and names of plants; visuospatial skills for the layout of borders, arrangements; praxis, for the handling of plants and garden implements; and executive function, interest in the subject and ability to plan ahead. Any or all of these may be affected in dementia syndromes, and differential deficits may differentially affect abilities to garden (see, for example, the patient with semantic dementia). Hence, if gardening is contemplated as a component of occupational therapy for dementia patients, an individual approach tailored to cognitive abilities and deficits may be required.

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Ziprasidone-induced hypersensitivity syndrome in an aged schizophrenia patient

Dear Editor

Hypersensitivity syndrome is an idiosyncratic drug reaction characterized by rash, fever and internal organ involvement, and mostly occurs with the administration of anticonvulsants (Bonnetblanc, 1998; Schlienger and Shear, 1998). Ziprasidone, an atypical antipsychotic agent with minimal extrapyramidal adverse effects and a favorable metabolic safety profile (Daniel, 2003), is now commonly used for the treatment of aged psychosis. To our knowledge, hypersensitivity syndrome caused by ziprasidone has not been reported previously. Herein, we report the case of an elderly patient who developed severe skin rash over her whole body, with fever accompanied by toxic hepatitis and jaundice 11 days after starting treatment with ziprasidone.

CASE REPORT

The patient was a 69-year-old woman who had suffered from chronic paranoid schizophrenia for more than 40 years and had not received any psychotropic treatment for the previous three years. She was admitted to the hospital because of auditory hallucinations, erotic delusions, and aggressive behaviors toward her caregiver. On admission, she was in generally good health, as determined on physical examination, serum chemical tests, hematology, urine analysis, chest radiography, and electrocardiography. Treatment with oral ziprasidone 40 mg/d was initiated and then increased to 80 mg/d after 1 week.

Eleven days after starting treatment with ziprasidone, she developed a skin rash over cheeks, neck, trunk, and four limbs. Her temperature was 38.9°C,

and her pulse was 102 beats per min. Soon thereafter she became jaundiced and had clay-colored stool. She then underwent comprehensive laboratory investigation, which showed the following abnormal levels: alanine aminotransferase, 72 U/L (reference range, 0–40 U/L); aspartate aminotransferase, 212 U/L (reference range, 5–45 U/L); gamma-glutamyltransferase, 396 U/L (reference range, 4–51 U/L); alkaline phosphatase, 398 U/L (reference range, 10–100 U/L); lactic dehydrogenase, 437 U/L (reference range, 95–213 U/L); total bilirubin, 4.4 mg/dL (reference range, 0.2–1.6 mg/dL); direct bilirubin, 3.5 mg/dL (reference range, 0–0.3 mg/dL); eosinophil count, 5% (reference range, 1–3%), and immunoglobulin E, 324 IU/mL (reference range, < 200 IU/mL).

Blood and urine cultures were sterile. Results of a virology screen, including tests for anti-hepatitis A immunoglobulin M (IgM), hepatitis B surface antigen, IgM anti-hepatitis B core antigen, cytomegalovirus IgM, herpes simplex virus IgM, Epstein-Barr virus IgM, and anti-hepatitis C, were negative. Both ceruloplasmin and serum carcinoembryonic antigen levels were normal.

Computed tomography and sonography of abdomen showed no evidence of biliary tree dilatation, no stones in the gall bladder, no enlarged lymph nodes in the abdomen, and no signs of obstruction of biliary tract. The administration of ziprasidone was discontinued on day 12 after its initiation. The patient's vital signs and rash gradually improved. Her liver function returned to normal levels within 3 weeks. Her treatment was switched to olanzapine 20 mg daily. Her fever, rash, and abnormal liver function results did not recur.

DISCUSSION

Hypersensitivity syndrome is a rare but potentially fatal adverse drug reaction most often caused by anticonvulsants. The literature includes one report of olanzapine-induced hypersensitivity syndrome (Raz *et al.*, 2001). To our knowledge, ours is the first report of ziprasidone-induced hypersensitivity syndrome.

Experience with anticonvulsant-induced hypersensitivity syndrome suggests that the triad of fever, rash, and internal organ involvement occurs 1–8 weeks after exposure to the medication (Knowles *et al.*, 1999). Fever is often the first sign, followed by a rash, which can range from a simple exanthem to toxic epidermal necrolysis. Internal organ involvement usually involves the liver, although other organs, such as the kidney, CNS or lungs, may also be involved. In our case, the patient developed fever and rash 11 days after starting treatment with ziprasidone, while the previous patient with olanzapine-induced hypersensitivity syndrome developed symptoms 60 days after ingesting the drug (Raz *et al.*, 2001). Our patient later developed jaundice and abnormal liver function.

The pathophysiology of hypersensitivity syndrome is still unknown, but it may be linked to a genetically determined inability to detoxify reactive drug metabolites (Verrotti *et al.*, 2002). In the management of hypersensitivity syndrome, early recognition of the first clinical signs of the syndrome and rapid discontinuation of the drug often prevents the progression of symptoms (Knowles *et al.*, 1999; Verrotti *et al.*, 2002). Corticosteroids are usually administered if symptoms are severe. In addition, a battery of laboratory tests, such as liver function tests, complete blood count and serum creatinine determinations, and urinalysis, should be performed. In our case, the patient's fever and skin rash resolved soon after the termination of ziprasidone treatment without corticosteroid treatment, and her liver function returned to normal levels within three weeks.

After recovering from hypersensitivity syndrome, our patient's treatment was switched to olanzapine, with no reappearance of fever, rash, or abnormal liver function. In the previous case of olanzapine-induced hypersensitivity syndrome, treatment was safely switched to risperidone (Raz *et al.*, 2001). The experience from these two cases suggests no evidence of a cross-reaction between the atypical antipsychotics.

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