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Very rare coexistence of hypertrophic cardiomyopathy and achalasia

Nadir görülen bir birliktelik: Akalazya ve hipertrofik kardiyomiyopati

To the Editor,

Achalasia is a rare disease that is characterized by the deterioration in esophageal peristalsis and a poorly relaxing lower esophageal sphincter (LES) due to increased LES pressure, with an incidence of 1/100.000 (1). The main symptoms are dysphagia to solids and liquids, regurgitation and chest pain. Heartburn occurs in 27-42% of achalasia patients.

In the literature, achalasia and the coexistence of some cardiovascular diseases has been reported. The coexistence of achalasia with cardiac pre-excitation, pneumopericardium and esophagopericardial fistula presenting as pericarditis, left atrial thrombus, takotsubo cardiomyopathy, and mitral stenosis was previously reported (2-6). One of the remarkable previous reports is about achalasia as a rare cause of congestive heart failure via severe compression of the left atrium (7). Moreover, there were also reports about cardiac arrhythmia during pneumatic dilatation of achalasia or fatal heart block following treatment with botulinum toxin (8,9). However, in the literature, to the best of our knowledge, the coexistence of hypertrophic cardiomyopathy (HCM) and achalasia has not been reported before.

Hypertrophic cardiomyopathy, a disease with a prevalence of 1:500, is characterized by left ventricle (LV) hypertrophy, without dilatation, usually asymmetrical and mainly septal, in the absence of any other cardiac or systemic diseases that can lead to a LV hypertrophy (10). Heartburn and chest pain are frequent symptoms.

The coexistence of HCM and achalasia in the same patient is very unusual. We had the experience of managing a 38-year-old male patient with HCM and achalasia. He had complaints of retrosternal pain, heartburn and exercise intolerance. He had been treated previously by his family physician with proton pump inhibitors for one month but symptoms did not resolve. Finally, he was referred to a cardiologist for further evaluation after electrocardiogram (ECG) was obtained because of deep negative T waves in the precordial and lateral leads and LV hypertrophy with a strain pattern. The transthoracic echocardiographic study showed an asymmetric type of LV hypertrophy (anterior ventricular septum: 30 mm, posterior wall 11 mm) (Figure 1). The diagnosis of HCM was made. There was a moderate LV outflow gradient (mean gradient: 30 mmHg). Myocardial perfusion scintigraphy (SPECT) was planned on the suspicion of coronary ischemia, but no signs of ischemia or perfusion defects were detected. He was treated with 100 mg metoprolol and 100 mg acetylsalicylic acid once a day; however, on the 20th day of the treat-

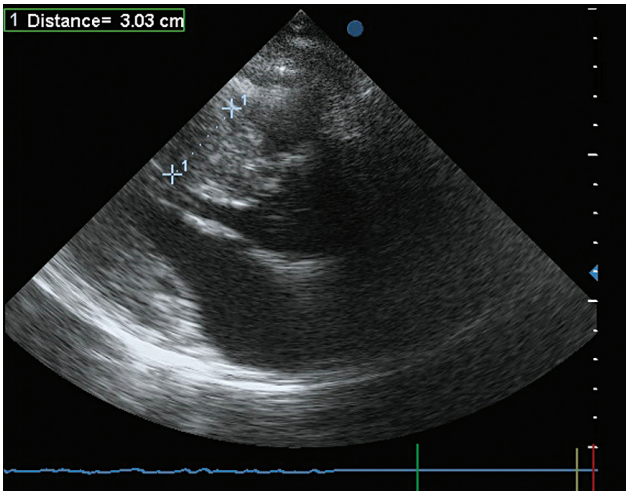

Figure 1. The parasternal long-axis echocardiographic image of the asymmetric type LV hypertrophy (note the extraordinary thickness of the anterior ventricular septum: 30 mm).

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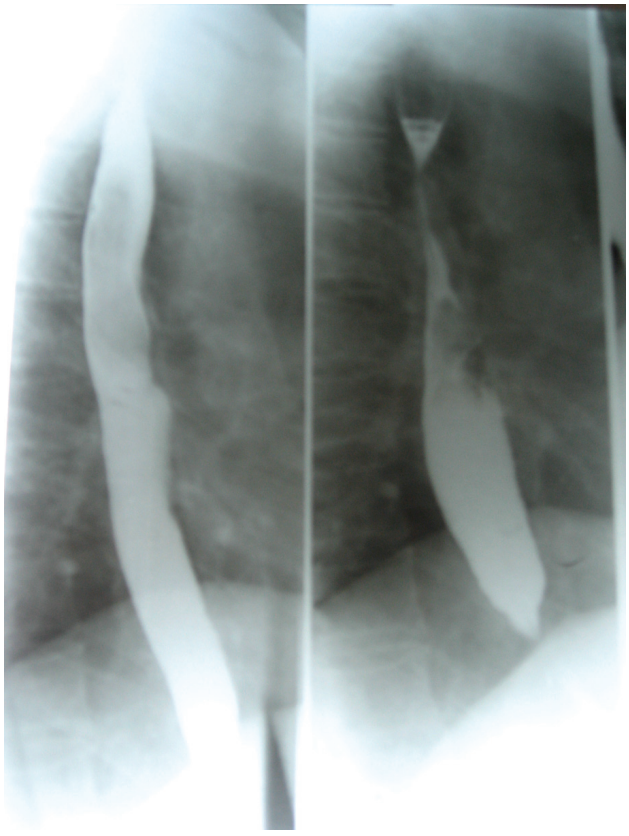

Figure 2. Barium esophagogram demonstrating the narrowed ending of the esophagus, resembling a bird's beak, and the accompanying dilated esophagus.

ment, he returned with a deteriorating heartburn and progressive dysphagia. He was referred to a gastroenterologist. The upper gastrointestinal endoscopy was normal. However, barium esophagogram revealed the diagnosis of achalasia with a narrowed ending of the esophagus, resembling a bird's beak, and a dilated esophagus with delayed emptying of the barium into the stomach (Figure 2). With the diagnosis of achalasia, pneumatic balloon dilatation was performed. His medication was changed to verapamil 120 mg once a day and metoprolol was stopped due to its possible augmentative effects on LES contractility.

In this particular patient, we think that the initial metoprolol therapy after the diagnosis of HCM may have accelerated the symptoms of achalasia due to its augmentative effects on LES contractility.

The coexistence of these diseases also drew our attention to some interesting common physiopathological pathways. Vasoactive intestinal polypeptide (VIP) and the VIP receptor 1 gene, which is highly polymorphic, were suggested to play a role in late-onset idiopathic achalasia (11). Increased degradation of VIP in the heart with fibrosis was also demonstrated previously (12). Furthermore, there are some reports suggesting that the impaired neuronal nitric oxide (NO) synthesis of the myenteric plexus may be a contributing factor in the pathogenesis of achalasia (13). There is also a growing body of evidence about NO playing an important role in the physiopathology of HCM. Decreased expression of myocardial endothelial NO synthase among dogs with HCM was previously described by Piech et al. (14). Moreover, different protein kinase C (PKC) isozymes were shown to mediate LES tone and phasic contraction of esophageal circular smooth muscle (15); PKC-α was shown to induce cardiomyocyte hypertrophy by an increase in protein synthesis, protein-DNA ratio, and cell surface area (16). The crucial roles of the VIP signaling system, NO and PKC in the physiopathology of both diseases may require further investigation.

We believe it is important for the clinician to be aware of the presence of this entity. HCM patients with deteriorating chest pain or new-onset dysphagia during the follow-up, especially while under therapy with beta-blockers, should undergo further examination in consideration of achalasia, which should necessitate a gastroenterology consultation.

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A high chromogranin A: Is it always a tumor?

Yüksek kromogranin A düzeyleri her zaman tümör varlığına mı işaret eder?

To the Editor,

Human chromogranin A (CgA) is a secretory protein that is used as a tissue marker for neuroendocrine tumors (NETs) (1,2). In patients with carcinoids and pheochromocytomas, CgA is a more stable marker than plasma levels of serotonin, catecholamines and their urinary metabolites (3). It may also be elevated due to several other causes; however, the use of proton pump inhibitors (PPIs) is the most important reason if elevated CgA level is not caused by a NET (4).

A 65-year-old woman was referred for endocrine evaluation of an incidentally discovered right-sided adrenal mass measuring 1 cm. She had a medical history of type 2 diabetes mellitus and hypertension for 20 years and long-standing gastroesophageal reflux disease (GERD). She was treated with intensive insulin therapy and metformin for diabetes and had been receiving lansoprazole for six months for GERD. She reported that she had been suffering from abdominal pain, bloating, recurrent diarrhea, and constipation for the last year. Hormonal evaluation showed normal plasma aldosterone/renin ratio and overnight dexamethasone suppression test. Urinary meta and normetanephrines were normal. We concluded that the patient's unilateral adrenal mass was nonfunctional. According to the patient's history, a clear conclusion could not be drawn on the association of her diarrheal episodes and her vague symptoms of carcinoid syndrome. Therefore, serum CgA levels, urinary 5-hydroxyindoleacetic acid (5-HIAA) and serotonin levels were measured. Serum CgA level was >1000 ng/ml (normal: <100 ng/ml), while urinary 5-HIAA and serotonin levels were normal. A whole body Indium-111 octreotide scintigraphy was negative. Due to the marked elevation of CgA, thorax and abdominopelvic computed tomography (CT) scan, upper endoscopy and colonoscopy were performed to rule out a NET. Colonoscopy revealed a tubular adenoma in the sigmoid colon, and endoscopy showed esophageal varices and pangastritis. Biopsy samples of gastric mucosa did not indicate enterochromaffin-like (ECL) cell hyperplasia. The presence of elevated liver enzymes, pancytopenia, imaging consistent with chronic liver disease, and esophageal varices on endoscopy suggested liver failure. As for the elevated CgA levels, the possible causes identified were liver failure, diabetes and PPI therapy. After cessation of PPI therapy for one week, serum CgA level plummeted from >1000 ng/ml to 176 ng/ml (0-100 ng/ml) and remained normal (43 ng/ml) one year after stopping PPI treatment.

Hypochlorhydria-induced hypergastrinemia can have a trophic action on ECL cells; thus, CgA can be released into the blood circulation as a consequence of the activation and proliferation of these ECL cells in the stomach. Treatment with PPIs

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