

# Herbst Triad: A rare clinical manifestation of a common pathology

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## OPEN ACCESS

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## Abstract

The Herbst triad is a rare manifestation of gastroesophageal reflux disease and other esophageal pathologies. It is characterized by the presence of anemia, digital clubbing, and protein-losing enteropathy. Since evidence on this condition is anecdotal, the available information is mostly derived from case reports and its physiopathology remains unclear. The following is the case of a schoolchild, whose symptoms were reversed once she underwent surgery.

## Keywords

Gastroesophageal reflux; Hypoproteinemia; Protein-losing enteropathies; Hypertrophic osteoarthropathy; Iron deficiency anemia.

## INTRODUCTION

Herbst triad is a rare manifestation of gastroesophageal reflux disease (GERD) and other esophageal disorders. Despite its rarity, it should be included as part of the differential diagnoses of clubbing and protein losing enteropathy in patients with gastrointestinal symptoms. Although its clinical features are well established, its physiopathology is still unclear.

## CASE REPORT

This is the case of a 9-year-old female patient, who started experiencing symptoms of regurgitation and occasional

emesis with blood at age 4. At age 5, the girl had an episode of hematemesis. At first, she was assessed by the gastroenterology and pediatrics services of another medical center and received a prescription of omeprazole since she had a diagnosis of GERD for several months.

From age 4 to 9, the patient underwent 4 esophagogastroduodenoscopies (EGD), which reported grade C esophagitis, according to the Los Angeles classification. Given the persistence of the symptoms, and despite treatment with a proton pump inhibitor, she was prescribed with alginate and domperidone.

Simultaneously, since the age of 7, the patient had iron deficiency anemia (hemoglobin): 7.4 g/dL; hematocrit:

24.4%; mean corpuscular volume [MCV]: 65.9 fL, and ferritin: 2 ng/mL). Thus, she was treated with the oral administration of iron in different presentations, but she had a poor tolerance, and no response was observed, requiring transfusion support.

In addition, clubbing, associated with anemia, appeared in both hands (**Figure 1**), as well as hypoalbuminemia (3 g/dL), and chronic acute malnutrition. In view of these symptoms, she was assessed by the pneumology, hematology, rheumatology, and genetics services, which requested multiple studies, but the cause was not found.



**Figure 1.** Digital clubbing initially documented (left), and post-treatment improvement (right).

Before visiting our center for consultation, the patient experienced a decrease in the frequency of emesis, but she still had chest pain and halitosis, and dysphagia appeared. Taking these symptoms and signs into account, she was referred to our health institution for being assessed by the gastroenterology and pediatric surgery services.

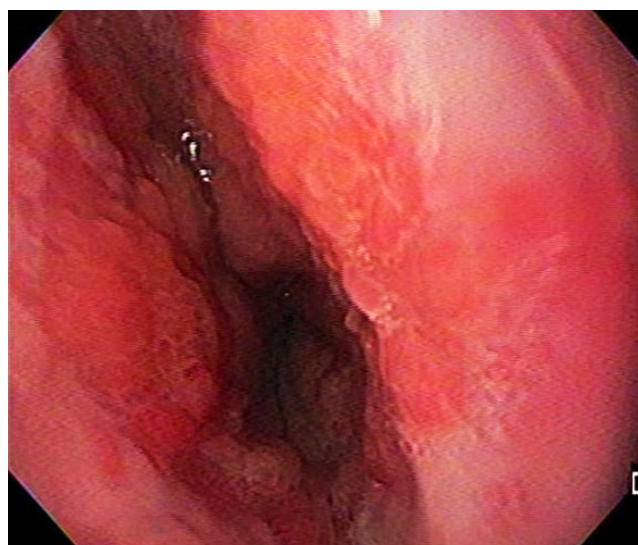
Physical examination on admission revealed a patient with a height-for-age ratio of -1.84 standard deviations (SD) and a body mass index-for-age of -2.7 (SD). Moreover, marked paleness was observed, as well as permanent left neck lateral flexion and digital clubbing.

Due to the recent development of dysphagia, several studies were requested. First, an X-ray of the upper digestive tract was performed, which showed an increase in the diameter of the esophagus, severe reflux, and alteration of tertiary peristalsis (**Figure 2**). An EGD was performed, which allowed finding grade D esophagitis (according to the Los Angeles classification), a hyperplastic polyp, a small hiatal hernia, antral follicular gastritis, and normal duodenum (**Figure 3**).

Biopsies performed during the procedures showed compatibility with severe acute peptic esophagitis, extensive ulceration, and granulation tissue, while the high-resolution esophageal manometry showed hypotonic lower esophageal sphincter and esophageal aperistalsis, according to the Chicago Classification v3.0 (**Figure 4**).



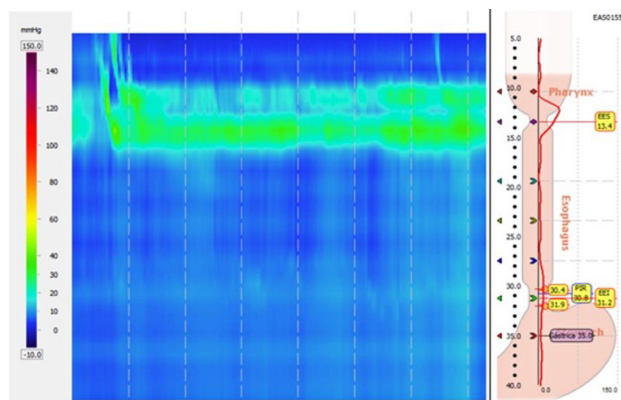
**Figure 2.** X-ray of the upper digestive tract, where increased diameter of the esophagus, severe reflux and alteration of tertiary peristalsis are observed.



**Figure 3.** Endoscopy of the upper digestive tract, with grade D esophagitis (according to the Los Angeles classification).

Consequently, a search was conducted in order to correlate gastrointestinal involvement with findings in the limbs, refractory anemia, hypoalbuminemia, and nutritional involvement. It was also suspected that the symptoms and signs observed in the patient were associated with Herbst triad.

The case was presented to the multidisciplinary board and pre-surgical preparation with placement of iron infusion and



**Figure 4.** High-resolution esophageal manometry. The lower esophageal sphincter is almost imperceptible due to hypotonia and esophageal aperistalsis.

Nissen fundoplication was decided; reconstruction of the lower esophageal sphincter was also decided. This decision was made considering that in pediatric patients with severe GERD, and despite the low casuistry, it has been reported that esophageal motility disorders other than achalasia do not contraindicate anti-reflux surgery. Therefore, the least ablative surgery was chosen. While performing the procedure, severe periesophagitis was observed.

During postoperative follow-up, there was a cervical straightening on the third day, and the resolution of dyspepsia was observed after 15 days, as well as weight gain and improvement of her nutritional status. After 3 months, the patient's BMI-for-age parameters were normal (-0.5 SD), as well as albumin (4 g/dL) and erythrocyte levels

(hemoglobin): 14.6 g/dL; hematocrit: 41.6 %; MCV: 80.6 fL, and ferritin: 36.7 ng/mL). At that point, digital clubbing had completely disappeared (**Figure 1**). These results allowed the patient to return to school life, which had been interrupted in the last 2 years.

## DISCUSSION

Herbst triad is a rare manifestation of GERD and other esophageal disorders (1). It is characterized by the presence of iron deficiency anemia, protein losing enteropathy or hypoalbuminemia, and digital clubbing (1, 2). This triad was first described in 1976 by Herbst et al. (2), although Botha had already briefly mentioned the cases of 2 children with hiatal hernia and digital clubbing who improved after surgery (3, 4).

With respect to its epidemiology, it cannot be established with certainty since it is an anecdotal and, perhaps, under-diagnosed condition (1). **Table 1** summarizes the characteristics of patients with Herbst triad reported in the literature to date (1-7).

According to what has been reported in the literature, the course of the disease prior to its diagnosis ranges from 6 months (1) to 5 and a half years (2). In the present case, this period was 5 years. Frequently, patients were assessed by other specialties such as cardiology, hematology, rheumatology (4) and pneumology, which conducted an etiological search before reaching a final diagnosis (1).

Iron-deficiency is the type of anemia associated with Herbst triad; it can be moderate to severe, with hemoglobin (Hb) levels between 5.3 (5) and 8.1 mg/dL (1, 2). According to the existing literature, it is refractory to oral

**Table 1.** Demographic characteristics of patients with Herbst triad described in the existing literature

Date of publication	Author	Age	Sex	Place of origin	Other characteristics
1976	Herbst (2)	4 years and a half	Male	United States	
1976	Herbst (2)	5 years and a half	Male	United States	White
1976	Herbst (2)	11 years	Male	United States	Intellectual disability
1990	Sacher (5)	4 years	Female	Switzerland	Cerebral palsy
1990	Sacher (5)	1 year and a half	Female	Switzerland	
1996	Greenwald (4)	9 years	Female	Canada	Caucasian; spastic cerebral palsy due to anoxia
1998	Rosario (6)	4 years	Male	Brazil	
2004	Calcado et al. (1)	6 years	Male	Rio de Janeiro (Brazil)	White
2007	Guerrero (7)	6 years	Female	Spain	

iron therapy (1, 2) and symptomatic with manifestations such as pallor (1, 2, 5), dyspnea (1), fatigue (4), and irritability (2). These signs were observed in our patient.

Another manifestation is protein-losing enteropathy, which occurs with hypoalbuminemia in a variable range (1). Prior to Herbst's first report, the only esophageal disorder that had been associated with protein-losing enteropathy was esophageal cancer (2). It was subsequently associated with other conditions such as achalasia, polyps, and leiomyoma (6). This protein-losing enteropathy has been documented by tests such as fecal excretion of radioactive chromium bound to albumin following intravenous injection. These tests were not performed on our patient (2).

In turn, digital clubbing (or acropachy) has been described in both upper and lower limbs, in either side, without cyanosis (1). The pathophysiology of digital clubbing and protein-losing enteropathy is still unknown. However, these conditions are clearly related to esophageal involvement. It should be noted that these findings are reversed with surgical correction and resolution of esophagitis (1, 2, 4).

One report has described that other manifestations of Herbst triad that had improved after surgery recur when the hernia reappears (4). It has been proposed that the synthesis of neurogenic factors, increasing growth factors, and alterations in blood flow are involved in the appearance of hypertrophic osteopathy, which appears with the changes of the fingers (4).

On the other hand, gastrointestinal manifestations are typical of GERD, and include frequent vomiting and regurgitation episodes (even from birth) (1, 2), epigastric pain (1), heartburn (7), hiccups (1, 5), retrosternal chest pain (1, 2), diffuse abdominal pain (5), and hematemesis (2).

The association between Sandifer syndrome and dystonic cephalic and cervical movements after meals has also been described, presenting with reflux exacerbation (as in our case) (1, 2, 5) and rumination syndrome (2, 5). All of the patients described required extensive studies prior to diagnosis, similar to what happened in our case.

The micro and macroscopic findings observed include severe esophagitis with thickening of the esophagus and significant edema, as well as a local reaction of the mediastinum, which is considerable (2). Histopathology reports may show severe ulcerated chronic esophagitis, esophageal

granulation tissue (4), mild gastritis (2), normal stomach (4), and, sometimes, moderate chronic inflammatory enteropathy (1). Small bowel biopsy reports are normal (2, 4). All these findings were described in our patient.

It is noteworthy that anemia or serum proteins in most patients with Herbst triad reported so far did not improve through pharmacological treatment for GERD or oral iron substitution (2, 5).

With regard to surgical treatment, several strategies have been developed to correct reflux and hiatal hernia, such as the combination of the Boerman and Nissen techniques (2), and Nissen fundoplication (4, 5, 7).

In the original case series, surgical repair resulted in an immediate improvement of Sandifer syndrome, reflux, anemia and return of proteins to normal levels, with a decrease in digital clubbing after one year (2). This is a very similar scenario to that of our patient.

In the description of these cases, the first symptom that was resolved was cephalic movements, which in our case, improved on the third day after surgery, followed by reflux and rumination symptoms, which improved after a week. Normalization of serum proteins took place between 1 and 2 weeks after surgery (5), while anemia improved at 6 weeks with oral ferrous sulphate. Finally, digital clubbing decreased after 9 months to 1 year on average (2, 5, 7).

## CONCLUSIONS

Hiatal hernia and esophagitis, in the context of severe GERD, should be included in the differential diagnoses of digital clubbing and protein losing enteropathy. Timely treatment avoids the occurrence of complications and reverses, in its entirety, the clinical and laboratory alterations that patients develop. This improves the quality of life of these children and their families.

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## Conflict of interest

None declared by the authors.

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