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Intractable hiccups caused by pulmonary embolism.

A case report

Abstract

The list of signs and symptoms of pulmonary embolism is very long. However, none of the authors has previously reported that pulmonary embolism may be the cause of intractable hiccups. We present here the case of a 58-year-old man with lung cancer, who consulted us because of intractable, continuous hiccups which had been uninterrupted for four weeks. None of the known pharmacological therapies was successful. Thrombosis of the vena cava inferior was found on the abdominal ultrasound, and despite the lack of any evidence it was thought that thrombosis and probable pulmonary emboli may be related to the hiccups. The patient was treated with Deltaparin sodium and the hiccups stopped after 48 hours. As the patient deteriorated a couple of weeks later, the hiccups reappeared when Deltaparin was discontinued. He passed away peacefully.

Key words: pulmonary embolism, hiccup, singultus, fractionated heparin, deltaparin sodium

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Introduction

Intractable hiccups or singultus can be induced by inflammation, damage or mechanical irritation of the nerves contributing to the hiccup reflex [1]. The hiccup reflex on the afferent side consists of the phrenic and vagal nerves plus a sympathetic chain at the level of T₆–T₁₂. All but the phrenic nerve also innervate the lungs and pleura. It is thus conceivable that lung and pleural pathology can be related to the onset of intractable hiccups.


The list of the causes of hiccups is very long [2]. Slightly shorter is the list of the recognized signs and symptoms of pulmonary embolism [3, 4]. Among them are chest pain, breathlessness with decreased haemoglobin saturation, cough, sometimes with blood, pleural rub and fainting.

Here we report on the first case suggesting that intractable hiccups may occasionally be a symptom of pulmonary embolism. Specific diagnosis and treatment may result in symptom control.

Case description

The patient was 58 years of age. He was a heavy smoker for more than 40 years and was known to have severe COPD (FEV₁ < 62% of predicted value). After a period of haemoptysis, he was diagnosed with non-small cell lung cancer of the left upper lobe six months prior to death. Unfortunately, the tumour was inoperable at the time of diagnosis and the patient was treated with palliative radiotherapy to the left upper lobe in order to reduce the haemoptysis. After radiotherapy, he

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experienced improvement in some of his symptoms. However, his appetite was still poor and he was losing weight (at first consultation: 11% of the original body weight). He experienced severe hiccups which had persisted uninterrupted for four weeks. When the non-pharmacological methods of treatment failed, he was prescribed the following sequentially: omeprazole, metoclopramide, baclofen, metoclopramide, gabapentin, chlorpromazine and dexamethazone. Nothing helped. The patient became desperate and even threatened to his doctor that he would commit suicide. He was referred to the Clinic of Pain and Symptom Management. He appeared cachexic on physical examination. His abdomen was soft, but the liver was apparently enlarged. There were a couple of venous dilatations on the abdominal wall. Both legs were swollen but no signs of peripheral thromboembolism were found.

The patient was subjected to bedside abdominal ultrasonography, which is a routine examination in nearly all patients referred to the palliative care clinic. Upon ultrasonography, the liver was mildly enlarged and there was no cholelithiasis. No liver metastases were found. The spleen was of normal size. A typical floating thrombus was found in the vena cava inferior. Doppler investigation of the peripheral leg veins did not suggest thromboembolism.

There were no other realistic options in the treatment of the hiccups, so the patient was started at home on a therapeutic dose of Deltaparin sodium administered SC (12500 U/day). The hiccups disappeared 48 hours after commencing this treatment. He remained at home for three weeks. The single hiccup salvos came back from time to time, but were nowhere near as severe as the previous episode. Finally, he developed a chest infection and became breathless. He was treated with oral antibiotics but his condition deteriorated rapidly. All oral medicines were discontinued and he was started on an SC syringe driver with morphine sulphate 10 mg and midazolam 10 mg, both per 24 hours, which controlled his breathlessness. At his own request, because of pain at the injection sites, the Deltaparin injections were discontinued, which resulted in the recurrence of hiccups within 12 hours. The doses of morphine sulphate and midazolam were up-titrated to 30 mg morphine sulphate and 20 mg midazolam, both per 24 hours, until the patient was comfortable and the hiccups disappeared. He lost consciousness and passed away at home two days later.

Discussion

In principle, any pathology involving the lungs, pleura and mediastinum can be complicated by hiccups [5]. Some hiccups may be drug induced, so careful analysis of the medication and its reduction may lead to resolution of the symptom [6]. In this context, dexamethazone and benzodiazepines are notorious, although, paradoxically, the same drugs may be used to control hiccups. As it is believed that hiccups result from a lowered threshold for electrical discharges either on the periphery (diaphragm, phrenic nerve, pleura or lung) or centrally (brain tumours, brain abscesses, plaques, metabolic causes, etc.), the main objective is to decrease the discharge activity using anticonvulsant drugs such as baclofen [7], valproic acid or more recently gabapentin [8, 9]. Various other treatments have been described. However, most of them are empirical therapies not backed by any form of controlled data.

In the case described above, the striking and sole finding on physical examination and ultrasonography of the abdomen was vena cava inferior thrombosis. The doctor assisting the patient went to his office and searched the databases for "pulmonary embolism" and "hiccups". Although this delivered 98,000 hits, no peer-reviewed articles in medical journals could be identified. There was only one; a non-peer-reviewed article where hiccups were mentioned as a symptom of pulmonary embolism [10].

Based on this, it was decided to treat the patient with SC Deltaparin sodium. To the relief of the patient, and his doctor, the hiccups stopped two days later and did not bother the patient until the last days of his life. When the Deltaparin was discontinued, the hiccups started again. Although we do not have direct proof that the patient suffered from pulmonary embolism, both the ultrasonography and the response to Deltaparin are strongly suggestive. Alternatively, the cause of the hiccups could have been inferior vena cava thrombosis and distension at the level of the diaphragm. We suggest that inferior vena cava thrombosis, with or without pulmonary embolism, may be underdiagnosed in patients with intractable hiccups. Occasionally, abdominal ultrasonography may be worthwhile as it may reveal a treatable diagnosis, as in the case described above.

References

1. Friedman N.L. Hiccups: a treatment review. *Pharmacotherapy* 1996; 16: 986–995.
2. Souadjian J.V., Cain J.C. Intractable hiccup. Etiologic factors in 220 cases. *Postgrad. Med.* 1968; 43: 72–77.

3. English J.B. Prodromal signs and symptoms of a venous pulmonary embolism. *Medsurg. Nurs.* 2006; 15: 352–356.
4. Soderberg M., Hedstrom U., Sjunnesson M., Larfars G., Jorup-Ronstrom C. Initial symptoms in pulmonary embolism differ from those in pneumonia: a retrospective study during seven years. *Eur. J. Emerg. Med.* 2006; 13: 225–229.
5. Cymet T.C. Retrospective analysis of hiccups in patients at a community hospital from 1995-2000. *J. Natl. Med. Assoc.* 2002; 94: 480–483.
6. Thompson D.F., Landry J.P. Drug-induced hiccups. *Ann. Pharmacother.* 1997; 31: 367–379.
7. Walker P, Watanabe S., Bruera E. Baclofen, a treatment for chronic hiccup. *J. Pain Symptom. Manage.* 1998; 16: 125–132.
8. Petroianu G., Hein G., Stegmeier-Petroianu A., Bergler W., Rufer R. Gabapentin “add-on therapy” for idiopathic chronic hiccup (ICH). *J. Clin. Gastroenterol.* 2000; 30: 321–324.
9. Tegeler M.L., Baumrucker S.J. Gabapentin for intractable hiccups in palliative care. *Am. J. Hosp. Palliat. Care* 2008; 25: 52–54.
10. Available on: http://www.trialimagestore.com/article_pulmonary_embolism.html.

