Reflex myoclonus in olivopontocerebellar atrophy

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Abstract

The presence of reflex myoclonus in response to touching and pinpricking the wrist or stretching the fingers and to photic stimulation was assessed in 24 patients with a presumed diagnosis of olivopontocerebellar atrophy (OPCA) and in 30 age matched control subjects. Reflex myoclonus to somatosensory stimulation was found in 23 patients and in none of the controls. Photic myoclonus was present in 12 patients and in none of the controls. Electrophysiological study of the reflex myoclonus showed enhanced (> 10 μV) somatosensory evoked potentials and an associated reflex electromyographic discharge (C-wave) in 15 patients. These findings indicate that reflex myoclonus is common in OPCA and probably of cortical origin.

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Myoclonus is a brief, shock-like muscle jerk arising in the CNS. It can be classified according to its clinical presentation as spontaneous, action, or reflex. Reflex is the term applied to muscle jerks produced by pin pricking, touching, or stretching a body part, or visual and auditory stimulation. Reflex myoclonus is usually focal or generalised. The neuronal discharge responsible for reflex myoclonus most commonly lies in the sensorimotor cortex (cortical reflex myoclonus) or in the brainstem (reticular reflex myoclonus).

Myoclonus has rarely been reported in patients with olivopontocerebellar atrophy (OPCA). In the few published instances, only severe action and spontaneous myoclonus were described. We were impressed a few years ago by the unusually high frequency of cortical reflex myoclonus in patients with multiple system atrophy, particularly those with presumed OPCA. We have therefore conducted a prospective study to assess the presence and clinical and electrophysiological features of reflex myoclonus in a large group of patients with OPCA and compared the findings with a control group.

Methods

SUBJECTS

The study groups were made up of 24 patients (18 women and six men) with a clinical diagnosis of OPCA and a mean (SD) age of 62 (7) years and 30 age-matched (mean (SD) age 59 (10) years) normal volunteers (usually the patient’s spouse). A positive family history was present in two patients. All other patients were sporadic cases. The diagnosis of OPCA was established by the presence of a typical clinical picture (table 1); absence by history and laboratory tests of other causes of a cerebellar syndrome (trauma, anoxia, hypothyroidism; vitamin E deficiency; GM-2 gangliosidoses; adrenoleucodystrophy, etc); as well as a normal muscle biopsy in eight patients; and particularly by the presence on the CT brain scan of a pronounced and selective atrophy of the brainstem and cerebellum (fig 1). It must be taken into consideration that OPCA is actually a pathological diagnosis. In this sense, it would be most appropriate to consider our patients under the more general diagnostic category of multiple system atrophy, which comprises progressive autonomic failure (Shy-Drager syndrome), nigrostriatal degeneration, and OPCA. We prefer to continue using OPCA to refer to our patient population because all of them had clearcut signs of cerebellopontine damage at the time of study; this is not necessarily the case in patients with nigrostriatal degeneration and Shy-Drager’s disease.

CLINICAL ASSESSMENT

Two of us (MER, JAO) carried out a full neurological examination of all the patients. The presence of reflex myoclonus was investigated in the hands by stimulating with a light touch and by pin-pricking the palmar surface of the wrist and the metacarpal region of the index finger with a sharpened clip (not a thin needle such as the ones commonly used for parenteral drug administration). The effect of muscle stretching was studied by tapping the

| Feature | No (%)
<table>
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<tbody>
<tr>
<td>Postural instability</td>
<td>24 (100)</td>
</tr>
<tr>
<td>Somaesthetic reflex myoclonus</td>
<td>23 (95)</td>
</tr>
<tr>
<td>Bradykinesia</td>
<td>22 (91-6)</td>
</tr>
<tr>
<td>Gait ataxia</td>
<td>16 (66-6)</td>
</tr>
<tr>
<td>Dysarthria</td>
<td>16 (66-6)</td>
</tr>
<tr>
<td>Dysmetria</td>
<td>15 (62-5)</td>
</tr>
<tr>
<td>Urinary incontinence</td>
<td>14 (58-3)</td>
</tr>
<tr>
<td>Photic reflex myoclonus</td>
<td>13 (54)</td>
</tr>
<tr>
<td>Rigidity</td>
<td>12 (50)</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>10 (42-5)</td>
</tr>
<tr>
<td>Ocular square wave jerks</td>
<td>10 (42-5)</td>
</tr>
<tr>
<td>Focal dystonia</td>
<td>9 (37-5)</td>
</tr>
<tr>
<td>Hypertreflexia</td>
<td>8 (31-6)</td>
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<tr>
<td>Resting tremor</td>
<td>6 (25)</td>
</tr>
<tr>
<td>Spontaneous myoclonus</td>
<td>3 (12-5)</td>
</tr>
<tr>
<td>Action myoclonus</td>
<td>3 (12-5)</td>
</tr>
<tr>
<td>Orthostatic hypotension</td>
<td>3 (12-5)</td>
</tr>
</tbody>
</table>

Table 1 Clinical features in 24 patients with olivopontocerebellar atrophy
Reflex myoclonus was elicited by threshold electrical stimulation (0.1 ms duration, frequency <0.5 Hz) of the median nerve in the wrist, and recorded by bipolar surface electrodes placed on the forearm flexor and extensor muscles, simultaneously with the somatosensory evoked potentials recorded from the scalp. Subjects were comfortably seated on a couch with the limb totally at rest. A five channel Mystro (Medelec) machine was used.

ELECTROPHYSIOLOGICAL ASSESSMENT
The methods used have been described in detail. Reflex myoclonus was considered as definite when a visible muscle jerk was consecutively present after five identical stimuli in the same area of the hand.

CT BRAIN SCAN
The diagnosis of OPCA was mainly based on the findings by CT of the typical neuroradiological signs of cerebellar and brainstem atrophy. Atrophy of vermian structures was diagnosed when two or more sulci were clearly visible and by measuring the maximum width and surface of the superior cerebellar cistern. Atrophy of the cerebellar cortex was diagnosed when hemispheric sulci were seen. The median width of the sulci was also estimated. Measurements were made of the maximum width and surface area of the fourth ventricle. The relative size of the brain-
stem was expressed as the width of the pre-

toine cistern divided by the distance

between the posterior clinoid and the fourth

ventricle.1011 The cerebellopontine angle cistern was measured at its maximal width. The presence of cortical atrophy was assessed by

the Evans' index. All measures were esti-

mated directly from the films and converted

into actual values by means of the CT scale.

Table 2 summarises the CT findings. Severe

atrophy of the cerebellum and brainstem with

sparing of supratentorial structures (fig 1) was

present in the OPCA group but not in the

control group.

STATISTICS

Differences in the neuroradiological and

electrophysiological findings between the

groups were analysed by one-way ANOVA. A

χ2 test was used for analysis of the presence or

absence of reflex myoclonus.

Results

Somaesthetic stimulation of the hand caused

reflex myoclonus in 23 of the 24 patients and

in none of the controls (p < 0·001). The jerks were focal and therefore restricted to the

forearm muscles on the stimulated side in 18

patients. In these 18 patients, reflex

myoclonus was produced in either hand. Five

patients showed a generalised jerk after local

stimulation. Pin pricking provoked reflex

myoclonus in the 23 patients. Touching the

wrist or palmar surface of the hand elicited

myoclonus in 17 patients (75%) and stretch-
ing the finger flexors was accompanied by

myoclonus in three patients (18-7%). In most

patients the reflex myoclonus consisted of

several repetitive jerks produced by a single

stimulus. Such discharges could be seen by

visual inspection or felt by the examiner while

holding the hand of the patient.

Electrical stimulation of the wrist was

accompanied by a reflex muscle discharge (c-

wave) recorded from the relaxed forearm

muscles in 16 patients (fig 2). The mean

(SD) latency of this response was 39·9

(6·5) ms (range 30–50). In none of the

control subjects was a similar response obtained

during relaxation. The somaesthetic evoked

potentials were of normal latency in the

OPCA group (table 3) but the mean ampli-

tude of the N20/P25 and P25/N33 waves was

significantly increased (fig 2) with respect to

the controls (table 3). The N20/P25 and the

P25/N33 waves were greater than 10 μV in

15 and 12 patients respectively. All patients

with a C-wave had a “giant” somatosensory

evoked potential.

Discussion

We found a high incidence of focal reflex

myoclonus to somatoesthetic stimuli in patients

with multiple system atrophy of the OPCA

type. This response was brisk, usually

localised to the forearm flexor and extensor

muscles, did not adapt to slow repetitive

stimulation (<1 stimulus per second), and

very often one single stimulus triggered sev-

eral muscle jerks. All these characteristics

are typical and compatible with a myoclonic

response and allow the differentiation of this

form of myoclonus from cutaneous reflexes.12

EMG recording corroborated the phasic and

short lasting character of the myoclonic dis-

charge. Photically induced myoclonus is also

fairly frequent in OPCA.314 By contrast,

spontaneous and action myoclonus were only

present in 12·5% of the patients. This figure

coincides with previous estimations of

myoclonus in OPCA.3 The existence of

reflex myoclonus has to be actively deter-

mined by the examiner, as this sign is often

free of symptoms.

Our finding indicates that reflex myoclonus

is common in OPCA and clearly a pathologi-

cal finding. We did not find this response in

the age-matched normal population. Further-

more, in a prospective study1315 we found

reflex myoclonus (either somatoesthetic or

photic) in a very small proportion of patients

with typical signs and evolution of

Parkinson's disease. Chen et al have also

reported a pathological exaggeration of the

long latency cutaneous reflex (E2) in patients

with multiple system atrophy,16 but less often

in patients with Parkinson's disease. These

findings suggest that reflex myoclonus and

EMG responses evoked by electrical stimula-

tion may be useful signs in the differential

diagnosis of Parkinsonism.1516

Electrical stimulation of the median nerve

evoked an EMG response (c-wave) in 16 of

the 23 patients with OPCA in whom there

was a reflex response clinically. This seem-

ingly lesser power of the electrical stimulus to

evoke reflex myoclonus in the hands may be
more apparent than real. It is possible that different stimulus characteristics, such as longer pulse duration and higher stimulation frequency, could increase the number of patients with a C-reflex. The latency of the C-reflex was around 40 ms in our patients. These data and the increased amplitude of the somatosensory evoked potentials in 15 patients strongly suggest a cortical origin for the visually evoked myoclonus. In cortical reflex myoclonus after electrical stimulation of a peripheral nerve the abnormal discharge arises in the sensorimotor cortex and in photic reflex myoclonus the paroxysmal discharge probably originates in the premotor areas. The finding of two types of cortical reflex myoclonus in patients with OPCA may suggest a generalised disorder of cortical excitability. The histological appearance of the cortex seemed totally normal in two of our patients as has been the case in other examples of cortical myoclonus. The pathophysiological basis of cortical myoclonus is not well understood. The cerebellum is the single CNS structure most often associated with myoclonus. It is tempting to suggest that cerebellar dysfunction could increase the gain of transcortical pathways leading to the pathophysiological emergence of cortical myoclonus. There are, however, several problems in concluding that cerebellar pathology is the only basis of cortical reflex myoclonus. Firstly, the same type of jerk can be recognised clinically in patients with cortical-basal ganglionic degeneration, Parkinsonism, and dementia, and progressive supranuclear palsy (personal observations), in whom the predominant pathology is not in the cerebellum. Secondly, and probably most important, the pathology in multiple system atrophy with OPCA predominance is by no means restricted to the cerebellum. Thirdly, in patients with a “pure” cerebellar degeneration, myoclonus is not necessarily present, and not even focal reflex myoclonus may be seen.

In summary, reflex myoclonus is a common finding in patients with presumed OPCA. This phenomenon has not been clearly recognised previously because of its scarce clinical impact but should be added to the phenomenology of multiple system atrophy with OPCA predominance. Ms María del Mar López, Isabel Sánchez, and Carol Ehlsen edited the article for publication.