Idiopathic Multiple Cranial Neuropathy A Twenty Year Experience

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A report on 8 patients with idiopathic multiple cranial neuropathy is presented. The syndrome consists of headache, facial pain and diplopia preceding the onset of cranial nerve palsy. The cranial nerves most frequently involved were the third, fifth and seventh. All patients were treated with corticosteroid therapy. The symptoms were self-limiting in their course and corticosteroid therapy appeared to hasten recovery of function. Only in a few cases a noticeable neurological deficiency remained. Differential diagnosis and etiological considerations are discussed.

Key words: Idiopathic multiple cranial neuropathy, Etiology, Guillain-Barré syndrome, Tolosa-Hunt syndrome

The etiology and pathogenesis of idiopathic multiple cranial neuropathy (IMCN) is often obscure (1-4). In a few cases the syndrome is associated with sarcoidosis (5), diabetes mellitus (6), and tuberculosis (7). Many of the cases have been reported from Asia. Typically, the clinical syndrome is acute in the onset and is characterized by multiple cranial nerve palsy mostly affecting the oculomotor and facial nerves. Symptoms are self-limiting and respond well to the corticosteroid therapy. Sometimes the onset of cranial nerve dysfunction is preceded by infectious process and therefore the possibility of Guillain-Barré syndrome is emphasized as an etiological factor (8). There are also same cases in which the syndrome has been shown to be inherited (9). However, there are many possible etiological factors, which may cause the syndrome, in most of the cases the etiology remains unknown in spite of extensive investigations. In this paper, we report our own data on 8 patients with IMCN during a span of twenty years.

MATERIALS AND METHODS

The patients materials for this paper consists of 8 patients with symptoms and signs of dysfunction of more than one cranial nerve without other pathological findings in neurological examination or any extension in the neurological signs during a long-term follow-up (1). Cases with involvement of a single cranial nerve, congenital cases and those associated with trauma, demyelinating, neuromuscular and cerebrovascular disease were excluded. In spite of extensive investigations, which were properly considered in each case, no clear etiology could be derived. Eight cases of IMCN were identified. The patients were examined many times at the out and in-departments. Both neuro-otological and neuro-ophthalmological examinations were carried out in all of the patients. The following investigations were carried out in all of the patients: Detailed neurological examination, erythrocyte sedimentation rate (ESR), Veneral disease research laboratory tests (VDRL), white blood cell counts (WBC), antinuclear antibody tests (ANA), analysis of cerebrospinal fluid (CSF), skull X-ray, angiography and computed

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cranial tomography (CT). Also, other routine and special laboratory investigations such as glucose tolerance test, hormonal and immunological tests were carried out.

RESULTS

There were 4 men and 4 women with IMCN aged 13 to 48 years, though half of cases were in the 3rd decade (Table 1). All of the patients had previously been in good health and were not exposed to toxic or noxious agents. None had a family history of illness or neurological disorder.

Headache, diplopia and facial pain

Seven patients had headache. Headache was usually the initial symptom, and tended to be unilateral, usually in the frontal or temporal areas. Five patients had diplopia. Six patients exhibited facial pain. Usually pain commenced few days before the nerve palsy. The pain was aching and unrelating, but never throbbing. In the individual case pain was localized in the earlobe and cheek. Nausea was present only in case 2. Case 5 had

dysarthria. None had periorbital edema and conjunctivitis.

Cranial nerves

Neurological symptoms referable to the affected cranial nerves were usually abrupt in the onset. They included diplopia, ptosis, altered facial sensation and others as might be expected.

The nerves involved were II (2/8), III (7/8), IV (3/8), V (6/8), VI (4/8), VII (6/8), IX (1/8) and X (1/8). The VIII, XI and XII were not involved in any of our patients. The most common finding was unilateral ophthalmoplegia and facial palsy on the painful side. Cases 2 and 6 had a transient decrease in vision, although resolved. Unequally reactive pupils were present in 2 of 8 cases. None had papilledema. Ptosis was present in 6 of 8 cases.

Laboratory tests

Table 2 illustrates a summary of etiological investigations. None had symptoms of diabetes mellitus. All had normal glucose tolerance tests and normal fasting blood sugar concentration. Erythrocyte sedimentation rate (ESR) was normal in 7 cases,

Table 1. Summary of 8 patients with idiopathic multiple cranial neuropathy

Case	Age	Sex	Duration	Symptoms	CN affected											
			before CN	before												
			Palsies	admission	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII	
1	68	F	5 days	headache diplopia facial pain	L	X	X	X(V1)	X							
2	33	M	2 days	nausea headache	L X	X				X	X					
3	49	F	10 days	headache diplopia	R L	X	X				X X					
4	13	M	8 days	headache facial pain	L	X		X(V1)								
5	39	M	10 days	facial pain dysarthria	L R					X X(V3)	X X		X X			
6	39	F	5 days	headache diplopia facial pain	L X R	X X		X(V1)	X	X X						
7	52	F	3 days	headache diplopia facial pain	L	X		X(V1)	X	X						
8	33	M	35 days	headache diplopia facial pain	R	X	X	X(V1)		X						

CN=cranial nerve. F=female. M=male. L=left. R=right

Table 2. Summary of etiological investigations

Case	ESR (mm/hr)	VDRL	WBC	ANA	CSF		Radiology		
					Cells ₃ (cumm ³)	Proteins (mg/dl)	Skull X-ray	Angiography	CT
1	12	Neg	5800	Neg	5	65	N1	N1	N1
2	26	Neg	6000	Neg	4	22	N1	N1	N1
3	8	Neg	5800	Neg	10	37	N1	N1	N1
4	7	Neg	7400	Neg	ND	ND	N1	N1	N1
5	9	Neg	6200	Neg	140	154	N1	N1	N1
6	5	Neg	3800	Neg	7	22	N1	N1	N1
7	3	Neg	4200	Neg	1	44	N1	N1	N1
8	4	Neg	5600	Neg	12	31	N1	N1	N1

ESR = erythrocyte sedimentation rate. VDRL = venereal disease research laboratory tests. WBC = white blood cell counts. ANA = antinuclear antibody tests. CSF = cerebrospinal fluid. CT = computed cranial tomography. ND = not determined. Neg = negative. N1 = normal.

while in case 2 it was 26mm/h. Venereal disease research laboratory tests (VDRL) and antinuclear antibody tests (ANA) were negative in all cases. All patients had a normal white blood cell count (WBC).

Cerebrospinal fluid

The cerebrospinal fluid (CSF) was abnormal in 3 of 7 cases with elevation of protein or/and pleocytosis. Protein count was elevated in cases 1, 5, and 7. Case 5 and 140 mononuclear cells/cumm³. Cultures for bacteria and fungi, and cytology were negative in all patients. All showed negative testing results for viral agents.

Neuroradiology

Skull X-ray, angiography and computed cranial tomography (CT) were normal in all cases.

Corticosteroid response

Every patient received prednisolone 30 to 60 mg per day. In 6 of them, improvement began within 7 days and in five cases recovery was complete by two months. Case 6 continued to have dilated pupil two years later. There were no reported complications. No patients died and none had recurrence (Table 3).

Table 3. Summary of corticosteroid response

Case	Beginning of recovery	Duration of CN deficit	Residual deficit	Steroid response	Relapse	Follow-up (months)
1	5 days	25 days	None	Yes	No	60
2	5 days	45 days	None	Yes	No	42
3	14 days	> 1 year	diplopia	Yes	No	18
4	None	> 1.5 years	dysesthesia of face	No	No	24
5	6 days	30 days	None	Yes	No	31
6	7 days	2 years	dilated pupils	Yes	No	27
7	3 days	7 days	None	Yes	No	23
8	7 days	30 days	None	Yes	No	21

CN = cranial nerve.

DISCUSSION

Multiple cranial nerve palsy may be a manifestation of several known disorders and may occur in sarcoidosis (5), diabetic neuropathy (6), tuberculous meningitis (7), Guillain-Barré syndrome (8) and others; however, many cases remain undiagnosed after extensive investigations. As a clinical entity it is a distinctive syndrome without any underlying disease, and also known as migrating disseminated multiple cranial neuropathy (4). The reports of such are not uncommon in some tropical and a few non-tropical areas. We reviewed all cases of IMCN encountered over twenty years. In the literature women were more often affected than men (1, 2, 4), in our series the male to female ratio was equal. The age of the patients was similar to other cases (1, 2, 4).

Headache, diplopia and facial pain frequently precede the onset of neurological symptoms. While any of the motor and sensory cranial nerves might be affected, involvement of 3rd, 5th and facial nerves was most common. The VIIIth, IXth and hypoglossal nerves were spared. Facial nerve palsy was seen in six of eight patients and Hokkanen et al. (2) stated that the facial nerve was frequently affected. The symptoms were self-limiting in the course and in most cases full recovery reached in some weeks (2). Corticosteroids hastened the recovery in most cases. Five of our patients (case 1, 2, 5, 7 and 8) full recovery was seen within 2 months, otherwise neurological symptoms and signs has been continued for 1 year in two patients (case 3 and 6), and case 4 showed no improvement over a period of years. It is considered that most of cases with IMCN is a clinically benign course but some of IMCN exhibit protracted symptoms and sign in spite of corticosteroid treatment. It should be kept in mind that there is a poor or no steroid responsive cases with IMCN, the resulting spectrum of illness probably reflecting diverse etiologies.

The syndrome of IMCN was recognized by Gowers in this textbook at as early as time 1888 (10). Collier commented (11) on the self-limiting nature of the syndrome and its tendency to recur. In our series, none had a recurrence. Most patients presented a history of headache and facial pain without upper respiratory tract infection preceding the acute onset of the cranial nerve palsy.

In most cases no significant abnormalities were found in blood, CSF and neuroradiology. The CSF showed an albumino-cytologic dissociation with an elevation of protein content and normal count of cells in case 1 and 7, but the Guillain-Barré syndrome could not be verified in either case. Some cases of multiple cranial nerve palsy may represent oligo-symptomatic forms of the Guillain-Barré syndrome (8).

Nevertheless, in their patients, pain was not a feature, and they frequently exhibited cerebellar symptoms and signs in addition to cranial nerve palsy. None of our patients showed cerebellar symptoms and signs. Although cranial nerve palsy has been reported as a complication of diabetes mellitus (6), none of our patients had abnormal fasting blood sugar concentration and glucose tolerance tests. A careful search for evidence of tuberculosis, fungi, sarcoidosis and dysglobulinemia proved negative, nor could collagen disease be verified in patients with suspicious history of illness. Viral infections have been reported to cause isolated cranial nerve abnormalities (12, 13), but all showed negative in serological and CSF testing for viral agents. Carcinomatous meningitis may cause multiple cranial nerve signs (14), but in our cases no atypical cells were seen by CSF cytology.

In 1961 Hunt et al. (15) reported six cases from the United States who suffered a syndrome of focal cranial nerve palsy by recurrent unilateral retro-orbital pain with ocular palsy, hypoaesthesia in the area supplied by the first division of the trigeminal nerve, and occasional blindness. Headache or eye pain preceded the ophthalmoplegia, symptoms lasted from several days to weeks, spontaneous remission occurred, and attacks recurred at irregular intervals over several years.

The only distinguishing criterion from IMCN therefore, requires that structures involved be confined to the cavernous sinus. Steele and Vasuvat noted (3) that their cases of IMCN were similar to cases designated as the Tolosa-Hunt syndrome.

Further, pathological confirmation is needed to clarify these two clinical syndromes.

The patients of the present series represent IMCN. A careful search for systemic diseases proved negative. It should be clear that recognition of the syndrome of IMCN allows few diagnostic shortcuts,

suggesting the etiologically nonspecific nature of its presentation.

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