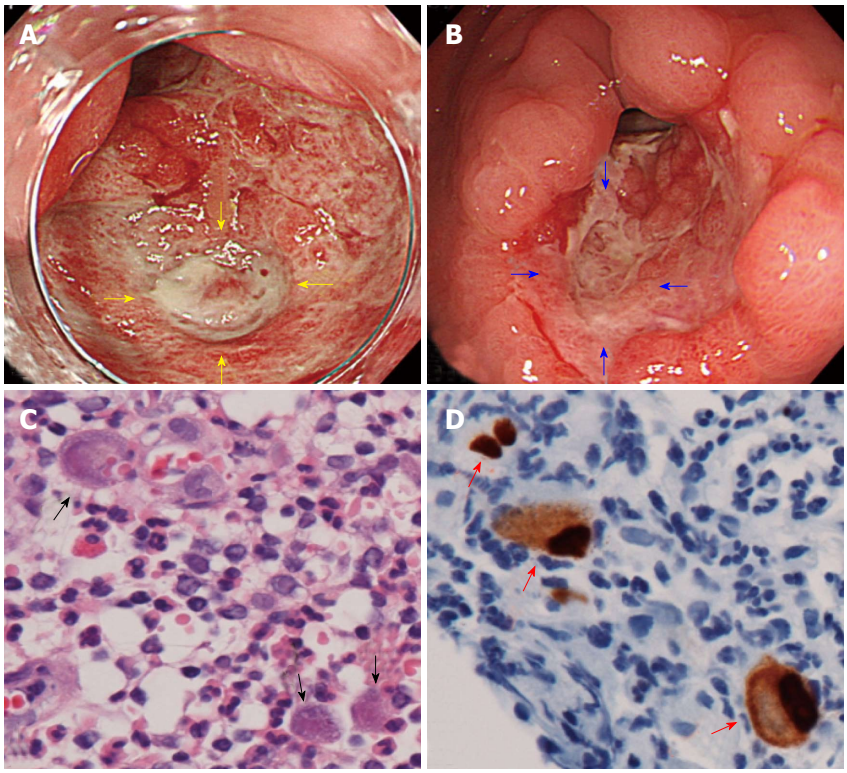

Figure 2 Endoscopic findings of cytomegalovirus associated ulcer and microscopic examination. A: Artificial ulcer on postoperative day 12, showing the formation of abundant granulation tissue and a 10-mm-deep ulcer at the center of the granulation tissue (yellow arrows); B: The healing process of the deep ulcer (blue arrows) on postoperative day 15; C: A biopsy from the deeper ulcer margin revealed large cells with intranuclear inclusion bodies (black arrow, HE staining, × 600); D: Large cells with intranuclear inclusion bodies stained positive for anti-cytomegalovirus (CMV) antibodies (red arrows, anti-CMV antibody immunohistochemical staining, × 600).

collagen component[13]; in this way, the local TA injection promoted the formation of flat and sufficient granulation tissue without fibrotic contraction. However, no infections or adverse effects were reported following local steroid injection into the post-ESD artificial esophageal or gastric ulcer floor. Subclinical CMV infection is high among Japanese infants (about 90%). Latent infection, which is established in the granulocytes and monocytes, can be reactivated by administering potent immunosuppressants, such as steroids[14]. Although the CMV ulcers generally occurred in compromised hosts, in our case, the formation of a CMV ulcer was likely caused by an inflammatory reaction in the post-ESD ulcer and reactivation of the latently infected granulocytes and monocytes, which had migrated to phagocytize the necrotic and granulation tissues on the ulcer floor. Ulcer healing occurred after 14-21 d when the TA effects had subsided. The local injection of TA is effective in preventing post-ESD esophageal stricture or pyloric stenosis; however, after the CMV is reactivated, the long-acting nature of TA may delay the healing process. CMV is recognized an important pathogen of severe infections in immunocompromised hosts, and causes CMV mononucleosis with multi-organ involvements. In general, CMV-related ulcers might make multiple and deeper lesions in digestive tract in upper gastrointestinal endoscopy[15].

In this case, the ulcer located at the center of the post-ESD artificial ulcer floor which was limited and local area under focal immunosuppressive condition by TA.

In conclusion, the local steroid injection might be an etiological factor for CMV-associated ulcers. We advise that clinicians observe the ulcer floor following TA injections and quickly treat CMV-associated ulcers with ganciclovir if needed.

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