LEADING ARTICLE

JUVENILE MYOCLONIC EPILEPSY

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INTRODUCTION

Historically, juvenile myoclonic epilepsy (JME) was first described more than 100 years ago by Herpin. In 1867, Herpin described *maladie de secousse* after observing myoclonic jerks (*secousse*) in his son. Some 30 years later, in 1899, Rabot described the intermittent nature of the jerks which involved the neck and shoulder muscles. He termed these myoclonic jerks "impulsion". Janz in 1985 gave a detailed description of this disorder which is also known as impulsive petit mal of Janz.

THE CLINICAL FEATURES OF JME

The prevalence of this epileptic syndrome has been variously quoted to be between 4-7% by different studies, and is almost as common as classical childhood absence (petit mal)[1,2]. Clinical reports on JME have hitherto been largely on Caucasian populations. The report from the University Hospital, Malaysia[3], of a small series of 11 cases has revealed that this genetic syndrome is as much a problem amongst those of Chinese, Malay and Indian heritage as it is amongst Caucasians. The clinical features of JME are characteristic. There is an age related onset of seizures between 12-18 years of age. In 17% of patients, the seizure pattern consists of myoclonic jerks alone. Fifty-eight percent of the cases present with a combination of myoclonic jerks and generalised tonic-clonic seizures (GTCS). In the remaining 25% myoclonic jerks, GTCS and absences are seen[2]. The myoclonic jerks and GTCS occur almost exclusively within half to one hour of awakening. This is the hallmark of the diagnosis of JME. Sudden morning jerks cause patients to drop whatever they are carrying. However, the subtle nature of the myoclonic jerks, ascribed to nervousness and jitters by patients often go unnoticed. The presenting problem to the doctors is often the GTCS which occur on an average of 24 months later[4]. Diagnosis may be further confirmed on electroencephalogram (EEG) which shows ictal discharges of polyspike and wave at 4-6Hz in an otherwise normal background. Discharges may be activated by photic stimulation in 30-40% of patients and it is noteworthy that there is no other epileptic syndrome so closely related to photosensitivity as JME[5]. Effective treatment is available for the majority of patients with JME. Eighty to ninety percent respond well and very specifically to therapy with sodium valproate[2,4]. However, there is a high incidence of relapse on withdrawal from antiepileptic therapy and Janz has reported this to occur in 91% of patients[6]. The relapse rate with antiepileptic drug withdrawal is among the highest of all epilepsies.

LACK OF AWARENESS AND ERRORS IN DIAGNOSIS

Although JME has been relatively well characterised as an epileptic syndrome, it is generally not well recognised by medical practitioners, in both the local as well as in the international scene. In all patients, this form of epilepsy was not recognised by the referring doctors[1,7,8] which include consultant paediatricians and neurologists. It took an average of 8.5 years from the first myoclonic jerks and 6.5 years from the first GTCS before the correct diagnosis of JME was made[7]. Three of the 11 patients reported in the Malaysian series[3] have taken between 23 to 30 years for a correct diagnosis of JME to be made. This is a testimony that the lack of awareness of this epileptic syndrome is a major obstacle towards proper management of patients with JME. The many years of stress and burden of their epilepsy on their social lives could have been curtailed if only an early diagnosis has been made. It is only in the past several years that neurologists and epileptologists began to appreciate the significance of this syndrome, not only for its clinical importance but also in its relevance in the understanding of the genetics of epilepsy.

It is therefore timely that clinicians be made aware of the diagnostic, therapeutic, natural history and prognostic issues of JME. Accurate diagnosis can be ascertained only by obtaining a thorough, exhaustive history and confirming the diagnosis on electroencephalogram (EEG) showing the typical polyspike-wave pattern characteristic of the syndrome. Errors and delay in diagnosis and treatment preclude good seizure control and dim the possibility of normal lifestyle. The onus to early diagnosis of JME does not lie only with the doctors. Those affected need to identify themselves to their doctors for treatment. To the lay person GTCS may be the only form of seizures. There is therefore a need for greater public awareness to the many other less well recognised and sometimes subtle manifestations of seizures. This is necessary not only in the context of JME but also for other forms of non-convulsive seizures. Health education is the only avenue to promote better public understanding and awareness. Health education and in particular patient education is again important in conditions like JME in which a life-time of medical treatment is deemed necessary for personal well-being and safety. In JME, modification of lifestyle can remove stress factors which make patients vulnerable to recurrence of seizures despite appropriate antiepileptic therapy. Such factors known to precipitate seizures in JME include non-compliance to medication, emotional stress, sleep deprivation, keeping late nights studying or at parties, photic stimulation from sources such as discotheques, computer/video games, and consumption of alcohol and other stimulants including caffeine. The self-imposed conformity, emotional upheaval, provocativeness and defiance of authority characteristic of the adolescent make the adolescent patient population affected by JME especially vulnerable to seizure exacerbation by such lifestyle precipitants. To have to counsel these adolescents and advise them on these restrictions in lifestyle can be a significant challenge to clinicians.

THE GENETIC DIAGNOSIS - JME AS THE MODEL FOR MOLECULAR GENETIC STUDIES

JME is a genetically determined epileptic syndrome in which the seizures themselves constitute the disease. There is ab-

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sence of any identifiable underlying pathology. As in all primary epilepsies, there is a family history of a similar age-related seizure pattern, normal intellectual and psychological development and absence of neurological abnormality.

Research in the genetics of epilepsies has entered a new era. A recent advancement in epileptology is the molecular diagnosis of primary (genetic) epilepsies. JME is the first of such epilepsies to be mapped to a chromosome, namely chromosome 6p21.3[9]. The study was done on the pedigrees of 68 JME probands. Genetic linkage studies were done on their symptomatic and asymptomatic siblings and parents. The mode of inheritance has yet to be confirmed although autosomal recessive[10] and polygenic hypotheses[9] have been considered likely. Studies are now being done to further localise the JME site on chromosome 6. There is, in addition, very strong evidence for linkage of JME to the Bf-HLA loci on chromosome 6. This exciting evidence has brought the diagnosis of epilepsy to the molecular level.

Such breakthrough in medical science can only come about with full cooperation and consent from members of the families concerned. In our local population, the diagnosis of epilepsy still confers a social stigma to the patient and this is greatly frowned upon if heredity of the seizures is implicated. The majority of our local families will shy away from such genetic studies and rather not have their bad heritage come to light. The perception of our local families to epilepsy and its inheritance has much to do with their cultural background and it may take several generations and much more understanding to sensitivity to the disease, to dispel feelings of guilt and shame. Education about epilepsy should extend beyond the patients and their families. Public education to change attitudes may have to be a long term project.

CONCLUSION

The purpose of this article is to bring to the attention of practising doctors a relatively common form of epilepsy that is not recognised. Encouraging results from the molecular genetics of JME will rationalise the diagnosis of a growing number of genetic epilepsies in the future. Some thoughts on the social implications of epilepsy were shared.

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