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CLINICAL CASE

An uncommon cause of dysphagia in pediatric age

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Abstract
Introduction: Achalasia is a rare disease in children of unknown etiology. For its rarity and diagnostic difficulty, the authors report the case of a teenager with achalasia.
Case report: 15-year-old boy, with unremarkable past medical history, was referred to the outpatient clinic with a 3-month history of regurgitation and dysphagia. An upper digestive endoscopy was performed, which was normal. The symptoms got worse and he lost 9% of weight. Considering the diagnosis of eating behavior disorder, he was admitted for further investigation. Laboratorial evaluation was unremarkable. Dysphagia characterization suggested a disorder of esophageal motility. Barium follow-through was compatible with achalasia and high-resolution esophageal manometry confirmed this diagnosis. He underwent laparoscopic Heller myotomy combined with Dor fundoplication with no symptom recurrence.
Comments: Achalasia is a rare disease associated with a challenging and delayed diagnosis. The normality of the upper digestive endoscopy and the hypothesis of an eating behavior disorder both led to a delayed diagnosis. It is important to proceed with investigation in the presence of unremitting dysphagia symptoms.

PALAVRAS-CHAVE
Acalásia;
Disfagia;
Manometria;
Adolescente

Uma causa de disfagia pouco comum em idade pediátrica

Resumo
Introdução: A acalásia é uma doença rara em idade pediátrica, de etiologia desconhecida. Pela sua raridade e dificuldade diagnóstica, os autores relatam o caso de um adolescente com acalásia.

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Caso clínico: Adolescente de 15 anos, sexo masculino, com antecedentes pessoais irrelevantes. Por queixas de regurgitação e disfagia com 3 meses de evolução, efetuou Endoscopia Digestiva Alta (EDA) que foi normal. Após agravamento das queixas, com perda ponderal (9%), foi colocada a hipótese diagnóstica de perturbação do comportamento alimentar, pelo que foi internado para esclarecimento do quadro. Analiticamente não apresentava alterações. As características da disfagia durante o internamento (inicialmente para líquidos e posteriormente também para sólidos) sugeriram alteração da motilidade esofágica, tendo sido realizado trânsito esofágico baritado, cujo resultado foi compatível com a hipótese de acalásia. A manometria esofágica de alta resolução confirmou este diagnóstico. Foi submetido a miotomia laparoscópica de Heller com fundoplicatura de Dor, sem recorrência das queixas.
Comentários: A acalásia é uma doença rara, associada a dificuldade e atraso no diagnóstico. A normalidade da EDA e a hipótese de perturbação do comportamento alimentar, contribuíram para atrasar o diagnóstico, pelo que, na presença de queixas persistentes de regurgitação ou disfagia é importante caracterizar exaustivamente os sintomas, pensar na doença e prosseguir com a investigação.

Introduction

Achalasia is a primary motor disorder of the esophagus characterized by insufficient relaxation of the lower esophageal sphincter (LES) and an absence of peristalsis in the esophageal body.[1,2] Its clinical manifestations are difficulty in the passage of food through the esophagogastric junction, without a true organic stenosis or an extrinsic compression, as in the case of a functional esophageal obstruction.[1–3] It leads to incomplete emptying of the esophagus, with a gradually esophageal dilatation and its consequences.[4]

The disease was first described by Thomas Willis in 1674 and, in 1953, King described the first case of achalasia in childhood, presenting the story of a 6-month-old infant.[2,4–6]

This is a rare condition, especially in the pediatric age range,[2] being more frequent in adults between 25 and 60 years old.[5] It is a disease with an incidence of 1:100,000 in the general population, with only 4–5% of these cases occurring in children.[3–7,12] Few patients present symptoms before 15 years of age.[6] In children, the average age at diagnosis is 8.8 years.[8]

The influence of genetic factors in the etiology of achalasia is suggested by the existence of this disease associated with some syndromes, such as Allgrove Syndrome, Rozycki Syndrome and Pierre–Robin Syndrome[3]. Reports of isolated familial achalasia represent less than 1% of all cases of this disease.[3]

The etiology of idiopathic achalasia is unknown.[1,2] There are some forms of secondary achalasia, such as pseudoachalasia secondary to infiltration by tumor, and Chagas Disease which is associated with infection by *Trypanosoma cruzi*.[1,7,9]

Regarding its pathophysiology, achalasia is associated with functional loss of ganglion cells of the myenteric plexus of the esophagus. This change appears to be caused by an autoimmune response involving cytotoxic T-cells and autoantibodies, which triggers a process of ganglionitis with neuron loss of the esophageal myenteric plexus. This trigger can be of an infectious nature associated with some viral infections (Herpes Simplex Virus type 1, measles) or from the direct effect of a toxin, in a susceptible host (immunogenic base).[3,5,9,10] The inflammation of the myenteric plexus leads to degeneration and dysfunction of postganglionic inhibitory neurons of the distal esophagus. The imbalance between nitric oxid and vasoactive intestinal peptide used by neurons as neurotransmitters translates in a deregulation in excitatory and inhibitory control of the LES and the adjacent esophagus, leading to achalasia.[9,10]

Given the rarity of this disease, especially in children[7], the description of new cases may contribute to a better knowledge of its clinical manifestations and evolution.

Case report

Male adolescent, 15-year-old, with no relevant past familiar or personal medical history, was referred to the Outpatient Clinic of Centro Hospitalar de Leiria by his attending physician because of borderline elevated TSH (5.81 μUI/mL). This analysis followed complaints of sporadic regurgitation of undigested food which started 3 months earlier. He denied anorexia, abdominal pain, change in stools, weight loss or fever. Approximately 2 months later he complained of dysphagia, initially for liquids and subsequently also for solid foods. He then stated daily nocturnal regurgitation of undigested food.

At physical exam he weighed 53.5 kg (p25–p50); Height – 174 cm (p50–p75); Body Mass Index (BMI) – 17.7 kg/m^2 (p10–p25). He was longilineal with no palpable thyroid or cutaneous lesions. He was flushed and hydrated. Cardiopulmonary auscultation and abdominal exam found no alterations.

Laboratory tests showed: WBC 9500/μL; Neutrophils 4200/μL; Lymphocytes 4300/μL; Eosinophils 300/μL; Hemoglobin 15.0 g/dL; VS 1 mm in 1st hour; TSH 3.39 μUI/mL and FT4 10,6 pmol/L. Liver function and biochemistry with

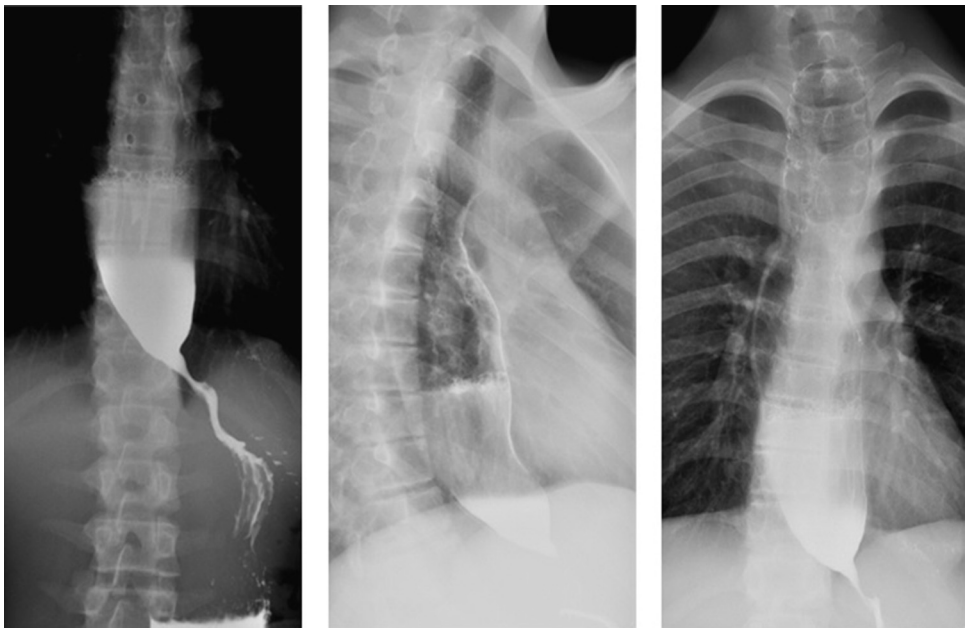

Figure 1 Images from barium follow-through that show a dilated esophagus in almost its entire length, absence of peristaltic waves and sudden decrease in esophageal caliber at the esophagogastric junction, a ''bird's beak'' appearance, with passage of a small amount of contrast to the gastric lumen. These findings are consistent with achalasia.

ions showed no alterations. The chest plain film showed no significant alterations.

The dysphagia worsened, and a diagnosis of eosinophilic esophagitis was considered, so an upper digestive endoscopy (UDE) was performed, which showed no alterations. There were no histological abnormalities found in the biopsies taken from the esophagus and stomach walls.

Two months later, he showed a weight loss of over 1 kg (comprising 9% of weight loss since he first showed symptoms), with a lower BMI (16.8 kg/m^2). Complaints of dysphagia became more frequent and he added nocturnal heartburn to his symptoms. He denied chest pain or respiratory symptoms, specifically nocturnal cough or dyspnea.

His weight loss associated with a normal UDE lead to the consideration of an eating disorder, so he was referred to a pedopsychiatric observation. He was found to have no psychiatric pathology, so he was admitted for further investigation.

During hospitalization, a careful characterization of the symptoms showed an initially selective dysphagia for liquids which gradually evolved into an indifferent dysphagia for all kinds of food. It was possible to observe nocturnal regurgitations. This symptoms lead to a probable diagnosis of an esophageal motility disorder. He performed an esophageal barium follow-through examination (Fig. 1), which showed a dilated esophagus in almost its entire length. There was an absence of peristaltic waves and a sudden decrease of esophageal caliber at the level of the esophagogastric junction, with a ''bird's beak'' appearance, and passage of a small amount of contrast to the gastric lumen. These findings were suggestive of achalasia so he did a high-resolution esophageal manometry which showed a LES with an elevated resting pressure of 48 mmHg (N: 8–35 mmHg), absence of normal LES relaxation and distal esophagus with a peristaltic waves. The Upper Esophageal Sphincter (UES) showed no alterations. These findings were consistent with a dysfunctional esophagogastric junction relaxation, corroborating the clinical and radiological hypothesis of achalasia. He repeated UDE which showed esophageal walls covered with residual food, with effortless passage of the endoscope through the LES into the stomach.

He was discharged from the hospital with a nasogastric feeding tube and a high-protein formula, and underwent laparoscopic Heller myotomy with Dor fundoplication about a month and a half after the diagnosis. He is now about a year and a half after surgery, with no complaints, recovering his previous weight and with no symptoms of gastroesophageal reflux, having not had the need to do any medication, specifically proton pump inhibitors.

Discussion

The clinical features of achalasia are variable depending on the duration of the disease and the age of onset,[3] the main symptoms being dysphagia for solid foods and liquids (>90%), regurgitation of undigested food (76–91%), retrosternal chest pain (25–64%), weight loss (35–91%), heartburn (18–52%) and respiratory complications, including cough (30%) and aspiration (8%).[1] In this case, the patient did not initially value dysphagia and presented with regurgitation, and only later complained of dysphagia and weight loss. Dysphagia is usually only a complaint of older children, such as it happened in this case. Generally, regurgitation occurs immediately after meals,[1] which is also consistent with symptoms reported by this adolescent. It is more common in the supine position, and the patient may wake up coughing and choking.[5] Again in this case the complaints were essentially of gastroesophageal reflux overnight. Cough may still occur, either due to aspiration of food or by compression

of the airway by a dilated esophagus.[4] The predominant symptoms in infantile achalasia are respiratory symptoms and regurgitations which can easily be confused with gastroesophageal reflux disease.[2] Thus, the diagnosis of achalasia should be considered in children with persistent vomiting or growth failure, particularly when associated with symptoms of food impact, dysphagia and weight loss.[6]

Secondary pulmonary disease can occur due to regurgitation and aspiration of the retained material in the esophagus, manifested by nocturnal cough, choking, frequent pulmonary infections, wheezing, atelectasis, and less likely, pulmonary empyema.[4] Some patients may develop hoarseness caused by direct compression of the recurrent laryngeal nerve by a distended esophagus.[4] A serious and potentially fatal complication of achalasia is tracheal obstruction by compression of a dilated esophagus, which may present as the only clinical manifestation of the disease.[4]

In a study by Zhang et al., which included 13 children with achalasia, the mean duration of symptoms was 31 months prior to the diagnosis.[7] This delay in diagnosis is probably due to the fact that children present unspecific complaints, and due to its rarity in this age group. In the presented case, the diagnosis was made about 5 months after the onset of symptoms.

The diagnosis of achalasia is suggested by typical clinical features and confirmed with specific testing, which include barium esophagogram, UDE and esophageal manometry.[1,5]

Typically, the evaluation starts by the esophagogram[1], which is the classic diagnostic exam and is very effective for early detection of the disease.[7] This exam also allows to exclude structural abnormalities, estimate the diameter of the esophagus and the existence of epiphrenic diverticulum.[10,11] The presence of a dilated esophagus with narrowing of the distal esophagus (''bird's beak'' appearance) displayed in this case is a late manifestation of the disease.[4]

A plain chest film may offer some clues to the diagnosis of achalasia.[2] It can show an absence of the gastric air bubble and sometimes widening of the mediastinum.[2] In the supine position, there can be an air fluid level in the mediastinum, often retrocardiac, that represents retained material in the esophagus.[2] In the case described the chest radiograph did not provide any diagnostic clues.

The UDE is essential to rule out or diagnose another esophageal pathology.[1] This exam may also demonstrate an enlarged esophagus, as well as retained food and/or secretions.[5] UDE also allows biopsies of the esophagus, and can also be used as a therapeutic method, by performing pneumatic dilation.[1,3]

It should be noted that 44% of patients with achalasia may show a normal UDE and the esophagogastric junction can easily be transposed, despite the high resting pressure of the LES.[5] In our case, the first UDE performed was normal and there was no obstacle or bump in the passage through the LES into the stomach.

Currently, the gold standard exam to confirm the diagnosis of achalasia is esophageal manometry, which may be performed as conventional or high resolution. The latter is preferred, as it allows to further categorize achalasia in three different types with therapeutic and prognostic implications.[10]

Findings compatible with achalasia diagnosis are absent or incomplete relaxation of the LES and absence of peristalsis in the body of the esophagus. The basal LES pressure may be normal, although is often elevated.[1] In the case presented both of these findings were identified.

The primary therapeutic goal in achalasia is to reduce LES pressure, facilitating the passage of food into the stomach.[5,7] This is essentially a palliative treatment aimed at relieving the patient's symptoms and improving esophageal emptying, thereby preventing the development of mega-esophagus.[2,5]

Pharmacological therapy of achalasia includes smooth muscle relaxants such as calcium channels blockers, nitrates and phosphodiesterase inhibitors.[1,5] However, these agents have not been used in children and in adults its use does not provide effective long-term results.[1]

Another possible treatment is the injection of botulinum toxin directly into LES.[1,5] This treatment also turns out to be ineffective at long-term and is usually reserved for cases with no surgical conditions.[1] Its utilization in pediatric cases is controversial.[3]

Pneumatic balloon dilatation, introduced in 1971 by VanTrapp[10], is another therapeutic option.[1,5] In the adult population, a multicenter study involving five European countries, showed that the efficacy of pneumatic dilation was comparable to laparoscopic Heller myotomy after 2 years of follow-up.[11] However, pneumatic dilatation has a higher rate of dysphagia recurrence at long-term, so that Heller myotomy is preferred in young patients.[10]

The treatment of choice in children, both for its safety and long-term effectiveness, remains the laparoscopic Heller myotomy, associated with an anti-reflux procedure, as it was done in this case.[1,5.7]

POEM (*Per Oral Endoscopic Myotomy*) has recently been introduced as a new minimally invasive treatment for achalasia.[10–12] However, there have not yet been any randomized clinical trials comparing this option with pneumatic dilatation and Heller myotomy. The results of a prospective, international, multicenter study of POEM, including a total of 70 patients, have been recently published and early results were actually spectacular, with 97% of patients reporting complete remission of dysphagia and chest pain.[12] This is far better than either surgery or balloon dilation, with no associated complications, aside from carbon dioxide gas extravasation (easily dealt by abdominal decompression with a Veress needle).[12] The other aspect of POEM is that it is essentially pain free and patients are able to resume normal activities in a matter of days.[12] Prospective comparative studies with laparoscopic Heller myotomy/balloon dilation will be needed to further define the potential long-term benefits of POEM and the therapeutic management of achalasia.[12]

As mentioned before, achalasia is a rare disease in children and its origin is generally unknown.[2,6] In childhood, rarity of this disease can frequently lead to a delayed diagnosis and treatment.[6] This disease should be considered in the differential diagnosis of children with signs and symptoms of esophageal obstruction.[2] This case illustrates the diagnostic difficulties in adolescents with a normal UDE, as a reminder that the normality of UDE should not exclude this hypothesis. The gold standard test for the diagnosis is esophageal manometry and the treatment of choice is Heller

cardiomiotomy associated with an anti-reflux procedure.[2] Although there is no definitive cure for the disease, surgical intervention allows children with achalasia to have a good quality of life.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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