Transient Global Amnesia: A Genetic Disorder?

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Dear Sir,

The pathogenesis of transient global amnesia (TGA) is still unknown although several hypotheses have been suggested in recent years. We describe a family (fig. 1) of whom 4 out of the 8 siblings had TGA and suggest a genetic predisposition.

The oldest sister (No. 4) is a 67-year-old woman who planned to go to the beach to swim in the sea. From the moment she cycled to the beach she could not remember anything. The next thing she recalled was when she returned home with a wet bathing suit. She felt strange about this amnesic episode and went to her family doctor. The general and neurological examinations were normal. The doctor diagnosed a TGA and did no extra tests. Her medical history did not reveal any abnormalities and she did not use any medication.

The brother (No. 6) is a 62-year-old healthy man who was gardening and suddenly could not remember what he was doing. His family brought him to a hospital, and during his stay at the emergency room, he repeatedly asked why he was wearing his working clothes. A neurological examination, an EEG and an MRI scan were normal. He was admitted to the neurology ward with the diagnosis of TGA and recovered completely within a day. His medical history revealed a fractured arm and herniated disk operation. He did not use any medication, but smoked moderately.

The second sister (No. 7), a 58-year-old woman, lived in Spain and was visiting her

Fig. 1. Family tree. Siblings with TGA are shaded in gray (No. 1, 4, 6, 7 and 9).

family in Holland. When she arrived at the airport, her family noticed she was confused and could not retain new information. She was brought to the hospital and an ongoing amnesia was substantiated. Besides her amnesia, no abnormalities were found on neurological examination. She was admitted to the neurological ward, and the next day her memory had normalized. The diagnosis was a TGA. She had no medical history and did not use any medication. A few years later, she had a similar episode of amnesia and a TGA was diagnosed again.

The third sister (No. 9), 55 years old, was working out in a health club like she used to do. Suddenly, her friends witnessed she reacted differently. She kept asking the same questions and had an amnesic episode, without other symptoms. She had no headache. They brought her home, and her

husband, a physician, diagnosed a TGA. Her medical history revealed migraine with aura, with her last migraine attack many years ago. She did not use any medication.

The mother (No. 1) of these siblings might have had a TGA as well. The day after her 75th birthday she wondered why she had so many flowers in her house and could not remember she had celebrated her birthday. The next morning she was healthy again. We cannot confirm this story since she is deceased.

TGA is a neurological syndrome defined by clinical features only. All family members had a clinical episode suggestive of TGA, as clinically defined. This family suggests a genetic predisposition to TGA. Since the incidence of TGA is relatively low (5–11 per 100,000) [1], a coincidence is not very likely. Another possibility is an un-

derestimation of the incidence of TGA in general. We think a TGA is distressing for both patients and family members, and most patients will seek medical attention.

Until now a responsible gene has not been detected. There are some earlier reports of families with a high incidence of TGA. Some suggest an underlying familial disease which makes family members more vulnerable to TGA, or a genetic component [2–5]. Nevertheless, in the literature or textbooks, a genetic basis for TGA is seldom mentioned.

Since the first description of TGA, several other pathogeneses have been suggest-

ed, including epilepsy, migraine, arterial ischemia and venous congestion [6–11]. None of these hypotheses have been proven or completely accepted. Interestingly, migraine is reported more frequently in TGA patients than in age-matched controls [12]. In the family we observed, 1 sister had a history of migraine. The relation of migraine to TGA is speculative. A common underlying mechanism of cortical spreading depression might be present, or a common genetic basis.

It is still poorly understood why the recurrence of TGA is so low. In case of a genetic predisposition, a higher recurrence

rate would be expected. In fact, the low recurrence risk of TGA is remarkable for any underlying cause.

We believe the described cases, in combination with earlier reports, might help to shed more light on the still poorly understood syndrome of TGA. We suggest a genetic predisposition might be part of the pathogenesis in a subgroup of TGA patients, but further genetic research is warranted to prove this hypothesis. These data might also help to encourage new multicenter studies on the basis of genomic screening.

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Erratum

The last name of the second author was misspelled in the article 'Transient global amnesia: a genetic disorder' (Eur Neurol 2010;63:186–187). It should read de Bruijn.

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Abstract

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