Hiccups and Multiple Sclerosis

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Hiccups is a rare and unfamiliar presenting symptom of multiple sclerosis. Patients admitted to Ramathibodi Hospital from 1969 to 1992 who had a clinical diagnosis of multiple sclerosis were reviewed. The presenting symptoms and neurological signs were analysed. The clinical features and course of the disease of cases who initially presented with intractable hiccups were studied in detail. There were 4 cases out of a total of 47 cases (8.5%) who presented with hiccups. These patients all had relapse and remission and two of them had a rather fulminant course of illness. Therefore, multiple sclerosis should be seriously considered as a possible cause of intractable hiccups. It may be of benign or malignant form. In the latter, the patients may develop quadriparesis within hours or days and respiratory failure may ensue.They usually respond well to high dose intravenous corticosteroids especially pulse methylprednisolone.

Keywords : *Hiccups, Multiple sclerosis, Brain stem*

J Med Assoc Thai 2004; 87(10): 1168-71
e-Journal: *http://www.medassocthai.org/journal*

Intractable hiccups may result from structural or functional disturbance of the medulla or of afferent or efferent nerves to respiratory muscles. Structural causes which have been reported before were structural lesions of the medulla such as infarct, hemorrhage, tumor, encephalitis, syringobulbia, demyelination and tuberculoma[1]. Brain stem form of multiple sclerosis often presented with dizziness, vertigo, double vision and unsteadiness of the gait. Hiccups is a rare and unfamiliar initial symptom which has been reported in multiple sclerosis[2-5]. The authors report here 4 cases of this disease who had intractable hiccups as their initial presentation and had rather fulminant course of illness.

Patients and Method

Patients admitted to Ramathibodi Hospital from 1969 to 1992 who had a clinical diagnosis of multiple sclerosis were reviewed. The presenting symptoms and neurological signs in the first episodes were analysed. Patients who presented with hiccups were identified and studied in detail.

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Results

The total number was 47; 6 men and 41 women with an age range of 14-68 years (mean 28.6 years). There were 4 cases who presented with intractable hiccups (3 women and 1 man). The presenting symptoms and signs in the first episode of all the cases are presented in Tables 1 and 2.

Case Report

Case 1

A 32-year-old female presented with hiccups for 1 month and vomiting and double vision for 1 week prior to admission. Three days after admission, she developed progressive quadriparesis.

Table 1. Presenting symptoms in the first episode of 47 cases of multiple sclerosis*

Symptoms	Percent of cases
Weakness	61.7
Numbness	53.2
Visual loss	44.7
Double vision	23.4
Gait difficulty	10.6
Vertigo	10.6
Hiccups	8.5

* There were more than one symptom in some cases

Table 2. Neurological signs in the first episode of 47 cases of multiple sclerosis

Signs	Percent of cases
Level sensory loss	53.2
Hemiparesis	44.7
Optic atrophy	38.2
Paraparesis	31.9
Nystagmus	25.2
Ataxia	17.0
Internuclear ophthalmoplegia	8.5
Quadriparesis	4.3
Lhermitte's sign	4.3

Physical examination revealed horizontal nystagmus, deviation of the tongue to the right with some fasciculations, quadriparesis, bilateral extensor plantar response and decreased pain sensation over C_2- L_2 region bilaterally. Cerebrospinal fluid contained 20 white cells/mm^3 with 75% mononuclear cells and 25% polymorphs. The protein was 30 mg% with gamma globulin of 8% of total protein. MRI of the brain showed high signal intensity at cervicomedullary junction on T2 - weighted imaging (Fig. 1).

She received intravenous pulse methylprednisolone with dramatic improvement within a few days. She was discharged with mild residual weakness of the extremities. Thereafter, she had a few more attacks of weakness of all four limbs in the next few months. She was treated with oral prednisolone with good response.

Case 2

A 14-year-old girl presented with intractable hiccups and vomiting for 6 weeks. Two weeks later, she developed right-sided weakness with difficulty in micturition. These were followed by weakness of the left side of the extremitics in a few days and respiratory failure one week after the onset of the weakness.

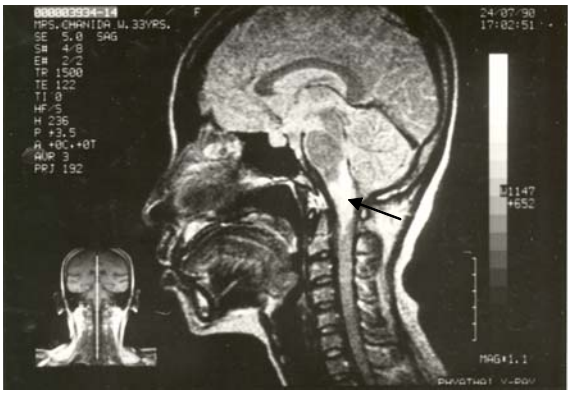

Fig. 1 MRI of the brain of case 1 showing high signal intensity at the cervicomedullary junction on T_2-weighted imaging (arrow)

Physical examination revealed horizontal and vertical nystagmus, fasciculations of the tongue, moderate weakness of the upper and lower extremities bilaterally, decreased pain sensation in the lower limbs and trunk up to T_2 level. Cerebrospinal fluid contained 65 white cells/mm^3 with 90% mononuclear cell and protein of 48 mg% with gamma globulin of 13% of total protein.

She received respiratory support and high dose intravenous dexamethasone with good response. One year later, she developed bilateral optic neuritis. This was followed by 9 exacerbating episodes of weakness of both lower extremities and urine retention in the next 3 years. Eventually, she suffered from septicemia and expired.

Case 3

A 25-year-old man came to the hospital because of persistent hiccups for 6 weeks. He had also suffered from vomiting and jerky vision for 1 week.

Physical examination revealed vertical nystagmus and mild truncal ataxia. There was no motor or sensory abnormality. Cerebrospinal fluid contained 40 white cells/mm^3, all being mononuclear cells. The protein was 89 mg% with gamma globulin of 6% of total protein. MRI of the brain was unremarkable. He received pulse methylprednisolone with rapid improvement.

Three months later, he developed bilateral retrobulbar optic neuritis. This was followed by neuralgic pain over C_{2-3} region and recurrent hiccups 5 months later.

Case 4

A 36-year-old Thai female presented with hiccups for 6 weeks followed by unsteadiness of the gait 2 weeks later. She also had blurring of vision for 1 month before admission.

Physical examination revealed normal visual acuity, optic discs and ocular movement. There were horizontal nystagmus and bilateral incoordination. The findings of the cerebrospinal fluid were unremarkable. The visual and auditory evoked potentials were normal.

She received high dose intravenous dexamethasone and was maintained with oral prednisolone with improvement in two months. Subsequently, she developed episodes of papillitis and recurrent ataxia one year and one and a half years later respectively. Three years after the first episode, she developed left-sided

weakness and numbness. On examination, there were pale optic discs bilaterally, mild left hemiparesis with generalized hyperreflexia, astereognosis on the left, Lhermitte's sign, incoordination on the left and ataxia. MRI of the brain showed high signal intensity on T_2 -weighted imaging from the medulla to C_{5-6} cord region.

Discussion

The pathophysiology of hiccups was not definitely clear. There were a few reports of multiple sclerosis associated with intractable hiccups which postulated that multiple sclerosis plague or other brain stem lesions might produce intractable hiccups by interfering with the normal descending inhibitory pathway (corticobulbar tracts) disinhibiting or releasing neurons responsible for the hiccups which then discharged spontaneously. These neurons may be those of the dorsal respiratory group (nucleus tractus solitarius) mediating inspiration and nucleus of vagus nerve mediating closure of the glottis. This results in the autonomous generation of discharges and involuntary movement with the features of myoclonic jerks[1,2]. Another explanation for intractable hiccups is the presence of an irritative lesion in the brain stem of multiple sclerosis and other diseases. Apart from a brain stem lesion, intractable hiccups together with syncope has been reported to result from a cervical cord lesion in a patient with multiple sclerosis[6].

In the present report, intractable hiccups was the initial presention of 4 patients who then went on to develop other neurological symptoms and signs. Two of them (case 1 and 2) had a fulminant course of illness on first admission. MRI of the brain of case 1 and 4 showed high signal intensity at the cervicomedullary junction on T_2-weighted imaging compatible with demyelination. MRI was not performed in case 2 and was unremarkable in case 3. All of them responded well to high dose intravenous methylprednisolone or high dose intravenous dexamethasone in the acute phase. They all had a relapse and remission course of illness.

The fact that some of these patients had rather fulminant course of illness on presentation followed by frequent relapses does not conform to a previous view that a brain stem lesion at the onset was associated with a benign prognosis[7]. In contrast, another study showed a markedly poorer prognosis for patients with vertigo as their initial symptom[8]. As regards treatment, these cases exemplify the view that high dose methylprednisolone provides early and prompt relief of symptoms and signs during acute exacerbation but does not prevent new lesions or alter the course of multiple sclerosis[9,10].

Hiccups have been documented to be a rare presentation or even rare manifestation of multiple sclerosis[2-5]. It is the presentation in 8.5 % of the patients in the present series. Hiccups (with or without vomiting) may have been present for weeks or months before other symptoms and signs of multiple sclerosis developed. It may be of benign or malignant form. In the latter, the patients may develop quadriparesis within hours or days and respiratory failure may ensue. They usually respond well to high dose intravenous corticosteroids especially pulse methylprednisolone. However, the course of the illness is often of a relapsing pattern either at the same or different locations typical of multiple sclerosis for years after the initial manifestation. Therefore, multiple sclerosis should be seriously considered as a possible cause of intractable hiccups.

References

1. Al Deeb SM, Sharif H, Moutaery A, Biary N. Intractable hiccups induced by brainstem lesion. J Neurol Sci 1991; 103; 144-50.
2. Mcfarling DA, Susac JO. Hoquet diabolique: Intractable hiccups as a manifestation of multiple sclerosis. Neurology 1979; 29: 797-801.
3. Birkhead R, Friedman JH. Hiccups and vomiting as initial manifestations of multiple sclerosis [letter]. J Neurol Neurosurg Psychiatry 1987; 50: 232-3.
4. Funakawa I, Hara K, Yasuda T, Terao A. Intractable hiccups and sleep apnea syndrome in multiple sclerosis: report of two cases. Acta Neurol Scand 1993; 88: 401-5.
5. Chang YY, Wu HS, Tsai TC, Liu JS. Intractable hiccups due to multiple sclerosis: MR imaging of medullary plaque. Can J Neurol Sci 1994; 21: 271-2.
6. Funakawa I, Terao A. Intractable hiccups and syncope in multiple sclerosis. Acta Neurol Scand 1998; 98: 136-9.
7. Phadke JG. Survival pattern and cause of death in patients with multiple sclerosis: results from an epidemiological survey in northeast Scotland. J Neurol Neurosurg Psychiatry 1987; 50: 523-31.
8. Riise T, Gronning M, Aarli JA, Nyland H, Larsen JP, Edland A. Prognostic factors for life expectancy in multiple sclerosis analysed by cox-models. J Clin Epidemiol 1988; 41: 1031-6.
9. Kesselring J, Miller DH, MacManus DG, et al. Quantitative magnetic resonance imaging in multiple sclerosis: the effect of high dose intravenous methylprednisolone. J Neurol Neurosurg Psychiatry 1989; 52: 14-7.
10. Anderson TJ, MacG Donaldson I, Sheat JM, George PM. Methylprednisolone in multiple sclerosis exacerbation: changes in CSF parameters. Aust NZ J Med 1990; 20: 794-7.

การสะอึกและโรคมัลติเพิลสเคลอโรสิส

รวิพรรณ วิทูรพณิชย์, บุษยา ภิรมย์ใหม่, สุพจน์ ตุลยาเดชานนท์

การสะอึกเป็นอาการนำที่แปลกและเกิดไม่บ่อยของโรคมัลติเพิลสเคลอโรสิส ผู้นิพนธ์ได้วิเคราะห์อาการและอาการแสดงของผู้ป่วยในของโรงพยาบาลรามาธิบดีที่ได้รับการวินิจฉัยว่าเป็นโรคมัลติเพิลสเคลอโรสิส ตั้งแต่ ค.ศ.1969-1992 และได้ศึกษาผู้ป่วยที่มีอาการสะอึกเป็นอาการนำอย่างละเอียด พบว่า มีผู้ป่วย 4 รายจาก 47 ราย (8.5%) ที่มาด้วยอาการสะอึก ผู้ป่วยกลุ่มนี้มีอาการทางระบบประสาทที่เป็น ๆ หาย ๆ และผู้ป่วย 2 รายมีอาการของโรคค่อนข้างรุนแรง ฉะนั้น ควรนึกถึงโรคมัลติเพิลสเคลอโรสิสเสมอในการวินิจฉัยแยกโรคผู้ป่วยที่มาด้วยอาการสะอึกต่อเนื่อง

การดำเนินโรคเป็นได้ทั้งแบบเบาและรุนแรง ในแบบรุนแรง ผู้ป่วยอาจมีอาการอ่อนแรงของแขนขาทั้งสี่ภายในเวลาเป็นชั่วโมง หรือ เป็นวันและอาจมีอาการหายใจลำบาก ผู้ป่วยเหล่านี้มักหายดีหลังจากได้รับยาคอร์ติโคสเตอรอยด์ขนาดสูงโดยเฉพาะมีทายล์เพรดนีโซโลน