Convulsions, Hypertension Crisis and Acute Renal Failure in Postpartum: Role of Bromocriptine?

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Dear Sir,

Bromocriptine mesylate (Parlodel®, San-doz) is a prolactin secretion inhibitor commonly used for suppression of puerperal lactation [1]. It is an ergoalkaloid derivate in which hydrogenation suppresses the usual α -adrenergic vasoconstrictive effect of these derivatives. Furthermore, it is a vasodilating drug by activation of the D₂ dopamine receptors [2] which has been even proposed in treatment of hypertension [3]. However, in certain conditions like acromegalia without hypopituitarism, Raynaud syndrome may occur in 36% of the patients taking bromocriptine [4] and numerous cases have been reported of ischemic neurological and cardiac complications linked to bromocriptine-favored vasospasm in predisposed patients [4-13]. The review of 1,813 women taking bromocriptine for lactation suppression by Watson et al. [14] has suggested that patients with previous pregnancy-induced hypertension were particularly at risk for bromocriptine-associated postpartum hypertension. We report here a case where a hypertensive crisis complicated with seizures and acute renal failure but without hyperuricemia, he-mostasis and liver disturbances, without brain CAT and RMI abnormality or renal histological changes, occurred 11 days after delivery of an uneventful pregnancy in a young primipara with only a sister history of preeclampsia as predisposing factor.

Valerie C. is a 31-year-old white woman, 1 gravida, 1 para, with familial preeclampsia history.

She had an uneventful pregnancy and an uncomplicated full-term spontaneous

Fig. 1. This CAT of the kidney shows no kidney enlargement but in the right kidney two cortical triangular images taking up the contrast media.

prescribed pipemidic acid (Pipram®) for 3 days at 400 mg twice a day. The urine culture revealed the presence of *Proteus mirabilis*. The patient was discharged on postpartum day 8 and pipemidic acid was discontinued. Three days later, she had severe headaches followed by seizures which motivated admission at the emergency unit. Blood pressure (BP) was 190/100 mm Hg. After consciousness recovery, clinical examination showed a normal vaginal delivery on December 7, 1992. Labor, delivery and immediate postpartum were normal. From day 1, she received 2.5 mg of bromocriptine twice a day for suppression of lactation. On day 5 of postpartum, she had a headache and a change in behavior but her blood pressure was

normal (130-80 mm Hg). Temperature was 37.8-38 ° C and therefore after a cytobacteriologic examination of her urine, the patient was

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tion was normal. Computed tomography of the brain was normal as well as cerebrospinal fluid. WBC was 10,500/mm³, hemoglobin 13.8g/100ml, platelets 275,000/mm³, he-mostasis and liver enzymes were normal. Serum creatinine was 247 µmol/l, blood urea 18 mmol/l, uric acid 272 µmol/l. There was no microscopic hematuria. Leukocyturia was 4/mm³ and urine culture was negative. Proteinuria was < 200 mg/l. Renal echogra-phy revealed a heterogeneous aspect of the cortex of the two kidneys but no enlargement. The following treatment was started: intravenous administration of nicardipine, MgSO₄, antibiotics, diazepam and low-molecular-weight heparin. Bromocriptine was discontinued. On days 12 and 13, the patient presented a spontaneous polyuria (diuresis was respectively 4,900 and 6,300 ml/day without any diuretic) explaining a body weight loss of 3 kg in 3 days. On day 14, serum creatinine was 158 µmol/l and blood urea 7.7 mmol/l. C-reactive protein was 12 mg/l. BP was well controled. Antibiotics and nicardipine were discontinued. Electroencephalogram showed a bitemporal suffering, but fundoscopy, cerebral RMI and angiography were normal. A second renal echography was performed and revealed nothing abnormal. Computed axial tomography of the kidneys (fig. 1) revealed also no enlargement, but showed in the median and upper part of the right kidney two triangular images with cortical basis and hilar summit taking up and keeping the contrast media with delay as it can be seen in acute pyelonephritis. Right renal puncture biopsy of the inferior pole was normal. The patient was discharged in a satisfactory condition without antihypertensive or antiepileptic treatment. Three, 6 and 12 months later, her serum creatinine was 105 µmol/l (creatinine clearance 65 ml/min/1.73 m²) and her blood pressure normal (120/80 mm Hg).

In our patients we can exclude other causes of postpartum seizures like a late onset eclampsia, cerebral thrombophlebitis and microangiopathy because brain CAT scan and RMI were normal and because renal insufficiency was not associated with proteinuria, hyperuricemia, hemostasis or liver disturbances nor with renal biopsy abnormalities. A tubular necrosis in relation with a circulatory shock was also excluded since blood pressure was never abnormally low. Acute pyelonephritis is unlikely because urines were sterile at admission and without leukocyturia. The cortical triangular images with late onset and late disappearance of the contrast media may be interpreted as a local consequence of the general vasospasm. On the other hand, the responsibility of pipe-midic acid in the occurrence of the seizures is unlikely since this quinolone drug with potential proconvulsant properties has no pressive effect and was discontinued 3 days before the occurrence of the seizures [15]. Therefore, by exclusion, the whole symptomatology of the patient suggests that bromocriptine was responsible for a general vasospasm. The spontaneous disappearance of hypertension with occurrence of polyuria after discontinuation of bromocriptine supports this hypothesis. To our knowledge, this is the first case of renal insufficiency due to bromocriptine-associated vasoconstriction. The only predisposing factor found in this patient was her familial preeclampsia history.

This case and brief review of the literature suggest to us that the pharmacovigilance about the use of this drug postpartum should be reinforced in those countries where San-doz has not voluntarily withdrawn bromocriptine for lactation inhibition such as in the USA and that not only

personal history of previous pregnancy-induced hypertension but also familial history of preeclampsia should be included as a contraindication of this drug in postpartum. All these women should be informed about the necessity to have their blood pressure rapidly measured in case of headaches. Bromocriptine treatment should be added to the etiological list of postpartum seizures which are so frequently reported of unknown origin (8 identifiable etiologies only out of 62 patients in the series of Lubarsky et al. [16] in which the responsibility of bromocriptine was not looked for).

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