

Extremely Severe Hyperprolactinemia in a Woman With Renal Failure Receiving Risperidone

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ABSTRACT

We present the case of an epileptic patient who experienced risperidone-induced hyperprolactinemia with chronic renal failure under hemodialysis. Her prolactin level was 1058 ng/ml, which was unexpectedly high. Because prolactin is mainly excreted in the urine, clinicians should pay more attention to chronic renal failure as one of the risk factors of hyperprolactinemia when prescribing risperidone.

Keywords: *hyperprolactinemia, risperidone, renal failure, epilepsy*

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INTRODUCTION

Hyperprolactinemia is an important adverse effect of antipsychotics. Hyperprolactinemia leads to an increase in hypoestrogenism and hypogonadism, and ultimately results in osteoporosis. Risperidone is an atypical antipsychotic that has fewer adverse effects than typical antipsychotics but tends to cause hyperprolactinemia [1]. Because prolactin (PRL) is excreted in urine, patients with chronic renal failure who require hemodialysis experience hyperprolactinemia [2]. In addition, elevation of PRL is found in post-epileptic seizure periods [3]. We report here the case of one epileptic patient who suffered from chronic renal failure under hemodialysis and experienced extremely severe hyperprolactinemia after risperidone treatment.

CASE PRESENTATION

The patient was a 55-year-old Japanese woman who

had experienced seizure events starting in junior high school student and had been treated with antiepileptics. However, she had experienced no clinical seizures since she was 20 years old, without drug treatment. She had been receiving hemodialysis three times per week because of renal failure of unknown etiology since she was 48 years old. She presented with auditory hallucinations, grandiose delusions, psychomotor excitement, and monologue at 55 years old, and refused to undergo hemodialysis. She was referred to our hospital for forced admission for hemodialysis treatment and to improve her psychiatric symptoms. She was alert, and no neurological findings were found on admission. Based on her symptoms, she was initially diagnosed with schizophrenia according to the DSM-IV-TR.

She resumed receiving hemodialysis three times per week because of worsened urine poisoning and started to receive olanzapine 5 mg/day for the treatment of psychosis. The olanzapine dose was increased up to 20 mg/day, but her psychiatric condition did not

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improve. She was then switched from olanzapine to risperidone. One mg per day of risperidone was prescribed on the 3rd day after hospitalization, and the risperidone dose was gradually increased up to 6 mg/day on day 32 after admission. The olanzapine dose was decreased until day 21 after admission, on which day olanzapine treatment was discontinued. Laboratory tests revealed an extremely elevated PRL level of 1058.9 ng/ml (normal range:

3.5–32.7 ng/ml) on day 42. Despite the hyperprolactinemia, the patient did not have any symptoms related to this condition. Because risperidone-induced hyperprolactinemia was suspected, the dose of risperidone was decreased, and risperidone treatment was discontinued on day 61. The patient's PRL levels gradually decreased, and normalized on day 93 (Fig. 1).

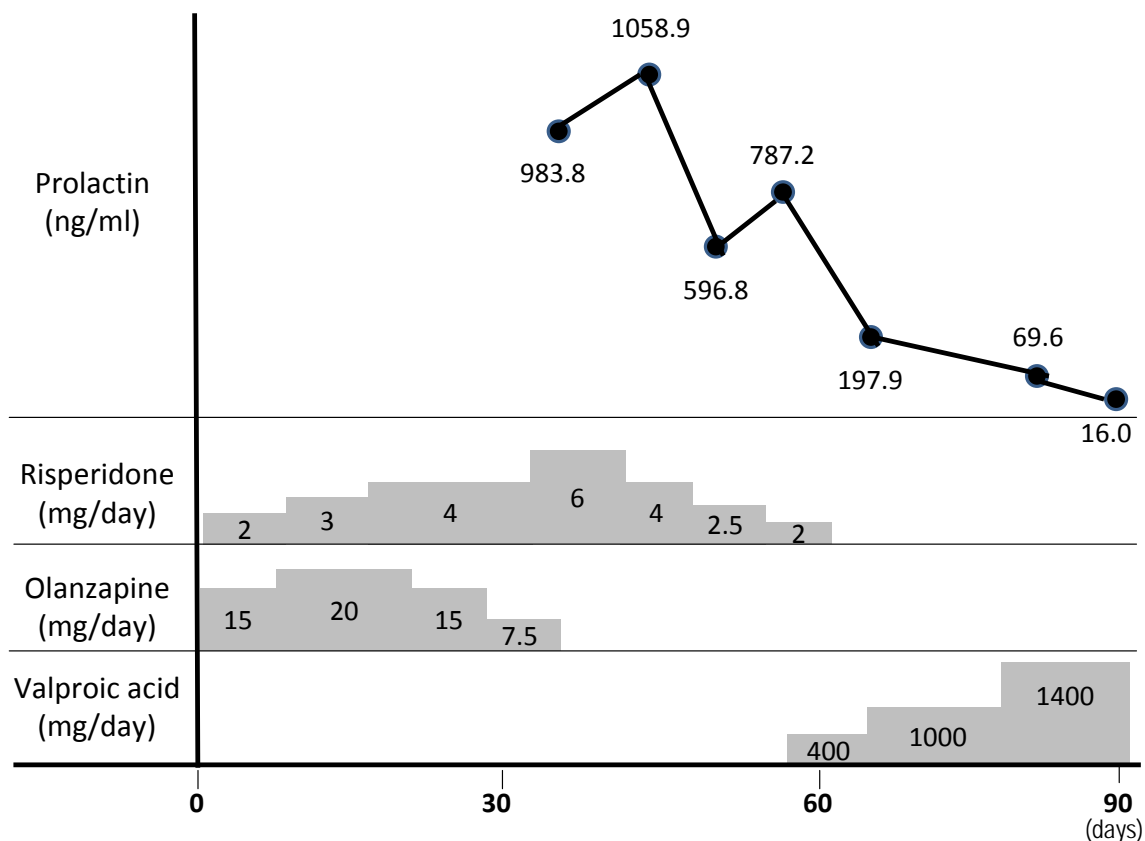


Figure 1. The change in the prolactin level and the treatment regimen for this case.

On day 63, the patient suddenly developed tonic seizures and lost consciousness. In an electroencephalogram (EEG) recording taken during the seizure, obvious seizure discharges (spike and wave complex) were observed. We arrived at a diagnosis of epileptic psychosis because her psychiatric symptoms were thought to be induced by irritative foci of frontal and/or temporal lobes, including limbic system hyperactivity. After the patient took 1000 mg/day of valproic acid (blood concentration: 112.84 $\mu\text{g/ml}$), her EEG recording returned to normal, and she no longer experienced any psychiatric symptoms or epileptic seizures. She was discharged on day 145.

DISCUSSION

Although atypical antipsychotics result in fewer extrapyramidal adverse effects than typical antipsy-

chotics, hyperprolactinemia is an unwanted effect of some atypical antipsychotics. Physicians should be aware of this situation, especially in patients on chronic antipsychotic medication. In the present case, extremely severe drug-induced hyperprolactinemia was observed. Risperidone is known to often induce hyperprolactinemia. To the best of our knowledge, the PRL level observed in our patient was unusually high. We assume that two factors were related to the severe drug-induced hyperprolactinemia in this patient. First, she had chronic renal failure requiring hemodialysis. Elevation of circulating PRL levels sometimes occurs with chronic renal failure because PRL is mainly excreted in urine. On admission, the patient's laboratory examinations showed moderate impairment in renal function (blood urea nitrogen level of 37 mg/dl, creatine level of 6.37 mg/dl, and estimated glomerular filtration rate of 6.0 ml/min/1.73²). Second,

risperidone and its active metabolite, 9-hydroxyrisperidone, stimulate PRL release by inhibition of dopamine neurons in the pituitary gland because they have similar antagonistic profiles for D₂ receptors [4, 5]. In patients with renal failure, the renal clearance of 9-hydroxyrisperidone is reduced, and its elimination half-life is prolonged [6]. Considering these two factors, lowered renal clearance of PRL and accumulation of the 9-hydroxy metabolite of risperidone due to chronic renal failure may have led to unexpectedly severe hyperprolactinemia.

We could not entirely rule out the effects of epileptic seizures on PRL levels. Our patient had a past history of epilepsy, and her EEG recording on admission indicated that she had complex partial epilepsy with ictal and/or interictal psychiatric symptoms. Bauer reported that postictal PRL levels were increased in 60% of patients (n = 80) with complex partial seizures [3]. He defined a postictal increase of PRL levels as an elevation of more than 18.9 ng/ml for a reliable criterion. However, PRL levels related to seizures appear modest, if there is any increase. Therefore, epileptic seizures may only have been partly responsible for hyperprolactinemia in the present case. There are several limitations of this case report. Unfortunately, we did not measure PRL levels on admission and could not compare PRL levels before and after risperidone treatment. However, PRL levels were decreased and normalized soon after dose reduction and withdrawal of risperidone (Fig. 1). The possibility that olanzapine treatment before risperidone might have affected the PRL response cannot be completely ruled out. However, risperidone appears to be the most likely causative agent for hyperprolactinemia because of its potent effects on PRL secretion from the pituitary gland and possible accumulation of its active metabolite, 9-hydroxyrisperidone, due to decreased renal excretion. Information about additional cases should be obtained to address to these possibilities. Regardless, findings from the present case suggest that risperidone treatment and chronic renal failure are combined risk factors that can cause extremely severe hyperprolactinemia. In conclusion, psychiatrists should focus on PRL monitoring in patients with chronic renal failure when prescribing risperidone.

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