Endoscopic Submucosal Dissection for Esophageal Squamous Cell High-grade Dysplasia in a Patient with Plummer Vinson Syndrome

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Abstract

A 35-year female with Plummer Vinson syndrome (PVS) presented with a history of progressive dysphagia over six months, not responding to iron therapy and endoscopic dilatations. Her upper gastrointestinal endoscopy showed a post-cricoid web dilated using a Savary-Gilliard dilator. On NBI, a long segment circumferential lesion with abnormal microvascular architecture was noted in the mid esophagus. Biopsy showed high-grade dysplastic squamous epithelium. The patient underwent minimally invasive, circumferential endoscopic submucosal dissection (ESD) and received oral prednisolone to prevent stricture formation. Resected margins were free of dysplasia. At follow-up there was no evidence of recurrence or stricture formation. To our knowledge, this is the first case of PVS with squamous proliferation with high-grade dysplasia that was successfully treated with circumferential ESD. Screening endoscopy helps in the downstaging of early cancer, and timely intervention helps to treat this with a minimally invasive approach like ESD.

Keywords
- endoscopic submucosal dissection
- esophageal cancer
- outcomes
- plummer-vinson syndrome

Introduction

Dysphagia to the passage of solids and liquids is an alarming symptom that needs timely evaluation and appropriate therapy.1 Characterizing the symptoms will help differentiate esophageal dysphagia from oropharyngeal dysphagia.2 Plummer-Vinson Syndrome (PVS) is identified by the presence of iron deficiency anemia (IDA), post-cricoid dysphagia, and esophageal web.3,4 It is commonly seen among middle-aged women and rarely in children and adolescents.5,6 Patients with esophageal rings or webs are usually asymptomatic. Symptomatic patients typically present with intermittent dysphagia to solids. The esophageal webs can rupture easily when the endoscope traverses the web. Dysphagia to solids due to strictures in the esophagus may need dilatation.7 The prevalence of PVS seems to have lowered due to early detection and treatment of underlying IDA. PVS recognition is vital to identify patients with an increased risk of squamous cell carcinoma of the pharynx and esophagus; hence is considered a precancerous disease.8 The frequency of post-cricoid carcinoma varies from 4–16% across studies.9,10 If diagnosed early, patients with esophageal cancer can be treated with esophagectomy or minimally invasive endoscopic resection.11,12 Herein, we present a unique case of PVS with superficial squamous proliferation with high-grade dysplasia in the mid esophagus, which was treated successfully with endoscopic submucosal dissection (ESD).
The Case

A 35-year female presented with progressive dysphagia to solids (Grade 2) associated with weight loss of ~10 kg in the last 6 months. An upper gastrointestinal endoscopy had initially shown post cricoid web (Fig. 1), dilated with CRE Wireguided Balloon Dilation (Boston Scientific, USA) done up to 12mm. The patient received oral iron supplements, pantoprazole 40mg, and sucralfate. However, her dysphagia was progressive; hence she showed up for an endoscopic procedure. The hemoglobin was 9.2 g/dl, the mean corpuscular volume was 60.6 fL, the white blood cell count was 9500/μl, and the platelet count was 450 x 10^3/μl.

At presentation, patient had IDA (serum iron 10 μg/dL, total iron-binding capacity 450 μg/dL, transferrin saturation 5.5%). Endoscopy showed post-cricoid web, which was negotiated using a Savary-Gilliard (Cook Medical, USA) dilator. At 25cms from the incisors, a flat circumferential lesion was seen extending up to 35cms. The lesion was flat (Paris O-IIa) and showed altered surface contour on the mucosal aspect without any elevated or ulcerated areas on white light imaging. On Narrow band imaging and magnification, areas of dilated interpapillary capillary loops (IPCL-B1 pattern – Magnified endoscopic classification of JES) with loop formation were noted. Lugols iodine was sprayed, and biopsy was taken from unstained areas, suggesting squamous proliferation with high-grade dysplasia. A computed tomography scan showed no evidence of thickening of the esophagus, local nodes, or metastatic disease. After discussing the available treatment modalities, the patient was planned for a circumferential ESD.

Under general anesthesia, with the patient in a supine position, the proximal and distal end of the lesion were marked using a Dual knife (Olympus, Tokyo, Japan) with a force-coagulation mode (effect 2, 40W) (VIO300D, ERBE Germany). A distal circumferential mucosal incision was done using a Dual knife (Olympus, Tokyo, Japan) (Endo Cut I) (Effect 2, Duration 3, Interval 3) after creating a submucosal cushion with saline and methylene blue with an endoscopic injection needle (NM-400L, Olympus, USA). The submucosal fibers were dissected to expose the muscularis all along the distal part of the lesion (Fig. 2). After that, a mucosal incision was done along the proximal aspect of the lesion on the posterior esophageal wall. The submucosal dissection was performed with a force-coagulation mode (effect 2, 40W), and a submucosal tunnel was created to join the proximal and distal mucosal incision. Another similar submucosal tunnel was created along the anterior aspect of the lesion. Both the tunnels were joined by lateral dissection, and the entire dysplastic area was meticulously resected en block (~6 cm) and submitted for a histopathology examination. Hemostasis was achieved with Coagrasper Hemostatic forceps (FD-410LR, Olympus, USA) using forced coagulation (60W). The procedure time was 210 mins. Postoperatively the patient was kept nil by mouth, and iv fluids were given. She had a low-grade fever which settled with paracetamol.

Fig. 1 (A) Post-cricoid web. (B) Post-cricoid web dilated with CRE Wireguided Balloon Dilation. (C) A flat circumferential lesion seen in esophagus extending up to 35cms. (D-F) Narrow band imaging showing areas of dilated interpapillary capillary loops (IPCL-B1 pattern – Magnified endoscopic classification of JES).
and antibiotics (cefixime). On the third postoperative day patient was started on clear liquids, which were tolerated well, and oral steroids (prednisolone 30mg daily) on tapering dosage for prevention of esophageal stricture. On Day 5 patient was discharged on liquids.

Biopsy was suggestive of high-grade squamous dysplasia confined to the muscularis mucosa (T1a), the vertical margins were negative, and there was no lymphovascular invasion. At follow-up endoscopy (1 month), the previous ESD site showed scarring with neovascularization. Healthy granulation tissue surrounding the ESD site was seen. There was a narrowing at 35cm from the incisors. CRE Wireguided Balloon Dilation (Boston Scientific, USA) was done up to 11mm; the scope was then negotiated across the stricture. The patient was encouraged to eat a well-balanced and nutritious diet. On follow-up at 6 months, the patient has gained weight, is tolerating an oral diet, and has no history of dysphagia or recurrence of the disease.

**Discussion**

The pathogenesis of PVS remains largely unknown. The most plausible etiologic factor is IDA which can precede dysphagia. The gastrointestinal tract is susceptible to iron deficiency leading to mucosa degeneration and web formation. These factors were also noted in our patient. Other etiologic factors such as genetic predisposition and malnutrition, are considered. These can be missed due to their proximity to the
upper esophageal sphincter. PVS is managed with iron supplementation, but severe obstruction by the esophageal web needs mechanical dilation. A single dilation helps treat dysphagia in most cases, but recurrent dysphagia is seen in those with an esophageal ring. In a study of 33 patients after dilation of an esophageal ring, recurrent dysphagia was reported in 89% of patients at 5 years.\textsuperscript{15} The patients must be followed closely as there is a high chance of recurrence. Surveillance endoscopy can be performed yearly, though no definitive recommendation exists.

The occurrence of esophageal cancer is increasing, and as per GLOBOCAN 2020 estimates, it ranks seventh and sixth in terms of incidence and overall mortality, respectively.\textsuperscript{16} ESD is an excellent modality for patients with early cancer but not advanced tumors. It utilizes endoscopic tools to dissect lesions from the submucosa like superficial esophageal cancer or those with high-grade dysplasia.\textsuperscript{17,18} So, ESD was chosen as the mode of therapy for this patient. Several studies have shown low mortality rates following ESD of isolated lesions. ESD helps to perform en bloc resection for histopathologic assessment. Five-year survival rates range from 76 to 100%.\textsuperscript{19,20} However, survival is lower in patients with lesions that extend beyond the lamina propria. Recurrences have been seen in 3 to 32% of patients.

Adverse events of ESD include mediastinal emphysema (suggesting perforation), ulcer bleeding, and esophageal stricture.\textsuperscript{21} Strictures are typically seen in patients with a mucosal defect involving more than three-fourths of the esophageal circumference. Triamcinolone injection during resection may decrease the risk of stricture formation. Strictures are typically treated with esophageal balloon dilation.\textsuperscript{22} We embarked on using a tunnel creation technique based on submucosal dissection principles performed during POEM. This technique was quicker than conventional ESD, and the lesion could be dissected easily without muscle injury. Steroid administration with either topical or local injection prevents stricture formation. In a small retrospective series, treating with esophageal balloon dilation plus an oral steroid was associated with a decreased risk of stricture formation. Triamcinolone injection during resection may decrease the risk of stricture formation. Strictures are typically treated with esophageal balloon dilation.\textsuperscript{22} We embarked on using a tunnel creation technique based on submucosal dissection principles performed during POEM. This technique was quicker than conventional ESD, and the lesion could be dissected easily without muscle injury. Steroid administration with either topical or local injection prevents stricture formation. In a small retrospective series, treating with esophageal balloon dilation plus an oral steroid was associated with a decreased risk of stricture formation.

A retrospective study over 18 years studied 135 patients with PVS; 86% were women with a mean age of 42 years; the common symptom was dysphagia. Mid and distal esophageal cancers were more common. The mean interval between diagnosis of PVS and squamous cell carcinoma was 6 years.\textsuperscript{24} Patil M et al. studied 132 cases of PVS over a 10-year period in which 4 patients showed concomitant esophageal tumors post dilatation of post cricoid web. Upper esophageal malignancy was seen in 4.5% of patients. ESD is now gaining popularity in Scandinavian countries for gastric lesions.\textsuperscript{25} Misjudgment of the indications or curability assessment can result in unfavorable patient outcomes.

To summarize, the present case of PVS was treated successfully with circumferential ESD. The procedure was safe to perform and effective in treating high-grade dysplasia. ESD may provide a non-surgical treatment option for patients with advanced tumors, which needs to be explored in well-designed controlled trials.

**Presentation at a Meeting**
Not presented.

**Author Contributions**
Concept – GP; Design – GP, AV; Performed case – GP, SV; Data Collection and/or Processing – GP, AV; Literature Review– AD, PH, AS, SP; Performed histopathological analysis – PG; Writing – AS, AV, GP; Critical Reviews - AM. All the authors reviewed and approved the final version of the manuscript.

**Consent**
Consent from the patient was obtained regarding the publication of this case.

**Funding**
None.

**Conflict of Interest**
None declared.

**Acknowledgments**
We thank Dr. Rajen Daftary for his dedicated anesthesia care during the procedure. We thank Mr. Milind Jadhav for editing the pictures to suit journal requirements.

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