pression and to a discontinuation of, or a change in, medication, with subsequent improvement in the patient's condition that may hinder the diagnosis of hepatotoxicity and explain the scarcity of reports, despite its continuous use.

In experimental animals, citalopram was found to induce a fatty liver. A metabolite generated through its first-pass metabolism has been suggested to be responsible for the liver toxicity (2). Taken together, these findings and the absence of hypersensitivity features suggest that a metabolically mediated mechanism is feasible.

Cross-hepatotoxicity has been reported with tricyclic antidepressants (3). Citalopram possesses a chemical structure unrelated to that of other antidepressants, which is consistent with the lack of cross-reactivity observed in this patient.

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ENRIQUE LÓPEZ-TORRES, M.D.
M. ISABEL LUCENA, M.D., PH.D.
JULIA SEOANE, M.D.
CARMEN VERGE, M.D.
RAÚL J. ANDRADE, M.D., PH.D.
Málaga, Spain

Is Multiple Cavernoma a Developmental Defect in Schizophrenia?

TO THE EDITOR: The neurodevelopmental hypothesis of schizophrenia suggests that the interaction between genetic and environmental events during critical periods of neuronal growth in utero may adversely affect neuronal architecture in adulthood (1). Multiple cavernoma (multiple cavernous hemangioma) is a developmental defect of small blood vessels that causes diffuse honeycombing of vascular spaces in the brain (2). This results in sedimentation, thrombosis, and calcification, which can be seen on magnetic resonance imaging (MRI). Here we present a case of schizophrenia with obsessive-compulsive symptoms in a woman with familial bilaterally diffuse cavernoma.

Ms. A, an 18-year-old unmarried woman, was admitted to our ward with psychosis and obsessive-compulsive symptoms. She had ego-dystonic mental obsessions (she reported having "ugly thoughts" about others) and an ego-syntonic delusion that others could read these thoughts. She reported an extensive family history. Her mother had a meningioma, and her brother and uncle suffered from cavernous hemangioma (cavernoma). Her brother also suffered from epilepsy. There was no family history of schizophrenia or obsessive-compulsive disorder. During high school, she was socially withdrawn and preferred to stay at home. One year before her admission, she developed paranoid delusions about her classmates but was not treated.

On admission, results of Ms. A's neurological and dilated ophthalmoscopic examinations were normal. A computerized tomography scan showed two suspected enhancements. Subsequent MRI demonstrated multiple cerebral cavernomas bilaterally, with typical "rings" visible on T_2 imaging. Cavernomas were most abundant in the temporal and frontal regions. Her EEG was normal. An exacerbation of her paranoid thoughts during the first hospital week did not respond to 5 weeks of risperidone treatment (maximum dose=6 mg/day). At that time, she was switched to olanzapine, 20 mg/day, with a remission of her psychosis within 3 weeks. The addition of sertraline, 50 mg/day, relieved her obsessive-compulsive symptoms after an additional 4 weeks.

Familial cavernoma is an autosomal dominant disorder with incomplete penetrance (3). The 7q locus might harbor the causative gene (4). Common clinical signs of multiple cavernoma include neurological deficits, seizures, and hemorrhage (2), although these were not present in this patient. It is possible that this patient's schizophrenia was causally linked to the developmental effects of her hereditary diffuse brain vessel malformation. Alternatively, this could represent an incidental and extremely rare comorbidity. (We found no such cases in the literature.)

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DAVID ISRAELI, M.D.
JOSEPH ZOHAR, M.D.
Tel Hashomer, Israel

Clozapine With Amisulpride for Refractory Schizophrenia

TO THE EDITOR: Only sparse data exist regarding combination treatments of clozapine with other psychiatric medications or ECT (1). Here we report on seven patients who received combined application of clozapine and amisulpride. Amisulpride is not marketed in the United States. It acts primarily on dopaminergic D_2 and D_3 receptors of the limbic system. Because of its lower induction of extrapyramidal symptoms and its better efficacy against negative symptoms (compared to typical neuroleptics), it is grouped among the atypical neuroleptics.

Seven patients (four men and three women) with a paranoid-hallucinatory (N=3) or schizoaffective psychosis (diagnosed according to DSM-III-R) gave written informed consent to be treated with clozapine combined with amisulpride. Their mean age was 41.3 years (SD=7.9, range=32–54). In the preceding 12–72 months, each had received neuroleptics from at least three different classes (butyrophenone, thioxanthene, and phenothiazine); in four cases, ECT was also applied. Since no significant improvement had occurred, all patients had been given monotherapy with clozapine; the average length of treatment was 30 weeks (range=8–52). With