CASE REPORT

Recurrent hiccups may signal brainstem pathology and should be investigated

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SUMMARY

While occasional hiccups are normal, their persistent recurrence is distressing and may have an underlying aetiology. Patients with recurrent hiccups may undergo a long journey and see many physicians before the diagnosis is finally made. The purpose of this report is to increase awareness of central nervous system lesions as a possible cause for recurrent hiccups and provide an illustrative case of an otherwise fit man presenting with ongoing hiccups caused by a medullary haemangioblastoma.

BACKGROUND

Hiccups (or singultus) are produced by intense contraction of the diaphragm and inspiratory intercostal muscles, with reciprocal inhibition of the expiratory intercostal muscles. Closure of the glottis milliseconds after the onset of the contraction produces the characteristic sound and sense of discomfort. While most hiccups will resolve spontaneously or with simple measures, those persisting beyond 24–48 hours should be investigated. Possible aetiologies of recurrent hiccups include structural or functional lesions of the central nervous system (CNS) or of the peripheral nerves controlling the respiratory muscles, metabolic and endocrine disorders, medications, general anaesthesia and psychogenic causes.^{1,2} Due to a wide range of differential diagnoses, establishing the underlying cause can be markedly delayed.

CASE PRESENTATION

A 67-year-old independent right-hand dominant electrical engineer was referred to the neurosurgical department with a history of recurrent hiccups. Over the 3 years that he had this problem, he was repeatedly seen by his general practitioner, underwent multiple investigations under an ear–nose–throat surgeon and was also reviewed by a neurologist.

There were no other symptoms; specifically, the patient denied any visual, speech or swallow disturbance and did not complain of headaches, nausea, imbalance, sensory or motor symptoms. His medical history was significant for diet-controlled diabetes and a neck of femur fracture. Family history was unremarkable. A thorough physical examination revealed no abnormal neurological findings.

INVESTIGATIONS

MRI head demonstrated an avidly enhancing mass lesion in the foramen of Magendie, posterior to the

medulla oblongata and measuring 13×13×10 mm (figure 1). There was no other abnormal enhancement, oedema, restricted diffusion or hydrocephalus, and MRI spine showed no syrinx or other lesions of the neuraxis (not shown).

DIFFERENTIAL DIAGNOSIS

Ependymoma was suggested by the reporting radiologist as the likely diagnosis. Differential included metastasis; however, this was less likely given the duration of symptoms.

TREATMENT

Following a multidisciplinary team discussion, the patient was offered surgery. The lesion was accessed through posterior fossa craniectomy and telovelar approach. An exophytic, avidly red mass with multiple draining veins and surrounding arachnoid adhesions was visualised at the inferior aspect of the floor of the fourth ventricle. After devascularising the tumour, a piecemeal removal was undertaken. The normal vascular anatomy of the region was fully preserved, including both posterior inferior cerebellar arteries.

OUTCOME AND FOLLOW-UP

Postoperatively, the patient was extubated and transferred to a high care ward. He continued to progress and started to mobilise independently. On day 4, he developed progressive agitation, confusion, slurred speech and swallowing issues. A diagnosis of hyponatraemia was made (serum Na 117 mmol/L). This was managed with hypertonic saline and repeated blood samples; however, his conscious level dropped a few hours later requiring intubation and transfer to intensive care unit. Haemorrhage, stroke and hydrocephalus were ruled out by CT scan. Following correction of sodium levels, the patient was successfully extubated and his confusion settled a few days later. After a period of observation, he was discharged home.

Histological examination demonstrated fragments of moderately cellular tumour showing rich vascularity, with reticulin outlining a honeycomb capillary network. Intervening stromal cells had polygonal nuclei showing degenerative atypia but no mitotic activity and pale/xanthomatous cytoplasm. No obvious necrosis was demonstrated. The specimen did not stain for metastatic (CAM5.2, CD10) or ependymal/glia (EMA, GFAP) markers, while S100 and vimentin were positive. Based on these findings, a diagnosis of haemangioblastoma (WHO grade I) was established.

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Figure 1 Post-gadolinium T1-weighted MRI images of the patient's head in sagittal, axial and coronal planes (left to right) demonstrating a well-defined, oval-shaped, vividly and homogeneously enhancing solid extra-axial lesion in the region of the medullary obex (yellow arrow). No mass effect, surrounding oedema, hydrocephalus or other lesions in neuraxis were identified (additional imaging not shown).

DISCUSSION

Depending on their duration, relapsing hiccups were classified by Steger *et al*² into an acute attack (<48 hours), persistent hiccups (>48 hours) and intractable hiccups (>1 month). While the epidemiology of persistent and intractable hiccups has not been studied, a retrospective study found that 55/100 000 patients attending a general hospital were given a primary diagnosis of hiccups.² Hiccups may present as the only symptom (such as described here) in which case a long history of diagnostic work-up and attempted treatment is not uncommon. Rarely, they can signal a serious underlying disease.^{3,4}

Knowledge of the 'hiccup reflex arc' is useful for understanding how different aetiologies can cause hiccups. The arc was first proposed by Bailey in 1943 and consists of the following^{2,5}:

- ▶ Afferent arm: the sensory component of the vagus and phrenic nerves, the pharyngeal branch of the glossopharyngeal nerve as well as the sympathetic fibres from T6 to T12.
- ▶ Central component: the C3–5 segments of the spinal cord, medulla, reticular formation and hypothalamus.
- ▶ Efferent arm: the phrenic nerves innervating their corresponding haemidiaphragms, the external intercostal nerves (T1–T11) supplying the intercostal muscles, and the scalenus anticus nerve to the scalene muscles. Additionally, the glottic closure is controlled by the recurrent laryngeal branch of the vagus.

Consequently, hiccups can be invoked by a process affecting any of the said components. The most common example is distention of the stomach, irritating the afferent limb of the arc, but the list of possible conditions is exhaustive.^{1,2}

A plethora of individual causes affecting the CNS has been associated with recurrent or intractable hiccups. A 1968 study of 220 patients with intractable hiccups found neurological causes in 38 patients (17%), with infarcts constituting the majority. Similarly, a review of 71 patients presenting to a neurology clinic over a 37-year period suggested that infarcts were the cause in 50 cases (66%).³ While lesions elsewhere in the CNS have been described, the medulla seems to be the most common location.³ Usually, disturbance of the nucleus tractus solitarius and/or nucleus ambiguus is implicated.⁵ A range of mass lesions has been documented as possible aetiology and includes cavernoma,^{6,7} glioma,^{3,7} choroid plexus papilloma of the fourth

ventricle,⁷ clival tumours (chordoma, plasmocytoma),³ metastasis (lymphoma, carcinoma),³ syringobulbia,⁸ large aneurysm of the posterior inferior cerebellar artery,⁹ cerebellar haemangioblastoma¹⁰ and tuberculoma⁷ (see Keane³ for more details).

Management is directed at establishing the underlying cause as generally the hiccups tend to resolve once this is treated. In the absence of identifiable pathology, or where no definitive treatment is possible, a range of physical and pharmacological measures have been proposed (for an overview, see Steger *et al*²), the choice generally directed by the pathology, the medical status of the patient and side effects.

In summary, chronic recurrent hiccups is a rare but distressing condition that should not be dismissed. CNS lesion may be involved in a considerable proportion of cases requiring timely investigation and appropriate referral. While in the present case the histology was benign, metastatic lesions and large aneurysms have also been reported as possible aetiology warranting urgent investigation.

Learning points

- ▶ The list of potential causes of recurrent hiccups is long and includes both systemic and focal pathology.
- ▶ Central nervous system lesions, particularly in the region of medulla oblongata, constitute one of the possible aetiologies.
- ▶ While occasional hiccups are normal, recurrent or persistent hiccups should be promptly and appropriately investigated.

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