Cancer Association of South Africa (CANSA)

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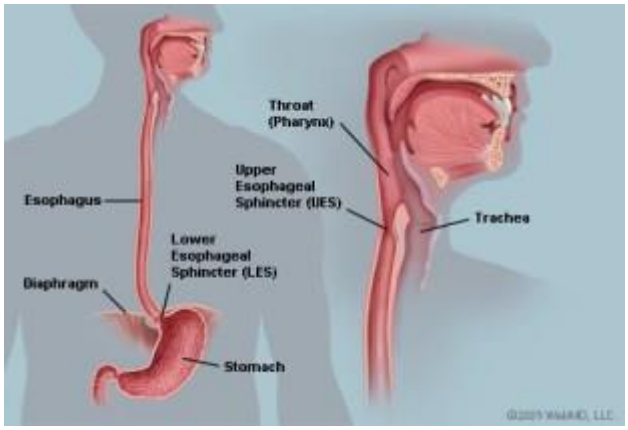
Fact Sheet
on
Sideropenic Dysphagia

Introduction

Sideropenic Dysphagia, also called Plummer–Vinson syndrome (PVS) or Paterson–Brown–Kelly syndrome, is a rare disease characterised by dysphagia (difficulty in swallowing), iron deficiency anaemia, and oesophageal webs. Treatment with iron supplementation and mechanical widening of the oesophagus generally provides an excellent outcome.



[Picture Credit: Oesophagus]

Nowadays, this syndrome has become extremely rare. It generally occurs in postmenopausal women. Its identification and follow-up is considered relevant due to increased risk of post-cricoid carcinoma and squamous cell carcinomas of the oesophagus and pharynx.
(Wikipedia; Patient.info).

Incidence of Sideropenic Dysphagia in South Africa

Because Sideropenic Dysphagia is not a cancerous condition in itself, the National Cancer Registry (2013) does not provide any information regarding the incidence of this condition.

Signs and Symptoms of Sideropenic Dysphagia

The list of signs and symptoms mentioned in various sources for Sideropenic Dysphagia includes the symptoms listed below:

- Throat pain during swallowing
- Burning sensation during swallowing
- Sensation of food stuck in larynx
- Fatigue
- Pallor

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- Pale inside of mouth
- Sideropenic anaemia
- Hypochromic anaemia
- Swallowing difficulty
- Mucosal webs in oesophagus
- Spoon-shaped fingernails
- Smooth tongue
- Red tongue
- Painful tongue

(Right Diagnosis)

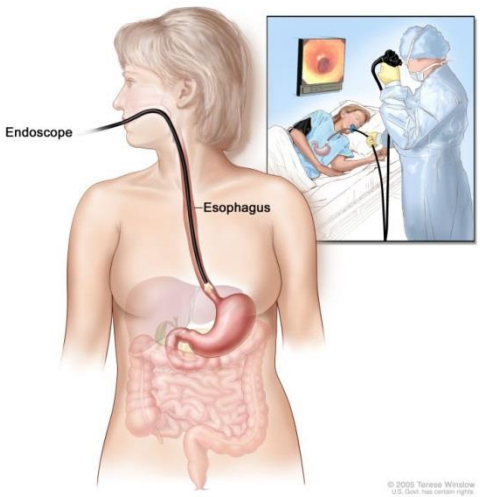
Sideropenic Dysphagia

Dysphagia is defined as difficulty swallowing foods at the oropharyngioesophageal level. This worrisome symptom requires evaluation.

The definition of *sideropenic dysphagia* is clinical and biologic: one symptom, upper oesophageal dysphagia, and one main biologic manifestation, iron deficiency anaemia. A group of less important features consists of changes in the skin and mucosa. In 1919 Paterson and Kelly described the association of iron deficiency anaemia, postcricoid dysphagia, and upper oesophageal stenosis secondary to oesophageal webs. Previously, Plummer reported cases of oesophageal spasm.

In 1922, Vinson reported cases with anaemia and iron deficiency that he considered secondary to dysphagia. The oesophageal webs are thin and transverse, protruding toward the lumen of the oesophagus. They are found in the anterior wall at the level of the cricopharyngeus muscle and spread laterally; sometimes they are circumferential, manifesting normal mucosa or subepithelial inflammatory reaction or epithelial atrophy with hyperkeratosis and intense mitotic activity. They may be single or multiple. The etiopathogenesis of the syndrome and, more specifically, of the oesophageal webs is unclear. A number of factors, such as genetic, environmental, nutritional, immunologic, and infectious, acting in concert with the iron deficiency may all play a role in the development of the syndrome.

[Picture Credit: Oesophagoscopy]



The diagnosis is clinical with progressive and long-standing dysphagia associated with iron deficiency anaemia. Only 10% of patients with these symptoms develop upper oesophageal webs, radiologic and endoscopic findings. The cineoesophagogram is the most effective and useful method for detecting the webs. We can observe them as a fine indentation on the barium column that comes from the anterior wall of the proximal oesophagus and that on occasion may be circumferential. Sometimes the webs are undetectable in a first study.

Oesophagoscopy shows the oesophageal web as a thin diaphragm with pale, fragile, or normal appearing mucosa that partially obstructs the lumen of the oesophagus. Oesophagoscopy is difficult to carry out in extreme stenosis. In the majority of cases, oral

iron treatment quickly improves the dysphagia, even before the anaemia is corrected, but there are very symptomatic cases with persistent dysphagia in which endoscopic dilation or rupture of the web is necessary. The prognosis is good, despite the fact that the syndrome is associated with increased risk for post-cricoid carcinoma, pharyngeal and oesophageal cancers.
(Journal of Pediatric Gastroenterology and Nutrition).

Causes of Sideropenic Dysphagia

The aetiology and pathogenesis of Plummer-Vinson syndrome has been attributed to numerous factors that include alterations in oesophageal innervation. There is agreement that prolonged iron deficiency is necessary for the development of the syndrome; however, only a minority of patients with iron deficiency manifests the syndrome. Individual factors acting together may play an important role in the development of the syndrome. Other factors that have been studied are environmental; genetic, with no demonstrated association with HLA; and immunologic. Chisholm investigated the relationship between autoimmunity and Plummer-Vinson syndrome to determine the incidence of autoantibodies in patients with iron deficiency, with or without webs, and compared them to a control group. A high incidence of antithyroid antibodies were found in both patient groups with iron deficiency compared with control subjects; however, no other autoimmune antibodies including antibodies specific to pharyngeal tissue were detected. No significant difference was found between patients with iron deficiency, with or without webs, confirming that autoimmune reactivity does not play a role in the pathogenesis of the syndrome.

With regard to the relationship between anaemia and dysphagia, evidence in the literature suggests that the oesophageal webs or stenosis are related to iron deficiency. Shamma'a *et al*. showed a 66% association between iron deficiency and oesophageal stenosis. Similar results were reported by a Swedish group. Cameron showed that analytically demonstrated anaemia preceded the onset of dysphagia in 20% of the cases.

The cause of dysphagia has been equally confusing because the webs often are undetected in the cases with anaemia and dysphagia. Some authors attribute this to a mechanical obstruction, whereas others believe that it is caused by a spasm of the upper oesophagus. Dysphagia in patients with a normal oesophagus also has been reported, attributed to muscular impairment in food propulsion with an increase in intrabolus pressure. Iron treatment normalised these pressures, as shown by manometric studies. Moreover, the disappearance of dysphagia after iron treatment precedes the reduction of oesophageal webs, as occurred in our patient. However, iron deficiency may produce myasthenic changes of the muscles related to deglutition. These changes are similar to those observed in progressive muscular dystrophy. Therefore, a lack of iron may clearly harm oesophageal motility. This supports the etiologic role of iron deficiency in the syndrome's pathogenesis and can explain why some patients with normal oesophagi shown in the endoscopy may note resolution of their symptoms with iron treatment alone.

The effect of iron deficiency on iron-dependent enzymes has not been taken into consideration, although clinical evidence suggested that changes in the haemoglobin content alone could not explain all the patients' abnormalities. Impairments of oxidative phosphorylation with a decrease in cytochrome c levels have been reported. This decrease parallels the reduction of muscular myoglobin. In organs with a high cell turnover, such as in the alimentary tract, the iron-dependent enzymes rapidly lose their activity with iron deficiency and are very sensitive to it. Therefore, histologic changes characteristic of this

iron deficiency may contribute to web formation. Iron treatment is tissue specific, and this high cell turnover permits rapid recovery, explaining the rapid improvement of dysphagia after therapy with iron (Journal of Pediatric Gastroenterology and Nutrition; Medscape).

The cause of Plummer-Vinson syndrome is unknown. Genetic factors and a lack of certain nutrients (nutritional deficiencies) may play a role. It is a rare disorder that can be linked to cancers of the oesophagus and throat. It is more common in women.
(MedLine Plus).

Diagnosis of Sideropenic Dysphagia

The following tests will assist in making a diagnosis:

- Full Blood Count (FBC) will show a microcytic, hypochromic anaemia.
- Low Ferritin.
- Barium swallow may show the web. This may need to be enhanced with videofluoroscopy.
- A biopsy may be required if malignancy is suspected clinically.

(Patient.co.uk).

Treatment of Sideropenic Dysphagia

Iron replacement can almost invariably be achieved by oral means. Adding vitamin C does not improve absorption significantly. There is rarely any need for parenteral iron. Supplements may be needed long-term because after correction it is important to maintain a normal iron status. Causes of blood loss like menorrhagia may require attention.

Endoscopic dilatation or argon plasma coagulation therapy of the oesophageal web is occasionally required in cases of persistent dysphagia.
(Patient.co.uk).

Iron replacement is necessary to correct the anaemia, if present, and to resolve most of the physical signs of iron deficiency. The necessity for continued iron treatment is doubtful other than for anaemia correction.

Dysphagia may improve with iron replacement alone, particularly in patients whose webs are not substantially obstructive. Dysphagia caused by more advanced webs is unlikely to respond to iron replacement alone and, thus, is managed with mechanical dilation.
Address the cause of the iron deficiency (e.g., celiac sprue, bleeding angiectasias).

Treat dysphagia and the oesophageal web:

- Aside from iron replacement, diet modification may be sufficient in mildly symptomatic patients (see Diet). Those with significant and long-standing dysphagia usually require mechanical dilation. The web can often be disrupted during simple passage of the endoscope into the oesophagus. Otherwise, passage of a bougie (e.g., Savary dilator) is quite effective. In most cases, passage of a single large dilator is adequate and is thought to be more effective than serial progressive dilations.

- Fluoroscopic guidance is usually not required unless a tight web precludes further passage of the endoscope. The proximal location of the webs in PVS makes endoscopic balloon dilation difficult, but it has been performed successfully by radiology under fluoroscopic guidance.
- ND:YAG laser therapy has also been reported as a successful means of disrupting an oesophageal web. This modality is rarely required.
- Needle-knife electroincision has been described as a therapeutic alternative to dilation.

(Medscape).

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