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Clinical and inheritance profile of familial childhood epilepsy in Jordan

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ABSTRACT

Purpose: To present the clinical profiles and inheritance patterns of familial childhood epilepsy in the highly consanguineous population of Jordan.
Methods: This retrospective study examined children diagnosed with epilepsy and having at least one epileptic parent or sibling. The epilepsy type was classified according to the criteria of the International League Against Epilepsy. Patients were monitored for a period of 6 months to 5 years.
Results: The study population included 39 children belonging to 31 families; 21 boys (53.8%) and 18 girls (46.2%). The age at onset ranged from one month to 16 years. Generalized seizures were observed in 23 patients (58.9%), partial seizures in 14 patients (35.8%); and generalized and partial seizures in two patients (5.1%). Seizure control was achieved in 33 patients (84.6%), and 13 patients (33.3%) were seizure-free for at least two years. Withdrawal of antiepileptic medication was successful in five of these 13 patients (38.5%), while seizures recurred in the other eight (61.5%) on withdrawal. The consanguinity rate among parents of affected children was 61.3%. Pedigree analysis suggested probable autosomal dominant (AD) inheritance with or without reduced penetrance in 13 families (41.9%), probable autosomal recessive (AR) inheritance in 6 families (19.4%), and an X-linked recessive inheritance (XR) in one family.
Conclusions: This is the first report on familial epilepsy involving first degree relatives in Jordan. Genetic testing including exome sequencing could help in reaching the accurate diagnosis and may also reveal novel autosomal recessive genes associated with pediatric idiopathic epilepsy.

1. Introduction

Consanguineous marriages comprise 20–40% of all marriages in Jordan[1–4] which may predispose offspring to rare autosomal recessive conditions.[5–7] Previous studies have indicated that consanguineous marriage is a major risk factor contributing to epilepsy in the neonatal and infancy periods.[8,9]

Genes implicated in idiopathic epilepsies include the *SCN1A* gene, encoding the voltage-gated Na channel α1 subunit ($Na_v1.1$), in some autosomal dominant epilepsies (prolonged, myoclonic, and absence seizures)[10] and the *TBC1D24* gene, encoding an AFR6-interacting protein, in autosomal recessive idiopathic epilepsy.[11] While the Jordanian population has a high rate of consanguineous marriages, to our knowledge there have been no reports describing the inheritance patterns of familial epilepsy.

This study aims to describe the inheritance patterns, clinical profiles, treatment responses, and prognoses of epileptic children with a positive history of epilepsy in their first degree relatives.

2. Patients and methods

This retrospective study was conducted at a child neurology clinic at Jordan University Hospital, a tertiary care referral hospital located in Amman, over a 10 years period from January 2001 to August 2010.

All children aged one month to 18 years presenting with epilepsy during the study period and with a positive family history of epilepsy in at least one first degree relative were included in this study. Identification of these patients was possible through a personal data base of the first author that includes all patients presenting to the child neurology clinic since January 2001. Files for all patients that were identified as epileptic and having a positive family history of epilepsy were revised. To fulfill the inclusion criteria, the pedigrees documented in the files were revised. In the child neurology clinic, family history is usually obtained by the child neurologist from the parent accompanying the child (father, mother or both) with pedigree constructed and stored in the file. Because of the high stigma of epilepsy in Jordan, it is common practice to rely on the parents' reports, without going further and interviewing other family members such as grandmothers or grandfathers who

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probably know more details about the family history. Patients for whom a parent was not available due to death, divorce or other reasons leading to inability to take full family history and difficulty in constructing a pedigree were excluded from the study. Postulation of mode of inheritance of epilepsy was based on the family pedigree that was documented in the file since genetic studies were not done for the families. Due to the retrospective nature of the study, it was not possible to recontact seven families who show pedigrees with data for only two generations (Fig. 1). Children with a family history of febrile convulsions only, a family history of epilepsy but not in first degree relatives, or a family history of epilepsy due to neurodegenerative or neurometabolic disorders or due to symptomatic epilepsy were excluded.

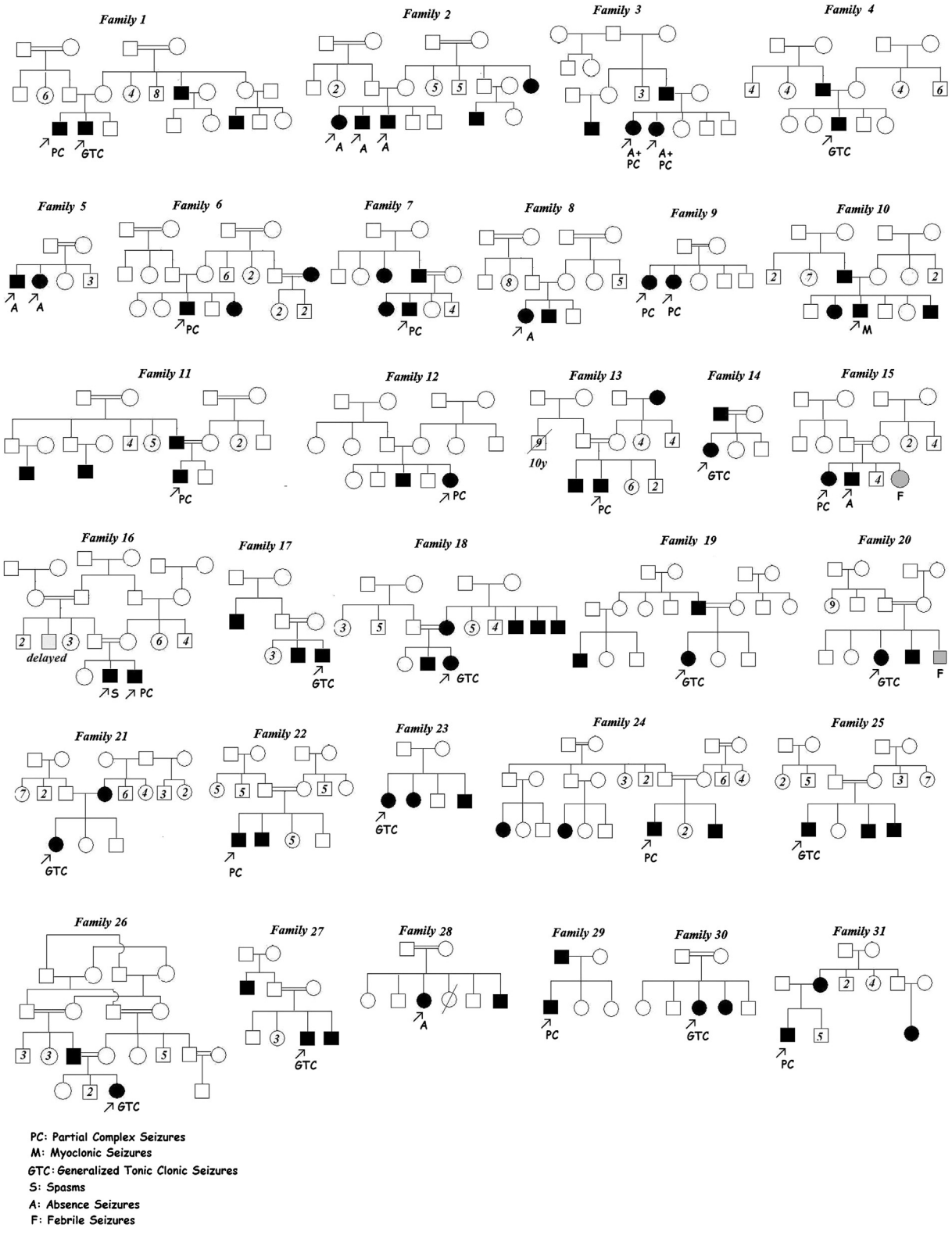

Fig. 1. Pedigrees of the 31 families.