



An Unusual Cause of Intractable Hiccups

Edward Butt, MD, MPH¹, Ernesto Zamora, MD², and J. Marc Shabot, MD²

¹Department of Internal Medicine, The University of Texas Medical Branch at Galveston, Galveston, TX

²Department of Gastroenterology and Hepatology, The University of Texas Medical Branch at Galveston, Galveston, TX

ABSTRACT

Hiccups are a minor nuisance for most people and usually resolve within minutes. However, for some, they can persist for years and result in severe symptoms and even death. This case report describes a patient found to have a mediastinal lipoma resulting in intractable hiccups. The discussion highlights the pathophysiology, etiologies, and treatments of hiccups.

KEYWORDS: case report; intractable hiccups; lipoma

INTRODUCTION

Persistent hiccups are defined as those which last for at least 48 hours while intractable hiccups are those that last for at least 2 months.¹ Intractable hiccups can result in a poor quality of life for patients and even death as the hiccups can precipitate fatal ventricular arrhythmias.²⁻⁵ Hiccups may cause symptoms such as dyspnea, dysphagia, emesis, and insomnia.¹ Knowledge of the reflex arc involved with hiccups may allow providers to better understand and investigate the underlying causes of hiccups.

CASE REPORT

A 58-year-old man with a medical history of gastroesophageal reflux disease (GERD) who presented for 10 years of intractable hiccups. The hiccups occurred daily and lasted for several hours or even days at a time. The hiccups were associated with dyspnea at rest, dysphagia with solids and liquids, and effortless emesis unrelated to meals. The duration of his hiccups was shortened from days at a time to several hours with baclofen 10 mg twice a day as needed.

A subsequent esophagogastroduodenoscopy was unremarkable. An ensuing escalation in treatment of GERD with omeprazole 40 mg twice a day had no effect on his hiccups. Neurologic etiologies were then investigated with brain and cervical spine magnetic resonance imaging. We ordered a chest computed tomography scan which demonstrated a well-encapsulated large 7.5 × 5 × 6 cm lipomatous anterosuperior mediastinal mass adjacent to the left phrenic nerve concerning for irritation of the nerve (Figures 1–3). The lipomatous mass was subsequently resected, and the patient's symptoms resolved on the first day after the operation.

DISCUSSION

Hiccups, which are self-limited, are believed to be caused by rapid distension of the stomach secondary to sudden changes in temperature of the upper gastrointestinal (GI) tract, carbonated drinks, eating too fast, overeating, or aerophagia.⁶ The mechanistic pathway that causes hiccups involves a neurological reflex arc which has 3 components: the afferent limb, the central processing unit, and the efferent limb. The afferent limb includes the vagus, glossopharyngeal, sympathetic, and phrenic nerves, which receive visceral and somatic sensory signals. The central processing unit involves the midbrain, which is involved in pupillary reflexes and movement regulation.⁷ The efferent limb involves the sending of signals in motor fibers of the phrenic nerves to the intercostal muscles and diaphragm.⁸ Intractable hiccups are caused by any abnormality involving the reflex arc.^{1,9}

Understanding the anatomy of the reflex arc can help determine the underlying etiology in a patient with intractable hiccups. For example, issues with the central unit of the pathway can result in hiccups. Patients with ischemia or edema of the brain have

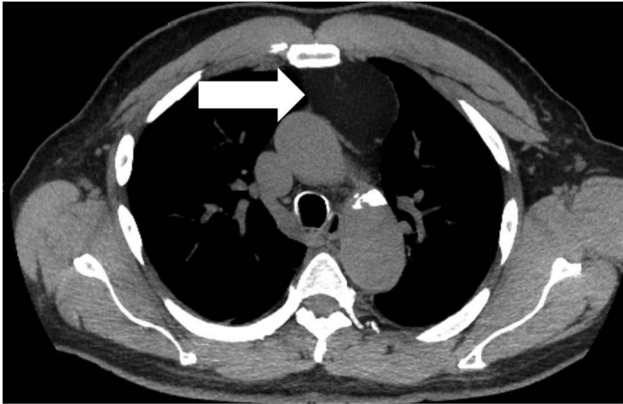


Figure 1. Thoracic computed tomography, transverse view. The arrow identifies a well-encapsulated large $7.5 \times 5 \times 6$ cm lipomatous anterosuperior mediastinal mass adjacent to the left phrenic nerve.

resolution of hiccups once the ischemia or edema improves.^{10,11} Other changes to the brain such as space-occupying lesions have resulted in intractable hiccups, which have resolved with surgical treatment.¹²

A multitude of diseases can involve the afferent and efferent limbs. Lesions that cause changes in pressure of the GI tract such as esophageal tumors can result in reflex activity of the efferent or afferent limbs.¹³ Other mechanisms that cause irritation of the diaphragm, such as volvulus and uterine stretching, can result in hiccups until the inciting cause is addressed.¹⁴

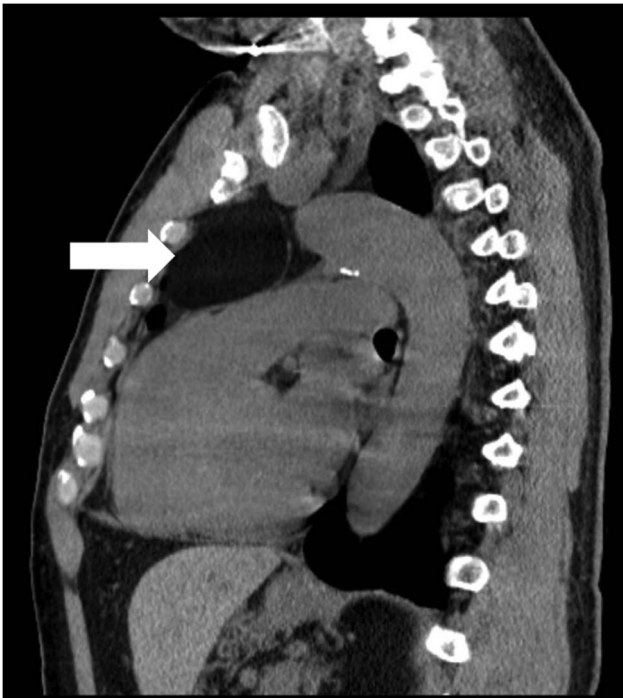


Figure 2. Thoracic computed tomography without contrast, sagittal view. The arrow identifies a well-encapsulated large $7.5 \times 5 \times 6$ cm lipomatous anterosuperior mediastinal mass adjacent to the left phrenic nerve.

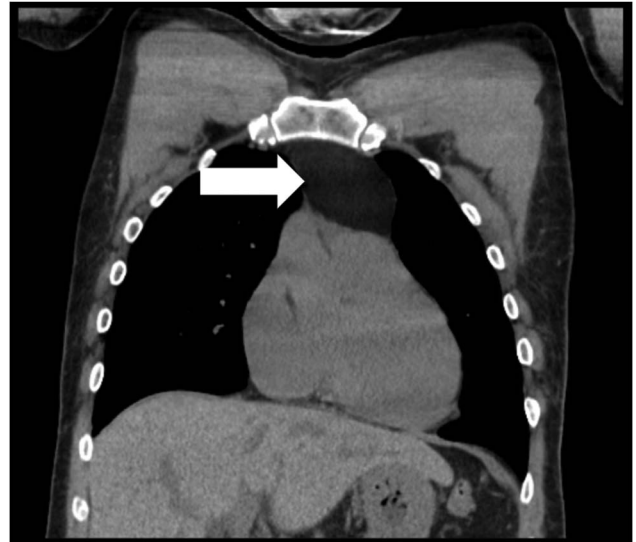


Figure 3. Thoracic computed tomography without contrast, coronal view. The arrow identifies a well-encapsulated large $7.5 \times 5 \times 6$ cm lipomatous anterosuperior mediastinal mass adjacent to the left phrenic nerve.

Interventions that involve the heart, such as ablations for atrial fibrillation, can induce hiccups because the right phrenic nerve comes into close contact with the right atrium.¹⁵ GERD is also noted by some as an etiology.¹⁶

The pharmacology of the pathway can help with investigating underlying etiologies as well. Drugs such as platin agents can cause hiccups due to 5-hydroxytryptamine release stimulating the vagus nerve and initiating the emetic reflex.¹⁷ Dopamine agonists can elicit hiccups because the reflex arc has abundant dopamine receptors.¹⁸ Steroids, opioids, and benzodiazepines can also lead to hiccups.^{19–21} Steroids can directly stimulate the reflex arc; benzodiazepines can directly stimulate the inspiratory muscles; and opioids can elicit hiccups by an unknown mechanism.^{19–21}

An unremarkable brain and cervical spine MRI scan ruled out lesions affecting our patient's central processing unit and afferent-efferent pathways in the cervical region. An esophagogastroduodenoscopy ruled out mechanical causes of hiccups in the upper GI tract. In addition, our patient was not on any medications known to cause hiccups, such as opioids, steroids, or benzodiazepines.

Mediastinal diseases affecting the afferent and efferent limbs have less commonly been documented to result in hiccups. Those that exist are often related to lymphadenopathy secondary to diseases such as sarcoidosis, which may cause compression of the phrenic nerve.²²

Lipomas are benign and common soft-tissue tumors which are solitary, painless, slow growing lesions that can present anywhere in the body. They typically present on the truncal region or extremities.²³ Most lipomas are discovered in the subcutaneous tissues.²³ However, some are located less commonly

in deeper tissues (15.5%), which require imaging to diagnose.²³ Primary mediastinal lipomas can present in the thoracic cavity, make up less than 2% of all mediastinal tumors, and rarely cause any symptoms.^{24,25} When they do, dyspnea and dysphagia can be seen, as in our patient whose mediastinal lipoma caused progressively worsening hiccups over years.

Several medications have been studied for intractable or persistent hiccups. Owing to gamma-aminobutyric acid (GABA) being involved in the neurologic pathway, gabapentin, which has structural similarities to GABA, can be an effective treatment in around three-fourths of cases.^{26,27} Baclofen, a GABA agonist, provides similar results. Dopamine antagonists such as metoclopramide can be effective because they block receptors located on the reflex arc.^{18,28} Finally, 5-hydroxytryptamine antagonism, through medications such as risperidone, has been shown to alleviate hiccups by decreasing stimulation of the vagus nerve.^{17,29} Nonpharmacological treatments, such as phrenic nerve blockage, have shown success, but it comes with dangerous risks including respiratory compromise.³⁰

When pharmacologic treatments fail and hiccups remain persistent or intractable, the search for its etiology is crucial. In our patient, his workup led to the resection of a mediastinal lipoma and resolution of his intractable hiccups.

Over 4,000 hospital admissions occur annually because of hiccups.⁸ Some cases result in death and others a poorer quality of life. Mediastinal pathology is rarely discussed as a cause of hiccups. This case highlights the importance of keeping in mind a broad differential when evaluating a patient with intractable hiccups to properly find and treat the etiology of the hiccups.

DISCLOSURES

Author contributions: E. Butt took a main role in writing and revising the report. E. Zamora had acquired the information in the case and aided with the writing and revision of the draft. M. Shabot analyzed and organized the report along with revising it multiple times. All authors approved the final version of it and agree to be accountable for all aspects of the work. E. Butt is the article guarantor.

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