and managed him as an outpatient for the following 18 months.

Comment

Considering all factors, such as the temporal relationship between the seizure onset and quetiapine intake, the exclusion of other possible etiology of seizures and their cessation after drug withdrawal, we judged that quetiapine precipitated seizure activity in both patients. These cases serve as a reminder that postmarketing surveillance of newly released medications, clinical awareness of seizure potential when using these medications, and the need for risk factor evaluation before starting psychotropic medications are essential.

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Familial Turner Mosaicism 46XX/45XO With Brain Calcification

SIR: A 72-year-old woman presented with mild diabetes mellitus, brain calcification with no obvious neurological deficit, and mosaic 45XO/46XX. Her daughter presented with mosaic 45XO/46XX Turner syndrome with deafness, facial involuntary movement, primary amenorrhea, and marked brain calcification with mild hypoparathyroidism.[1]

Her mother had experienced normal menarche, menstral cycle, and birth. The mother's serum calcium, phosphorus, and parathyroid hormone levels were within normal limits. The ratio of 46XX and 45XO was 85%:15% (40 cells examined) in the daughter and 75%:25% (20 cells examined) in the mother. Her symptoms were much milder than the daughter's, implying that their genetic defect yielded genetic anticipation. There had been some familial cases of brain calcinosis, known as Fahr disease, in which genetic anticipation had been often observed (i.e., descendent generation reveals severer phenotype). Recently, a locus around a tuberin-like protein gene 1 (*TULIP1*) at 14q.13-q21.1 was proposed as a candidate locus for Fahr disease.[2] Genetic anticipation has been observed in association with nucleotide repeat expansion,[3] and we searched the 14q.13-q21.1 region for nucleotide repeats through the NCBI BLAST Search (i.e., 10 kinds of trinucleotide-repeat, AAC, AAG, AAT, ACC, ACG, ACT, AGG, ATC, CAG, and CCG), and tetra-nucleotide CCTG[4] and penta-nucleotide repeat ATTCT,[5] which have been reported to cause diseases with genetic anticipation when they expand in certain genes. We identified 36 loci, including the nucleotide repeat in 14q.13-q21.1, but failed to detect any significant expansion of the analyzed nucleotide repeats in the patient and the patient's daughter.

Turner syndrome is characterized by impaired physical growth and hypogonadism. But some rare cases with 45XO or mosaicism of 45XO/46XX were reported to bear children, some of whom revealed chromosomal abnormality including mosaicism, implying that a genetic defect predisposing to chromosomal fragility yielding chromosomal aneuploidy was hereditarily transmitted to the descendents in those familial cases.[6,7] A few reported cases of Turner syndrome accompanied by brain calcification.[1] Some chromosomal instability syndromes with impaired DNA repair mechanisms, such as Cochayne syndrome and Fanconi anemia, which often reveal chromosomal aneuploidy,[8] accompany brain calcification.[9,10] The combination of chromosomal aneuploidy and brain calcification may be caused by a genetic defect concerning chromosomal instability.

The candidate locus for familial Fahr disease is proposed to locate around *TULIP1* at chromosome 14q.13-q21.1, but the *TULIP1* gene contains no nucleotide repeat. Impaired *TULIP1* function may be associated with structural alteration of unknown genes containing nucleotide repeats, or cause the genetic anticipation by an unknown mechanism. The genetic anticipation with Fahr disease may be yielded by an unknown mechanism other than nucleotide repeat expansion, or by nucleotide-repeat expansion coming out of 14q.13-q21.1, or by expansion of unknown nucleotide repeat other than analyzed here (i.e., dinucleotide or hexanucleotide repeat).

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Exploring the Relationship Between Panic Disorder and Parkinson's Disease

SIR: I read with interest the recent report by Matsui et al.[1] in which the authors highlighted a patient who was diagnosed with Parkinson's disease shortly after a panic attack. Though there is strong biological basis for the association of panic disorder with Parkinson's disease, the case report raises a number of unanswered questions. Based on the presentation, one cannot exclude the possibility of chance occurrence of the two conditions. The onset of parkinsonian symptoms in their patient may be much earlier than the date when the patient first noticed them. It may be more convincing if longitudinal data were available where it can be shown that the two problems progressed in tandem. Furthermore, availability of detailed information on the patient's premorbid personality and family history of psychiatric disorder would have been useful.

I think the more interesting clinical question would be to determine the proportion of Parkinson's disease patients who present with panic disorder before or at the time of diagnosis. To address that, I interviewed and examined 53 consecutive newly diagnosed Parkinson's disease patients in our movement disorders clinic for evidence and history of panic disorder prior to the diagnosis. This was carried out as part of our routine clinical care, and I also received institutional ethics approval for evaluation of nonmotor symptoms in Parkinson's disease. The patients' mean age of onset was 62 (SD = 11.5) years, with about 50% men and with the Hoehn and Yahr stage between 1 to 4. I found that none of our patients had history or evidence of panic disorder prior to Parkinson's disease diagnosis. This suggests that panic disorder as a presentation prior to the onset of Parkinson's disease symptoms was uncommon, at least in our population. Whether our finding reflects ethnicity-specific effects of phenotypic expression remains to be clarified.

However, I agree that psychiatric nonmotor symptoms, such as anxiety, depression, and panic disorder, can be disabling in Parkinson's disease patients,[2,3] and these are relatively less well studied than motor disability. Among anxiety disorders, it appears that generalized anxiety disorder, panic disorder and social phobias are most frequently encountered, and anxiety may develop before motor features.[3] To further our understanding of the pathophysiology of panic disorder in Parkinson's disease, more prospective studies are needed to examine their cause-effect relationship and the temporal relationship of panic disorder with other psychiatric and cognitive disturbances.

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