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Is endoscopic balloon dilatation and oral iron preparation treatment adequate in the treatment of Plummer-Vinson syndrome?

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ABSTRACT

Introduction: The main objective of this study is to present 10 Plummer-Vinson Syndrome cases treated and followed up at our clinic alongside cases in current literature.

Materials and Methods: The cases of 10 patients with prospective records of Plummer-Vinson Syndrome treated and followed up in the Gastroenterological Surgery Clinic of the hospital were evaluated.

Results: Seven (70%) of the patients were female, and three (30%) were male, with a mean age of 45±18. All the patients had a mean hemoglobin value of 8.4±0.94 g/dL and a mean erythrocyte volume level of 63±5.01 fL, and their ferritin levels were 6.5±5.42 ng/dL, which accounted for iron deficiency in the patients. With barium swallow studies before endoscopy, all patients were shown to have esophageal webs. All patients underwent endoscopic balloon dilatation under sedoanalgesia. Three cases of recurrence were observed, and those patients underwent the balloon dilatation process again. Squamous cell carcinoma in the distal esophagus was detected in one case in the 72nd month of follow-up.

Conclusion: Endoscopic balloon dilatation together with oral iron replacement is a safe, simple, and efficient mode of treatment. As Plummer-Vinson Syndrome is regarded as a precancerous condition, endoscopic follow-up is required for subsequent treatment.

Keywords: Dysphagia; Esophageal Web; Iron Deficiency Anemia; Plummer-Vinson Syndrome

Introduction

Plummer-Vinson Syndrome (PVS) is a rare condition also known as Paterson-Brown-Kelly Syndrome. Its main clinical features include web(s) in the upper esophagus, dysphagia, and iron deficiency anemia.[1-3] Although the pathogenesis of PVS remains largely unknown, it has been suggested that iron deficiency anemia, genetics, malnutrition, and autoimmune conditions are effective in its etiology.[4-7] It is generally seen more in middle-aged women.[8] On one hand, there are studies that argue that the most significant step in PVS treatment is iron replacement.[4,5] However, other studies in the literature report that endoscopic dilatation or incision should be performed in cases

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with esophageal webs that have been unresponsive to iron treatment.[6-8] The prognosis of PVS is almost perfect when it is not accompanied by hypopharynx and upper esophageal squamous cell carcinoma. If carcinoma develops, the prognosis dramatically deteriorates.[9]

Aim

This study presents 10 Plummer-Vinson Syndrome cases at our clinic that were treated with endoscopic balloon dilatation and were then followed up.

Materials and Methods

Study Design

The cases of 10 patients with prospective records of Plummer-Vinson syndrome treated and followed in the Gastroenterological Surgery Clinic were evaluated. The Clinical Research Evaluation Board approved the study protocol.

Study Population

Adult patients (>18 years of age) who presented to our clinic with dysphagia, who had a web in the proximal esophagus detected through barium swallow studies or endoscopy of the gastrointestinal system, and who had iron deficiency were regarded as having Plummer-Vinson Syndrome. Patients who had these criteria but who also had a history of pharynx or esophagus injury, surgery, or radiotherapy and/or who had missing file records were excluded from the study. Patients with hemoglobin levels below 12.0 g/dL for women and 13.0 g/dL for men, with serum ferritin levels below <30 µg/L and with mean corpuscular volume (MCV) below <80 fL were regarded to have iron deficiency anemia.[10]

The severity of dysphagia in the patients was classified according to their oral food intake. Those who were able to swallow solid food were assigned grade 0, those who ingested a semisolid diet, grade 1, those who could only take soft food, grade 2, and those who could only take liquid food, grade 3. Those who had complaints with any kind of food were classified as grade 4.

Instruments

Examinations were performed with a FUJINON VP-4450 & XL-4450 Endoscopy set. Dilatation was performed with multidiameter esophageal balloon catheters (CRE™; Fixed Wire, Boston Scientific).

Technique

All patients were given information prior to the procedures, and their informed consent forms were approved. Before the procedure, all the patients were shown through barium swallow studies to have a web. Endoscopic procedures were performed with propofol (Propofol ampoule, FRESENIUS KABI®) and fentanyl citrate (Talinat ampoule, VEM®) under sedoanalgesia. A guide wire was placed in the endoscope compartment. After that, dilatation was performed without fluoroscopy. In general, the dilator size was gradually increased. The first endoscopy and laboratory checks were done in the third month after the procedure. During the clinical follow-up, additional dilatation procedures were performed until symptomatic improvement was achieved if the esophageal web and dysphagia recurred.

Data

Patients' data with respect to age, gender, presenting complaints, physical examination results, laboratory results, radiological data, endoscopic results, accompanying upper gastrointestinal system malignity, recurrence, and follow-up duration (months) were recorded.

Statistical Analysis

The statistical analyses of the data collected were performed using the SPSS 21.0 package program. Categorical measurements were summarized in numbers and percentages, whereas continuous measurements were summarized in mean and standard deviation figures (also in median and minimum-maximum figures where necessary). Differences between laboratory values after iron treatment were compared using a paired samples T-test. The level of significance was set at $p<0.05$.

Results

Seven (70%) of the patients were female, and three (30%) were male, with a mean age of 47±18 years. All patients had dysphagia symptoms. Six (60%) of the cases had grade 1 dysphagia, three (30%) had grade 2, and one (10%) had grade 3. The mean duration of dysphagia complaints was 74.1±81.2 (9–240) months. Nine (90%) of the patients were suffering from weight loss. The clinical features of the patients have been summarized in Table 1.

The laboratory results of the patients revealed that all of them had hypochromic microcytic anemia. The pa-

Table 1. Clinical characteristics of patients

Case	Gender	Age	Dysphagia Score	Dysphagia time (month)	Weight Loss
1	F	18	1	12	Yes
2	F	34	2	84	Yes
3	M	34	1	120	Yes
4	F	51	3	240	Yes
5	F	45	1	12	Yes
6	M	71	2	24	Yes
7	F	67	1	9	No
8	F	56	2	180	Yes
9	M	45	1	36	Yes
10	F	44	1	24	Yes

F: Female; M: Male.

tients' mean hemoglobin level was found to be 8.4±0.94 g/dL, their MCV value was 63±5.01 fL, their ferritin level was 6.5±5.4 ng/dL, their iron-binding capacity was 479.3±80 µg/dL, and their iron level was 16.2±12.1 µg/dL. No distinctive features were found in their serum liver or kidney function tests. The hematological laboratory results of our patients have been summarized in Table 2.

A barium esophageal passage graph was performed for all patients before the endoscopy, and an outlook consistent with webs in the proximal esophagus was observed (Fig. 1). The esophagoscopy performed on all these patients demonstrated webbing in the cervical esophagus. All patients underwent endoscopic balloon dilatation under sedoanalgesia (Fig. 2). No complications were observed in the patients following the procedure. All the patients were started on an oral iron treatment after the procedure. Dysphagia complaints were eliminated in all the patients (Fig. 3).

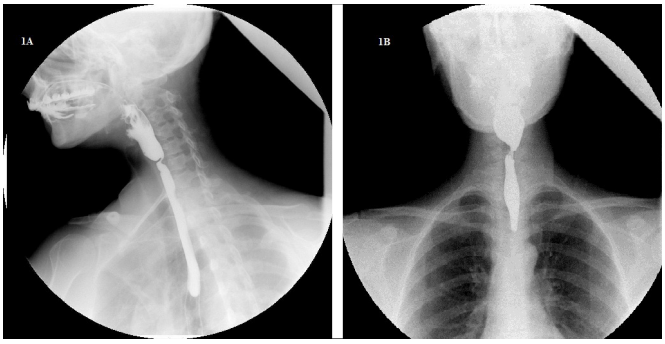

Figure 1 (a, b). Barium swallow showing esophageal web.

Table 2. Hematological datass of patient

Case	Hgb (g/dl)	MCV (fL)	Iron (µg/dl)	IBC (µg/dl)	Ferritin (ng/dl)
1	7	54	20	460	4
2	6,7	58	8	632	2
3	9	64	12	584	2
4	9,1	69	14	460	20
5	8,5	58	8	510	4
6	7,8	67	21	421	5
7	9	69	48	376	11
8	8,6	62	8	450	7
9	9	65	13	400	6
10	9,5	64	10	500	4

Hgb: Hemoglobin; MCV: mean corpuscular volume; IBC: iron-binding capacity.

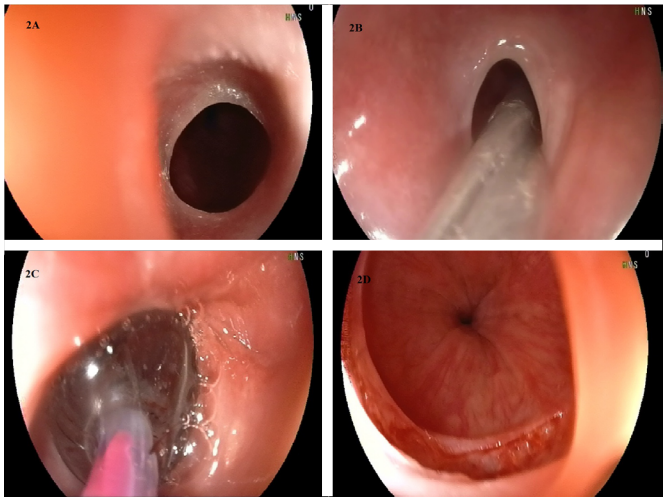

Figure 2 (a-d). An endoscopic view after successful sequential dilatation using balloon dilatation

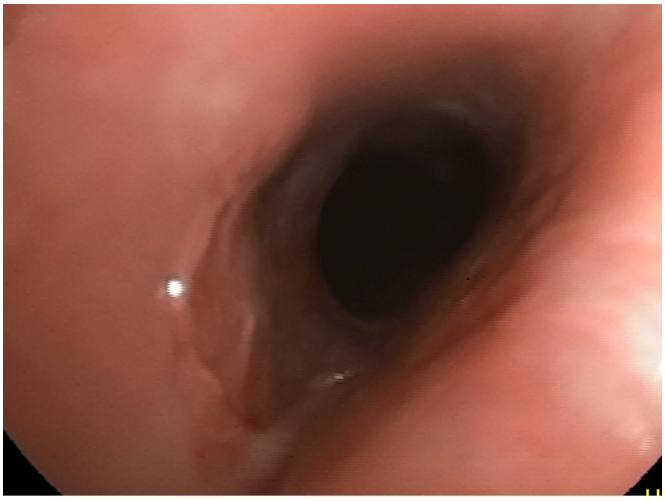

Figure 3. View of patient after six mounts of balloon dilatation treatment.

There was a statistically significant difference between the laboratory values of the patients before and after the oral iron therapy ($p<0.05$) (Table 3).

During a mean follow-up period of 29.6±24.4 months (range 6–84 months), recurrence was observed in three patients. These patients received balloon dilatation again. Squamous cell carcinoma (SCC) was detected at the lower end of the esophagus at the fourth year of follow-up endoscopy in one patient. Clinically, the patient was T3N+ following the radiological evaluation. After neoadjuvant chemoradiotherapy, the patient received an Ivor-Lewis esophagectomy. No recurrence or distant organ metastasis was found in the patient during the 12-month post-op follow-up. The follow-up and treatment features of the patients have been summarized in Table 4.

Table 3. Changes in laboratory values after iron therapy

Variable	Before oral iron therapy	After oral iron therapy	p
Hemoglobin (g/dL)	8.4±0.94	12.7±1.1	<0.001
Mean corpuscular volume (fL)	63±5.01	87.5±2.75	<0.001
Serum Ferritin (µg/L)	6.5±5.4	55.9±11.9	<0.001

Table 4. Follow-up of patients after endoscopic ballon dilation

Case	Recurrence	First Recurrence Time (Month)	Follow-up EBD number	Follow-up (month)	Malignancy during follow-up
1	No	-	-	12	No
2	Yes	6	1	14	No
3	Yes	24	1	84	Distal esophagus SCC
4	No	-	-	48	No
5	No	-	-	50	No
6	No	-	-	24	No
7	No	-	-	24	No
8	Yes	15	1	26	No
9	No	-	-	6	No
10	No	-	-	8	No

EBD: endoscopic ballon dilatation; SCC: squamous cell carcinoma.

Discussion

The syndrome's most commonly known name, Plummer-Vinson, is derived from physicians Henry Stanley Plummer (1874–1936) and Porter Paisley Vinson (1890–1959), who worked at the Mayo Clinic. They reported 91 cases with long-term iron deficiency anemia, dysphagia, and upper esophageal spasm without anatomic stenosis in their study published in 1912.[1] Paterson and Kelly, on the other hand, were the first ones to define this syndrome, known for features such as anemia, iron deficiency, dysphagia, glossitis, cheilitis, and koilonychia.[2,3]

The etiology of PVS still remains unclear. It has been suggested that the most probable mechanism in PVS is the rapid loss of iron-dependent enzymes related to iron deficiency and the consequent high level of cellular destruction. The loss of these enzymes causes mucosal degeneration, atrophic changes, and web formation related to dysphagia. Researchers have suggested that PVS-related dysphagia is generally related to iron deficiency, and studies demonstrating that iron supplements alleviated patients' complaints have been published as well.[4,5] Researchers have also reported that esophageal motility was upset in PVS, and they demonstrated that this motility disorder regressed with iron treatment.[5] Nutritional problems, genetics, and autoimmune causes can be listed among other causes.[6,7]

There is no exact data on the incidence and prevalence rates of the syndrome. PVS was common among Caucasians in the first half of the twentieth century in the northern hemisphere. Today, however, it is very rarely seen. The syndrome has been reported in the literature mostly in the form of case reports with a limited number of clinical studies.[11,12] There have only been a limited number of case reports from Turkey, and our study is the first clinical study to be published in the country.

While the syndrome is most often seen in middle-aged women in particular, other cases have also reported the syndrome in some people's seventh decade and in the population of children.[13-15] In Bakari et al.'s study,[12] 86.6% of their sample of 135 patients who had been diagnosed with PVS were female, with a mean age of 43 years. When we reviewed the literature on the subject and also included our own cases, we saw that the majority of cases were middle-aged female patients.

Dysphagia is generally painless, intermittent, or progressive over the years and is limited to solid food and is sometimes accompanied by weight loss. Goel et al.[11] reported that most of the 37 patients covered by their study had grade 1 and 2 dysphagia. The mean duration of dysphagia was 24 (4–324) months, and the mean body mass index was 18.3 (12.8–25.8) kg/m^2. In our study, however, 90% of the patients had weight loss, and the mean duration of dysphagia was 74.1 (9–240) months.

The major clinical and diagnostic criteria for PVS include post-cricoid dysphagia, upper esophageal web, and iron deficiency anemia. Although esophageal webs can be detected through barium passage graphs, the best method is video fluoroscop.[13,15] These rings can also be shown by endoscopy of the upper gastrointestinal system. Through the endoscopy, these rings are seen as planes that are smooth-surfaced, thin, or grey-colored. Endoscopic examination of the upper gastrointestinal system should be performed very carefully in case of suspected webs, since most webs are located in the proximal esophagus and can be ruptured because of their thin structure.[11,16]

Laboratory results are generally correlated with iron deficiency anemia. The levels of serum hemoglobin, hematocrit, MCV, serum iron, and ferritin decrease, while the total iron-binding capacity increases. Laboratory anomalies, except for these, cannot generally be defined.[11-13,17] In our study, hematological values consistent with iron deficiency anemia were detected in line with the literature, while no distinguishing features were detected in the other laboratory results. Pallor, fatigue, and tachycardia related to anemia can also be seen; glossitis, angular cheilitis, atrophic oral mucosa, and spoon nail (koilonychias) may also be encountered.[11]

Motility disorders such as achalasia, as well as esophageal diverticula, malignant tumors, benign strictures, spastic motility disorders, scleroderma, diabetes mellitus, gastroesophageal reflux disease, neuromuscular and skeletal muscle disorders, can be considered for differential diagnosis. After the differential diagnosis, which will differentiate the syndrome from other possible causes of iron deficiency and dysphagia, meaning that the disease has been clarified as PVS, the syndrome is then fundamentally treated by iron supplementation and esophageal dilatations.[14] Within the framework of dilatation treatment, dilatation can be performed for up to 17 mm after passing to the distal esophageal narrowness, especially using a guide wire. Although this problem can generally be treated at a single session, some patients need more than one session for treatment.[18] All the patients in our study

underwent guided endoscopic balloon dilatation. The dilatation began with a 12 mm balloon at the first stage, the balloon diameter was gradually increased and finished at 17 mm. Dilatation in all patients was successfully completed without complications. Seven (70%) cases did not require additional dilatation in endoscopy follow-up. In the three (30%) other patients, a second dilatation procedure was performed.

Goel et al.[11] reported that they performed endoscopic balloon dilatation for 31 patients and only two cases necessitated a second session. The authors also gave an oral iron preparation and folic acid to all their patients with iron deficiency anemia. We performed balloon dilatation in all cases; only three necessitated an additional session. We also started oral iron replacement treatment with all our patients.

Salihoun et al.[8] performed a total of 62 bougie dilatation procedures on 41 patients. No complications such as bleeding or perforation took place during the procedures, and the endoscope was easily able to pass through the esophagus after the procedure. The authors did not report any recurrences or malign degeneration during the mean follow-up duration of 31.5 (3–60) months.

Fall et al.[18] stated in their retrospective study covering 50 cases that they performed bougie dilatation on 36 patients with stricture and webs, with accidental endoscopic rupture for 6 out of 14 patients without stricture, and they only started 8 patients on iron treatments. The authors reported dysphagia recurrence during the follow-ups in seven patients who had received bougie dilatation only because of stricture. The authors also reported that only one of these patients developed esophageal stenosis following seven bougie dilatations within six years.

As PVS was associated with an increased incidence of post-cricoid carcinoma (4–16%) in a study published by Chisholm in 1974, the syndrome is considered precancerous for the hypopharynx and the cervical esophagus.[9] Apart from this study, esophagus and stomach cancer accompaniment with PVS have been reported, but the etiopathogenesis of the premalignant behavior of the syndrome is still unknown. Endoscopic follow-up is recommended[18,12] Within the scope of our study, one patient developed SCC in the distal esophagus in the 72nd month of follow-ups. The patient received an Ivor-Lewis esophagectomy. No recurrence or distant organ metastasis was detected during the post-op 12-month follow-up period. Based on this case and on the data presented in the literature, patients who only receive iron treatments and whose endoscopy cannot be fully performed should be given endoscopic follow-up even if their complaints are mechanically eliminated following treatment.

There are a few limitations to our study. The first and most important is that the study was done with a limited number of patients. Secondly, the median duration of the follow-up period was limited to 24 months. Because of these two limitations, we cannot comment on the risk of recurrence or malignancy. The third limitation is the absence of another treatment group to compare balloon dilatation therapy. The strong points of our study included the prospective records, the predefined diagnostic criteria, and implementation of the management strategy and the full follow-up of the participants.

Conclusion

PVS is a rarely seen clinical condition, with most information limited to case reports. When it does occur, it is frequently seen in middle-aged female patients. Oral iron replacement with endoscopic balloon dilatation is a safe, simple, and effective treatment method. Since PVS is regarded as a precancerous condition, endoscopic follow-up is necessary following treatment.

Disclosures

Ethichs Committee Approval: The study was approved by the Local Ethics Committee.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – E.G.; Design – Ö.Ö.; Supervision – S.G.; Materials – A.S.S.; Data collection and/or processing – M.D.; Analysis and/ or interpretation – E.G., E.P.; Literature search – M.D.; Writing – E.G.; Critical review – M.D.

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