Anticonvulsants Delaying the Diagnosis of Cushing's Syndrome in a Patient Who Presents with Schizophrenia

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To the Editor: In August 2013, a 22-year-old female was referred to a psychiatric hospital with 6 months history of insomnia, suicidal thought, social withdrawal, irritability and persecutory delusion. She was given the diagnosis of schizophrenia and started on risperidone and chlorpromazine, which were stopped abruptly after 1-week due to lack of any improvement in her mental state. Two days later, she developed recurrent episodes of generalized tonic-clonic seizures and was transferred to our hospital in a comatose state. She was emergently intubated and started on phenobarbital and valproic acid. Per family, the patient also had 6 months history of dizziness, fatigue, and scanty menses. Cushing's syndrome was suspected but serum cortisol was 534.6 nmol/L at 800 h, 445.5 nmol/L at 1600 h, and 382.7 nmol/L at 2400 h (normal range: 85.3–618.0 nmol/L); corticotrophin was 5.1 ng/L at 800 h, ≤5 ng/L at 1600 h, and ≤5 ng/L at 2400 h (normal range: 0–46.0 ng/L); 24 h urinary 17-hydroxysteroid was 15.7 μmol (normal range: 5.5–22.2 μmol/day).

Two weeks later, the patient recovered consciousness and had no more episodes of seizures, so antiepileptic drugs were discontinued. At the time of discharge, her mental state remained the same. At her 1-month follow-up, she was noticed to have cushingoid features including moon face, buffalo hump, and drumstick limbs. Repeat serum cortisol was high (1523.3 nmol/L) and not suppressed after 1 mg dexamethasone (1742.6 nmol/L). High-dose dexamethasone caused 50% suppression of serum cortisol, but not of 24 h urinary free cortisol. A diagnosis of Cushing's syndrome was made. Abdominal computed tomography showed a 2.5 cm × 3.5 cm right adrenal mass [Figure 1], which was removed. Pathology showed a benign adrenal adenoma. She was prescribed prednisolone. One week later, her mental state improved significantly and she returned to work.

Psychiatric symptoms are well-recognized in Cushing's syndrome, but schizophrenia as the initial presentation is rare. We found only seven reported cases in the literature.

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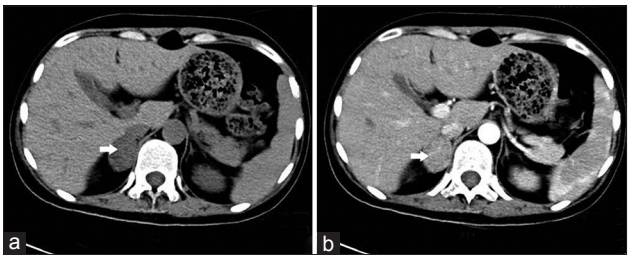

Figure 1: (a) Computed tomography (CT) of the abdomen shows a 2.5 cm × 3.5 cm sized, well-defined mass in the right adrenal gland; (b) Contrast-enhanced CT of the abdomen shows an enhancing mass.

All seven patients underwent surgery to remove their adrenal masses and showed either dramatic improvement or complete resolution of their psychotic symptoms within days to weeks postoperatively. Similarly, psychiatric symptoms improved rapidly after the normalization of cortisol level in our patient. In contrast, resolution of other psychiatric symptoms such as atypical depression has been reported to be variable after correction of the hypercortisolism.[1]

Seizures are an important adverse effect of antipsychotic medications. Our patient was given anticonvulsants for her seizures, which may have resulted in the delay of her diagnosis. It has been reported that anticonvulsants such as carbamazepine, phenytoin, valproic acid and phenobarbital can decrease cortisol level by inducing the liver p450 cytochrome enzyme system and stimulating steroid clearance.[2] In a study comparing anticonvulsant-treated epileptics with healthy controls, the half-life of cortisol in plasma and saliva was reduced significantly after intravenous administration of dexamethasone.[3] In our patient, elevated cortisol level was found only after these drugs were discontinued.

In conclusion, schizophrenia can be the initial presentation of Cushing's syndrome and may improve rapidly after excess cortisol is reduced. In addition, use of anticonvulsants can mask elevated cortisol levels. Cushing's syndrome should remain on the differential and cortisol levels repeated in these patients after anticonvulsants are discontinued.

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