

# Could Plummer–Vinson Syndrome Be Associated with Celiac Disease?

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**Abstract:** A 16-year-old female presented to our hospital clinic with a main complaint of difficulty swallowing. She reported mild dizziness and frequent fatigue and denied weight loss, fever, joint pain, or a history of diarrhea. Lab and physical results showed low weight; low hemoglobin, ferritin, and vitamin D levels; and a low red blood cell count. Swallowing assessment showed esophageal webs and swallowing difficulty, especially in the pharyngeal stage, and aspiration. It was initially suspected that clinical manifestations, including esophageal webs, iron deficiency anemia (IDA), and swallowing difficulty, were related to Plummer–Vinson syndrome (PVS). However, further investigations and pathological findings revealed several gastrointestinal manifestations consistent with celiac disease (CD). Based on this finding, the patient began a gluten-free diet for the management of CD. Afterward, she began to gain weight, followed by a resolution of swallowing difficulty. Therefore, clinicians should be familiar with the symptoms of CD when conducting a thorough clinical examination and maintain a high level of suspicion to rule out other causes and reach an accurate diagnosis. It is also recommended to screen all patients presenting with IDA, esophageal web, and dysphagia for CD even in the absence of diarrhea.

**Keywords:** Plummer–Vinson syndrome, celiac disease, dysphagia, esophageal web, iron deficiency anemia

## Introduction

Plummer–Vinson syndrome (PVS), also known as Brown–Kelly syndrome, is a rare disease characterized by post-cricoid dysphagia, iron deficiency anemia (IDA), and esophageal webs.<sup>1,2</sup> Dysphagia is usually progressive, intermittent, painless, and occasionally associated with weight loss. Esophageal webs are best detected by a videofluoroscopy swallow study (VFSS) but can also be identified using gastrointestinal endoscopy. In VFSS images, a web appears as a thin protrusion in the upper esophagus or post-cricoid region, with either a normal or noticeably narrowed distal portion and a dilated proximal segment.<sup>3,4</sup> The pathogenesis of PVS syndrome is unknown, but several studies have suggested etiological factors between iron deficiency and web formation.<sup>5,6</sup> Treatment with iron supplementation can completely resolve dysphagia and esophageal webs;<sup>5,6</sup> however, dysphagia can still persist in some patients due to severe narrowing of the esophageal lumen. As a solution, rupture, and dilation of the web cannot be avoided.

On the other hand, celiac disease (CD) is also a recognized cause of IDA. CD refers to a chronic gluten-sensitive condition marked by mucosal damage to the small intestine and malabsorption of important nutrients including iron. CD can also be manifested in several clinical presentations, including malabsorption syndrome (ie, abdominal pain, chronic diarrhea, and weight loss), short stature, or multiple gastrointestinal motor abnormalities. Patients with CD may rarely experience dysphagia; however, if it exists, the problem can persist for months or years.<sup>1,7–10</sup> Dysphagia in CD patients can manifest as difficulty swallowing solid foods and liquids, sometimes even their own saliva.<sup>10</sup> The pathogenesis of dysphagia that is

**Table 1** Differences in Dysphagia Between Celiac Disease (CD) and Plummer Vinson Syndrome (PVS)

CD	PVS
Dysphagia with solids, soft foods and liquids <sup>7,15</sup> Dysphagia is usually episodic and worsened over years <sup>15</sup> Tightness in throat and chest <sup>7</sup>	Dysphagia is limited to solid food and can include liquid if the condition is worsened <sup>11,16,17</sup> Gradual onset starting with solid foods and difficulty swallowing liquids after years of initial onset <sup>8,16</sup> Usually painless. <sup>8,16,18</sup>

related to CD might be due to neuropathy, which results in esophageal dysmotility.<sup>7</sup> According to Berry et al,<sup>7</sup> patients with CD may also complain of tightness in the chest. As with PVS, patients with CD can also have esophageal webs. Hence, in a study conducted by Kundumadam et al,<sup>11</sup> two esophageal imprints were found in the cervical region in a patient with CD during a modified barium swallow study (MBSS), which indicated esophageal webs. Studies report an association between cervical esophageal webs and CD.<sup>1,7,12,13</sup> The appearance of the web can be a direct consequence of IDA;<sup>5,6</sup> therefore, iron supplements can greatly improve swallowing difficulty.<sup>12</sup>

Although CD has been discussed in detail in the literature,<sup>12,14</sup> few studies have described the dysphagia features associated with CD and the similarities and differences between CD and PVS (Table 1). In this report, the similarity between CD and PVS was highlighted, with a focus on swallowing difficulties associated with both diseases, especially the pharyngeal stage of swallowing.

## Case Report

A 16-year-old female with a family history of celiac CD (aunt and uncle) presented to the family medicine clinic complaining mainly of difficulty swallowing solid food for six months. She described this condition as a sensation of food being stuck in her throat and chest; she also reported mild dizziness and frequent fatigue. She denied weight loss, fever, joint pain, and no history of diarrhea. However, upon examination, the patient's weight was 44.7 kg, which indicated that she is underweight based on her body mass index (BMI); the ideal body weight for her height (166 cm) is 59 kg. Upon clinical examination, there was no enlargement of the tonsils, no thyroid enlargement, and no palpable nodules. In addition, the patient underwent routine clinical labs and was found to have low levels of hemoglobin (66 g/L), ferritin (1.6), and vitamin D (34.4), and a low red blood cell count (4.15). The result of a thyroid ultrasound (US) was unremarkable. The family was contacted and advised that the patient needed to receive blood due to her low hemoglobin percentage. According to the lab results and clinical manifestation, she was diagnosed with chronic IDA. For further assessment, the patient underwent a barium swallow study performed by a radiologist, which showed aspiration into the trachea seen in the lateral view. No sign of reflux, no abnormal mucosal outline, no filling defects, and no abnormal narrowing or outpouching were observed. During this time, the patient received a (1 gram) one-week course of intravenous (IV) iron supplementation (1 g) and reported improvement in swallowing function. She was then referred by the family medicine department to the swallowing clinic for assessment and management due to the aspiration that was seen on the barium swallow study performed by the radiologist. Upon reviewing the barium study by the swallowing pathology team, a distinct web in the esophagus, which is similar to PVS, was noted. Therefore, the patient underwent a fiberoptic endoscopic evaluation of swallowing (FEES) and VFSS for a comprehensive assessment of her swallowing efficiency. The FEES was performed with volumes of thin and thick liquids at 1 mL, 3 mL, 5 mL, and 10 mL and with a teaspoon and a tablespoon of pureed and soft-textured foods. The FEES revealed pharyngeal dysphagia characterized by the following features: delayed swallowing trigger at the level of the vallecula with thin and thick liquids; residues in the vallecula with all consistencies; and silent aspiration with thin and thick liquids, but no aspiration with other consistencies during the study. Based on the results of the FEES study, the patient was diagnosed with pharyngeal dysphagia level 3 (moderate).<sup>19</sup>

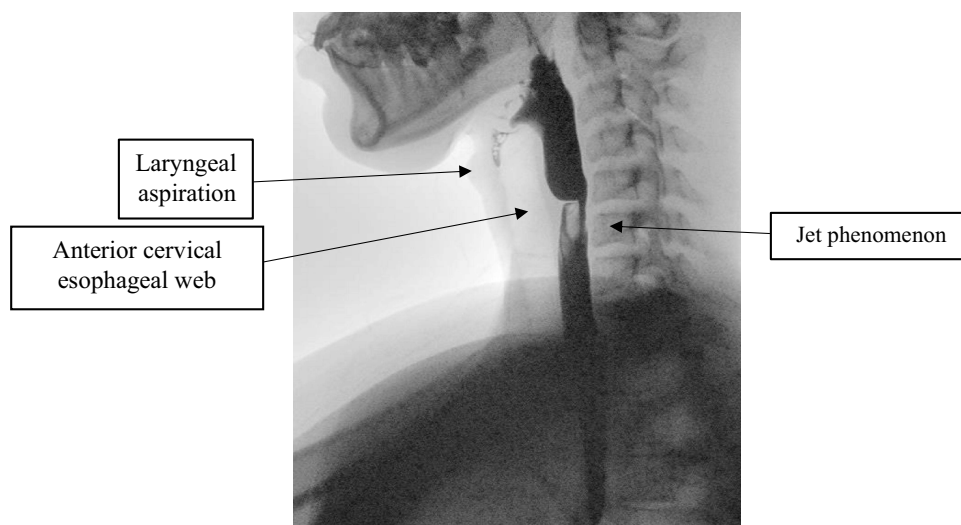
Given that a web was noted in the esophagus and that the patient had dysphagia and IDA, PVS was initially suspected, and this finding was discussed with the radiologist. One week later, a VFSS study was conducted by a specialized radiologist and a speech and language pathologist specializing in swallowing. An assessment of the oral, pharyngeal, and esophageal stages of swallowing was conducted with lateral and anteroposterior views using thin, thick,

and pureed consistencies. The VFSS was performed to verify the existence of the esophageal web noted in the earlier barium-meal imaging study.

From the perspective of the swallowing pathology team, the VFSS revealed several swallowing features, including delayed airway closure during swallowing leading to silent aspiration during swallowing of thin and thick liquids, penetration with puree, a delayed swallowing trigger at the level of the pyriform sinuses with all consistencies, residues in the vallecula grade 1 with thin and thick liquids, a large amount of residue with puree grade 2–3, which was graded based on Martin-Harris et al's<sup>14</sup> grading tool. However, there was no aspiration with puree. After the VFSS study was completed and the results were reviewed, it was concluded that the patient had level 3 (moderate) pharyngeal dysphagia characterized by silent aspiration with thin and thick liquids. During the study, there was an abnormality seen as a web in the esophagus, and it seemed that the patient had atypical dysphagia. Therefore, PVS was suspected due to the similarity of the clinical manifestation (ie, esophageal webs and IDA) and the video fluoroscopy imaging features.

From the radiologist's perspective, the VFSS also revealed a circumferential, thin, linear radiolucent defect in the upper third of the esophagus at the level of C5 near the cricopharyngeus muscle, which is suggestive of an esophageal web measuring approximately 0.2 cm (Figure 1). The web arises from the anterior esophageal wall and partially protrudes within the esophageal lumen posteriorly, causing mild dilatation, with characteristic jet-like contrast passage through the narrowed lumen, which is referred to as the esophageal "jet-phenomenon". Mild laryngeal aspiration can also be noted (Figure 1). Normal opacification of the remainder of the esophagus was noted, with no evidence of stricture or occlusion. Moreover, no other filling defects or obvious ulcerations could be seen. During the Trendelenburg maneuver, there was no indication of gastroesophageal reflux. The position of the gastroesophageal junction had not been altered, with no evidence of a hiatus hernia. A follow-up barium swallow study, after the patient was treated with intravenous iron supplementation, showed normal opacification of the esophagus with complete resolution of the esophageal web and no laryngeal aspiration (Figure 2).

In the clinical context of severe IDA and web formation, PVS may be suggested. Clinical correlation is recommended for conclusive results. Therefore, the case was referred to and discussed with the gastroenterology (GI) team to rule out PVS. Esophagogastroduodenoscopy was conducted and showed both a concentric esophageal ring at upper esophagus pancreatic rest at the prepyloric area and a scalloped appearance of D1 and D2. Multiple biopsies were taken from the esophagus, prepyloric area, and duodenum for a histopathology examination. The findings showed mild reflux esophagitis, negative dysplasia, and malignancy, moderate-to-severe chronic active gastritis, presence of helicobacter pylori organism, duodenum complete villus atrophy, crypt hyperplasia, positive serology for tissue transglutaminase IgA, and intraepithelial lymphocytosis; all of these are consistent with CD. Therefore, PVS was ruled out by the GI team, and CD was confirmed as the diagnosis of the condition. Upon diagnosis of CD, the patient started on a gluten-free diet.



**Figure 1** Barium swallow study, lateral view showing laryngeal aspiration, an anterior cervical esophageal web, and jet phenomena.



**Figure 2** Follow-up study after the patient was treated with complete resolution of the esophageal web and no laryngeal aspiration.

Afterward, the patient reported gaining weight and has had no swallowing complaints or further sensations of food being stuck in her throat or chest. A bedside assessment was performed and showed an unremarkable oral and pharyngeal stage, with no sign of aspiration during the assessment.

A VFSS was conducted after four months to reassess the patient, with thin and thick liquids of 1 mL, 3 mL, 5 mL, and 10 mL, and a tablespoon of pureed and soft textured foods. The main swallowing findings were delayed airway closure with thin liquid; delayed swallowing trigger at the level of pyriform sinuses with thin liquid delayed swallowing trigger at the level of the vallecula with thick liquid, puree, and soft food residues in the vallecula grade 1 with thin and thick liquids and puree no aspiration with any consistency; and deep penetration with thin liquids. The patient's speed of swallowing improved compared to the previous VFSS, as she presented with level 5 (mild) pharyngeal dysphagia with deep penetration of thin liquid. A VFSS was repeated two months later to re-evaluate the patient; the results showed only very mild residues in the vallecula with puree grade 1 and no aspiration with thin liquid, thick liquid, and puree, and a delayed swallowing trigger at the level of the vallecula with thin and thick liquids and puree. There was penetration with a thin liquid. The VFSS determined that the patient presented with normal swallowing (level 7). Consent of participation was obtained from the patient's guardian.

## Discussion

In this case report, the author described an interesting case of dysphagia whose IDA is associated with CD. The patient developed pharyngeal dysphagia level 3 (moderate), characterized by aspiration associated with iron deficiency as a symptom of CD. There was a distinct similarity between CD and PVS with regard to iron deficiency and the esophageal features seen in the VFSS. The VFSS revealed a web in the esophagus, which is characteristic of PVS.

In the current study, the patient presented with a sensation of food being stuck in her throat and chest. Similar studies reported a case of CD associated with dysphagia characterized by a sensation of solid food being stuck in the patient's chest and/or throat.<sup>15,20</sup> A delay in swallowing trigger can direct the bolus to pyriform sinuses, which may cause penetration or aspiration. In our case, the patient silently aspirated with thin and thick liquids due to reduced sensation and delayed swallowing trigger. As clearly noted in the MBSS, the delay in swallowing trigger caused a delay in airway closure and thus led to aspiration. Kahrilas<sup>21</sup> suggested that a delay in airway closure can cause swallowing problems.

Delayed laryngeal closure can occur due to anterior tilting of the arytenoid cartilages against the base of the epiglottis and reduced hyolaryngeal excursion due to descending of the epiglottis.

Patients with CD may suffer from dysphagia, which is characterized by chest tightness, as the initial presentation of the disease,<sup>7</sup> which was the case of the patient in the current study. Upon investigation, the patient presented with level 3 (moderate) pharyngeal dysphagia. Although many studies describe CD patients having swallowing difficulties, they did not specify the severity of the dysphagia or swallowing features in the FEES or VFSS, and almost no study reported aspiration associated with CD.

The VFSS was conducted 3 times in the current study. The first VFSS was performed to verify the existence of the unreported web in the barium meal study performed by the radiologist and to assess the oral pharyngeal phase. The second VFSS was performed four months after the dysphagia diagnosis, and the third VFSS was performed six months later. In the first VFSS, the patient presented with many aforementioned swallowing abnormalities. However, in the last VFSS, the features of dysphagia had significantly improved after proper management related to CD diagnosis.

As previously reported, a web was evident, and labs showed iron deficiency. According to the literature, iron deficiency can cause oral, pharyngeal, and esophageal dysphagia.<sup>22,23</sup> Chronic IDA can also be a direct cause of esophageal webs.<sup>5,6,24</sup> Webs can appear as thin protrusions or esophageal imprints in the upper esophagus or post-cricoid region in patients with CD.<sup>3,4,11</sup> Patients with webs typically present with oropharyngeal dysphagia for solids, but because of their proximal location, deglutitive aspiration may occur.<sup>25</sup> In our case, it seems that iron deficiency, which is caused by CD,<sup>26,27</sup> has indirectly contributed to the occurrence of dysphagia as the patient reported improvement in swallowing after receiving a (1 gram) one-week course of IV iron supplementation. Iron deficiency is also largely attributed to the formation of a web as the web has rapidly resolved the course of iron supplementation without any need for mechanical dilation to remove the web.

Several studies have reported complete disappearance of dysphagia after CD treatment.<sup>7,28</sup> For example, a study conducted by Lee et al<sup>15</sup> reported that the patient's swallowing difficulties were resolved after 8 months of CD management using gluten-free diet. Other studies reported mechanical dilation as a treatment method for esophageal stenosis associated with CD.<sup>12,29</sup> The CD management selected for the patient in the current study included a gluten-free diet and diet modification immediately after the diagnosis of CD. The diet was restricted to thick liquids and a soft diet. After a while, the patient started to improve, iron levels significantly increased, and the signs and symptoms of pharyngeal dysphagia completely disappeared. Moreover, the patient gained weight and had no further sensations of food being stuck in her throat or chest. Thus, all of these presentations indicate that dysphagia was caused by active CD.

It remains ambiguous whether CD and PVS are related. There is a lack of available information on VFSS features and their clinical manifestations, especially in our country. However, CD can be misdiagnosed as PVS in patients with dysphagia, iron deficiency, and esophageal webs.<sup>1</sup> A barium swallow study can be performed to diagnose the esophageal webs; however, if the esophagus is not sufficiently dilated, it can appear to be slightly narrowing, and therefore, the esophageal webs can be easily missed.<sup>30</sup> In the current case report, a VFSS was necessary because it offers a full assessment of the swallowing stages as the barium bolus travels from the mouth to the esophagus. Although the clinical manifestations and video fluoroscopy features are similar in CD and PVS, there is limited information in the literature investigating their similarities. According to Dickey and McConnell,<sup>1</sup> most individuals with cervical esophageal webs are not regularly examined for CD. Due to a lack of awareness, CD may have gone undiagnosed in many patients with cervical esophageal webs.<sup>1</sup> Another study conducted by Hefaihdh<sup>31</sup> described two cases of CD who presented as PVS, which underscores the importance of screening for CD in patients with PVS. Therefore, clinicians should be cautious and fully cognizant of this differential diagnosis when ruling out other causes and reaching an accurate diagnosis. Notably, one of the study's limitations is that the FEES study was conducted only once; it should have been repeated from another view rather than relying only on the improvement noted in the VFSS. Although the VFSS is considered the gold standard in assessing such cases, repeating the FEES to compare it with the first evaluation is strongly recommended.

## Conclusion

It is important to perform a careful investigation and to maintain a high level of suspicion to avoid misdiagnosis. It appears that CD and PVS have largely similar clinical manifestations, particularly in the presentation of swallowing difficulties, esophageal web, and iron deficiency. However, CD involves additional pathological findings related to gastrointestinal manifestations marked by mucosal damage to the small intestine and malabsorption of important nutrients including iron.

As shown in this case report, there is an association between iron deficiency, esophageal web, and CD. Therefore, all patients presenting with these symptoms should be screened for CD even in the absence of diarrhea. Iron supplementation was initially used for the patient in the present study and reported improvement in swallowing difficulty. After the diagnosis of CD, dysphagia has completely resolved after a gluten-free diet. In this report, we highlighted the similarity between CD and PVS and thoroughly described the swallowing difficulty presented by the patient, especially in the pharyngeal phase and aspiration. Further studies are needed to describe the clinical manifestations of PVS and CD and to understand the physiology and anatomical correlation between the two diseases, especially dysphagia in the pharyngeal and esophageal phases.

## Ethics Approval

The study was ethically approved by the Institutional Review Board (IRB) at Princess Nourah bint Abdulrahman University (IRB: 23-0103) and King Abdullah Bin Abdulaziz University Hospital (IRB: 23-0029), Riyadh, Saudi Arabia.

## Consent to Participate

Written informed consent was obtained from the patient's guardian to participate and publish this case report. On request, a copy of the written permission is available for review by the Editor-in-Chief of this journal.

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## Disclosure

The authors declare that they have no competing interests.

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