Juvenile myoclonic epilepsy

M J CLEMENT AND S J WALLACE

Department of Paediatric Neurology, University Hospital of Wales, Heath Park, Cardiff

SUMMARY The clinical and electroencephalographic features of 10 adolescents with juvenile myoclonic epilepsy are presented. The mean age on onset was 12.3 years. Myoclonic jerks, predominantly on awakening, occurred in all 10 and were associated with infrequent generalised tonic-clonic seizures in nine. Five had first degree relatives with seizures. The neurodevelopmental status was normal in eight and social integration good in seven. Waking interictal electroencephalograms showed normal background activity in nine, polyspike and wave in six, and single spike and wave in eight. Four were photosensitive. Failure to respond to other antiepileptic drugs was usual, but valproate monotherapy resulted in good or complete seizure control. Juvenile myoclonic epilepsy is a well defined clinical entity that responds well to valproate and is usually associated with a good outlook.

Of the childhood epilepsies, those which include myoclonic jerks cause most confusion, and especially in younger children are most likely to be drug resistant. Juvenile myoclonic epilepsy appears to be a distinct and relatively benign epileptic syndrome. Although well recognised in literature from continental Europe and the United States juvenile myoclonic epilepsy has apparently not been studied in detail in Britain.^{1–7} We aim to draw attention to this epileptic syndrome. Our findings in 10 patients with seizures typical of juvenile myoclonic epilepsy are presented. The clinical and electroencephalographic features, and responses to antiepileptic drugs, are reviewed.

Patients and methods

Between 1981 and 1987, 10 adolescents (five boys and five girls) with recent onset of myoclonic jerks, and in most cases associated generalised tonic-clonic seizures, attended the paediatric neurology clinic, University Hospital of Wales. Five were referred by general practitioners and five by consultant paediatricians. On presentation a full history of seizures was taken for both the patients and their first degree relatives. Information was collected on the perinatal and medical histories, as well as developmental, social, and educational details. General physical and full neurological examinations were performed on each patient and all had 'routine' 15 to 20 minute electroencephalographic recordings with hyperventilation and photic stimulation. The response to previous anticonvulsant treatment and to

the introduction of valproate monotherapy was assessed.

Results

SEIZURE TYPES AND CHARACTERISTICS

The seizure types at onset and the intervals between myoclonic jerking and generalised tonic-clonic seizures are shown in table 1, with the ages at onset. In eight patients the myoclonic seizures occurred almost exclusively on awakening in the morning. Similarly, six of the nine patients with generalised tonic-clonic seizures had their seizures predominantly in the early morning after a series of myoclonic jerks. Three of the four girls who had reached menarche described an increase in myoclonic jerking at menstruation. Two patients noticed that their jerks were induced by a television or computer screen.

PREVIOUS SEIZURES AND FAMILY HISTORY OF SEIZURES

Two boys had a history of febrile seizures. One girl had a history of unexplained 'fainting attacks' from 7 years of age. Five patients had a first degree relative with a history of seizures. In three cases there was a history of febrile seizures in siblings, one patient had a sibling with absence seizures, and in another the father had a history of infrequent, early morning generalised tonic-clonic seizures.

PERINATAL AND MEDICAL HISTORY

The perinatal course was uneventful in all but one boy, who had been born by emergency caesarean

Table 1 *Seizure types and characteristics*

<i>Patient No</i>	<i>Sex</i>	<i>Seizure type at onset</i>	<i>Age at onset (decimal years)</i>	<i>Age at first GTCS</i>	<i>Interval between onset myoclonus and first GTCS (months)</i>
1	M	GTCS+myoclonus	9.5	9.5	0
2	M	Myoclonus	10.8	11.7	10
3	M	Myoclonus	10.9	(GTCS did not develop)	
4	F	GTCS+myoclonus	11.6	11.6	0
5	F	GTCS+myoclonus	12.1	12.1	0
6	M	Myoclonus	12.7	12.9	3
7	F	Myoclonus	12.8	12.9	1
8	F	Myoclonus	13.5	14.1	7
9	M	Myoclonus	13.8	14.1	4
10	F	Myoclonus	15.7	15.8	1

GTCS=generalised tonic-clonic seizure.

Mean age at onset of seizures, 12.3; mean age at first GTCS, 12.7.

Mean interval from myoclonus to GTCS in those presenting with myoclonus alone was 4.3 months.

section at term; he had done well after 24 hours observation on a special care baby unit. The medical history was unremarkable in nine; one patient had a posterior fossa medulloblastoma removed at 2 years of age. He had had surgery followed by courses of radiotherapy and chemotherapy, which were completed six years before the onset of seizures.

DEVELOPMENTAL HISTORY

Although not seriously delayed, three patients had first walked after 17 months of age and one of these had also had mildly delayed speech. The developmental history was unobtainable in one girl; she may also have had some delay as, at presentation, she was receiving schooling for the educationally subnormal (moderate).

SCHOOLING, BEHAVIOUR, AND SOCIAL INTEGRATION

Nine patients attended normal school, of whom two required remedial teaching. One received schooling for the educationally subnormal (moderate). Overt behavioural disturbance was reported in two patients who had outbursts of uncontrollable rage. Social integration was appropriate for age in all but three patients. Two lacked confidence and were unreliable with tasks such as shopping. One girl was described as 'rude and rebellious' and did not mix well with her peers.

NEUROLOGICAL EXAMINATION

Neurological examination was normal in seven patients. Of the other three, one was mildly dyspraxic, a second had a minimal hemiparesis. Only the patient with a previous medulloblastoma had more than a minimal disability; he had pronounced dyspraxia.

GENERAL EXAMINATION

General examination was normal in all but one girl who was very short in stature due to unknown causes despite prior investigation.

RESULTS OF ELECTROENCEPHALOGRAPHY (TABLE 2)

The background rhythms were normal in nine patients. The records of six patients showed a generalised and symmetrical polyspike and wave pattern. Of the records of the remaining four, one showed spike and wave activity on hyperventilation, one showed bursts of generalised slow waves and sharp waves accentuated by hyperventilation, and one showed sharp waves and an isolated 'near spike' in the right temporal leads on hyperventilation. In the patient who had had a previous medulloblastoma, spike and wave with pronounced slow wave abnormalities, variable asymmetries, and bilateral phase reversals were recorded. Four patients displayed appreciable photosensitivity and of these, two had a myoclonic photoconvulsive response.

RESPONSE TO TREATMENT

Before attendance at the clinic six patients had been prescribed phenytoin, carbamazepine, or clonazepam, singly or in combination. One showed a partial response to phenytoin, but the dose required produced toxicity. Another showed an unsatisfactory partial response to combination treatment with carbamazepine and clonazepam. The remaining four showed no response to previous treatment. On the other hand, sodium valproate was effective and well tolerated in all our patients. Seven showed cessation of all seizures and in the remaining three cases there was an appreciable reduction in seizure frequency.

Table 2 Results of electroencephalography. (All recordings were made with the patient awake and interictal)

Patient No	Background activity	Isolated spikes	Polyspikes or polyspike/wave	Spike and wave	Abnormal bursts of slow waves	Sharp waves	Photosensitivity
1	Normal	+	+	+	+		*
2	Abnormal			+	+		
3	Normal	+	+	+			†
4	Normal			+			
5	Normal	+	+	+			†
6	Normal		+	+	+		
7	Normal	+				+	
8	Normal	+	+	+	+	+	
9	Normal				+	+	
10	Normal		+	+			*

+ = Present.

*Appreciably photosensitive; †very photosensitive with photoconvulsive jerks.

Discussion

The International Classification of Seizures into partial and generalised forms is well known.⁸ The characterisation of 'epileptic syndromes' by seizure type(s), together with specific findings on electroencephalography and particular neurological or intellectual abnormality,⁹ however, has been less widely practised. The recognition of an epileptic syndrome can help in determining the treatment most likely to control seizures, possible associated problems and the prognosis. Better known examples of such epileptic syndromes include West syndrome, Lennox-Gastaut syndrome, and 'benign partial epilepsy with centro-temporal (Rolandic) spikes'.

At a prevalence of between 4% and 5.4%,^{2 10 11} juvenile myoclonic epilepsy is almost as common as classical absence epilepsy (petit mal), which occurs in about 6% of epileptics.¹² Despite this it remains an underappreciated syndrome, usually unrecognised by the referring clinicians.²

Onset around puberty is a very characteristic feature.^{2 3 5 7 9-11 13 14} At least three quarters of all cases start in the second decade.^{7 10 11} The mean age of onset of myoclonias in the present series was somewhat younger than those from other reports,^{2 3 7 10 11} but the latter have included young adults in contrast with our purely paediatric case load.

In juvenile myoclonic epilepsy the seizures are virtually always of two types and occur almost exclusively on morning awakening.^{3 5 7 10 11 15} Bilateral single or repeated, arrhythmic, irregular myoclonic jerks without loss of consciousness are noted predominantly in the arms, and infrequent generalised tonic-clonic seizures, which may occur separately or more commonly follow a series of myoclonic jerks, can also be present.^{2 5 7 9-11 13 15} Sleep deprivation,

excessive alcohol intake,^{3 7 10 16} emotional stress,⁷ and menstruation^{7 10 11 13} may precipitate the seizures. Nine of our 10 cases had generalised tonic-clonic seizures as well as myoclonic jerks; a proportion comparable with that in other series.^{3 7 10 11} In most cases the myoclonic jerks are present for some time (months or years) before generalised tonic-clonic seizures occur and may then be erroneously considered to be hysterical.^{2 10} Reflecting the somewhat younger age in our cases, the onset of generalised tonic-clonic seizures followed relatively soon after the myoclonias. Four of our 10 patients had clinical or electroencephalographic responses to photic stimulation, in keeping with the observation that virtually no other epileptic syndrome is as closely related to photosensitivity as juvenile myoclonic epilepsy.¹⁴

Genetic factors are clearly of aetiological importance. Half of our cases had first degree relatives with seizure disorders. In other series between 25% and 50% of patients have a family history of seizures.^{3 7 10 11} Only one of our patients had more than minimal abnormalities on neurological examination and these were probably attributable to previous intracranial surgery, radiotherapy, and chemotherapy. The almost invariable normality of patients in other series has been emphasised.^{2 3 7 10 11 15} Almost all patients are reported to be of average intellect,^{2 3 5 6 10 15} and all but one of the children in our series were being educated in normal schools. There may, however, be a tendency to an immature personality trait and social maladjustment.^{6 7 10 15}

When abnormal, the electroencephalogram can provide very helpful confirmatory information. Interictally the background activity is nearly always normal,^{2 3 5 10 13} and epileptic discharges are characterised by multitudes of spikes occurring bilaterally.

ally, bilaterally synchronous spike and wave, and the particularly characteristic polyspike-wave complexes. Repetitive spike and wave complexes always occur at a frequency greater than 3 and usually at 3.5 to 4.5 cycles/second.^{2 3 5 7 10 13} Abnormalities are more likely to be found on records obtained early in the day,¹⁰ after sleep deprivation,^{2 3 10} or after plentiful intake of alcohol or coffee.¹⁰ Hyperventilation is not very provocative, but intermittent photic stimulation commonly produces polyspike-wave discharges.^{2 3 10 14}

The lack of neurological and intellectual deterioration in juvenile myoclonic epilepsy, together with a normal background electroencephalogram, help to distinguish it from the 'progressive myoclonic epilepsies' such as Baltic myoclonus epilepsy, Ramsay Hunt syndrome, myoclonic epilepsy with ragged red fibres, etc, in which progression to dementia and paralysis is almost invariable.¹⁷ Juvenile myoclonic epilepsy must also be differentiated from the rarer 'epilepsy with myoclonic absences' in which generalised, rhythmical, regular myoclonic jerking occurs during a period of altered consciousness and the electroencephalogram shows 3/second spike and wave.¹⁸

Absence seizures have been reported in association with juvenile myoclonic epilepsy but were not present in any of our patients.^{2 3 5 7 15 19} In some of these reports adolescents with absences as well as myoclonic jerks and generalised tonic-clonic seizures appear to have more severe seizure disorders,^{2 7} and it has been suggested that, rarely, transitional forms of myoclonic absences and juvenile myoclonic epilepsy may occur.¹⁵ On the basis of the very good outlook for those who have early morning myoclonias and generalised tonic-clonic seizures only, we suggest that patients with absences in addition should not be classified as having juvenile myoclonic epilepsy.

In the prevention of seizures in juvenile myoclonic epilepsy, it is clearly important to avoid sleep deprivation and excessive intake of alcohol or coffee. In addition, it is usually necessary to use antiepileptic treatment. In common with the findings of all other reports,^{2 3 13 15 20-22} the present series shows the very specific efficacy of valproate. Our patients are still too young for the long term outcome to be considered. In studies with long follow up periods, good control of seizures is maintained with continued valproate, but even after many years, recurrence of the seizures is almost invariable if valproate is withdrawn (J Roger, personal communication).^{7 15}

In conclusion, juvenile myoclonic epilepsy is a well defined epileptic syndrome in which myoclonic jerks and infrequent generalised tonic-clonic sei-

zures occurring on morning awakening start at puberty. A close family history of primary generalised seizures is common and the neurological and intellectual status is usually normal. The electroencephalogram may be normal but more usually, particularly if recorded early in the morning, shows multitudes of spikes, spike and wave, and polyspike-wave complexes, frequently with photosensitivity. The seizures respond well to valproate, but are resistant to other antiepileptic medication. The outlook for freedom from seizures is very good provided valproate is continued, but relapse is usual if treatment ceases.

References

- Aicardi J, Chevrie J-J. Myoclonic epilepsies of childhood. *Neuropadiatrie* 1971;3:177-90.
- Asconapé J, Penry JK. Some clinical and EEG aspects of benign juvenile myoclonic epilepsy. *Epilepsia* 1984;25:108-14.
- Delgado-Escueta AV, Enrile-Bacsal Fe. Juvenile myoclonic epilepsy of Janz. *Neurology* 1984;34:285-94.
- Janz D, Matthes A. Die impulsiv-petit-mal Epilepsie. New York: S. Karger, 1966:55-6.
- Loiseau P, Legroux M, Grimmond P, du Pasquier P, Henry P. Taxometric classification of myoclonic epilepsies. *Epilepsia* 1974;15:1-11.
- Reintoft H, Simonsen N, Lund M. A controlled sociological study of juvenile myoclonic epilepsy. In: Janz D, ed. *Epileptology*. Stuttgart: Georg Thieme, 1976:48-50.
- Simonsen N, Møllgaard V, Lund M. A controlled clinical and electroencephalographic study of myoclonic epilepsy (impulsiv-petit mal): preliminary report. In: Janz D, ed. *Epileptology*. Stuttgart: Georg Thieme, 1976:41-8.
- Commission on classification and terminology of the International League Against Epilepsy. Proposal for revised clinical and electroencephalographic classification of epileptic seizures. *Epilepsia* 1981;22:489-501.
- Commission on classification and terminology of the International League Against Epilepsy. Proposal for classification of epilepsies and epileptic syndromes. *Epilepsia* 1985;26:268-78.
- Janz D. *Die Epilepsien*. Stuttgart: Georg Thieme, 1969.
- Tsuboi T. Primary generalised epilepsy with sporadic myoclonias of the myoclonic petit mal type. In: Becker PE, Lenz W, Vogel F, Wendt GG, eds. *Topics in human genetics*. Vol 4. Stuttgart: Georg Thieme, 1977.
- Hauser WA, Kurland LT. The epidemiology of epilepsy in Rochester, Minnesota, 1935 through 1967. *Epilepsia* 1975;16:1-66.
- Jeavons P. Nosological problems of myoclonic epilepsies in childhood and adolescence. *Dev Med Child Neurol* 1977;19:3-8.
- Wolf P, Goosses R. Relationship of photosensitivity to epileptic syndromes. *J Neurol Neurosurg Psychiatry* 1986;49:1386-91.
- Wolf P. Juvenile myoclonic epilepsy. In: Roger J, Dravet C, Bureau M, Dreifuss FE, Wolf P, eds. *Epileptic syndromes in infancy, childhood and adolescence*. London: John Libbey Eurotext, 1985: 247-58.
- Touchon J, Besset A, Billiard M, Baldy-Moulinier M. Effects of spontaneous and provoked awakening on the frequency of polyspike and wave discharges in 'bilateral massive epileptic myoclonus'. In: Akimoto H, Kazatnatsuri H, Seino M, Ward AA, eds. *Advances in epileptology*. XIIIth Epilepsy International Symposium. New York: Raven Press, 1982:269-272.
- Roger J. Progressive myoclonic epilepsy in childhood and

- adolescence. In: Roger J, Dravet C, Bureau M, Dreifuss FE, Wolf P, eds. *Epileptic syndromes in infancy, childhood and adolescence*. London: John Libbey Eurotext, 1985: 302–10.
- ¹⁸ Tassinari CA, Bureau M. Epilepsy with myoclonic absences. In: Roger J, Dravet C, Bureau M, Dreifuss FE, Wolf P, eds. *Epileptic syndromes in infancy, childhood and adolescence*. London: John Libbey Eurotext, 1985:121–29.
- ¹⁹ Aicardi J. Myoclonic attacks in the epilepsies of adolescence. In: *Epilepsy in children*. New York: Raven Press, 1986:69–71.
- ²⁰ Jeavons PM, Clark JE, Maheshwari MC. Treatment of generalised epilepsies of childhood and adolescence with sodium valproate (Epilim). *Dev Med Child Neurol* 1977;**19**:9–25.
- ²¹ Jeavons PM, Covanis A, Gupta AK, Clarke JE. Monotherapy with sodium valproate in childhood epilepsy. In: Parsonage MJ, Caldwell ADS, eds. *The place of sodium valproate in the treatment of epilepsy*. No 30. Royal Society of Medicine Series, International Congress and Symposium Series, London 1980:53–60.
- ²² Jeavons P. Monotherapy with sodium valproate. In: Dam M, Gram L, Pedersen B, Orum H, eds. *Valproate in the treatment of seizures*. Hvidovre: Denmark Epilepsy Society, 1981:43–50.

Correspondence to Dr MJ Clement, 19 Mariners Drive, Backwell, Bristol BS19 3HT.

Accepted 3 May 1988