Amphotericin B-induced Nephrogenic Diabetes Insipidus

Key words: hypokalemia, tubular damage

Amphotericin B is the gold standard for antifungal treatment for the most severe mycoses. However, adverse effects are common with nephrotoxicity, which occurs early in the course of treatment, and results in a serious pathological condition. Renal tubular damage develops in association with amphotericin B therapy, and in particular, impairs the renal concentrating ability based on acquired nephrogenic diabetes insipidus (1). Fujita et al (2) reported in this issue a case of amphotericin B-induced nephrogenic diabetes insipidus in a patient with malignant lymphoma and cryptococemia. Urinary concentrating defect progressively occurred closely linked to the development of hypokalemia, and it is independent of the renal tubular damage. The serum potassium level rapidly decreased from 4.1 to 1.7 mmol/l in only two days, after starting amphotericin B. Accordingly, the urine volume enormously increased from 1,000 to 6,000 ml/day, and specific gravity of urine was reduced to below 1.005. Hypokalemia is one of the causes of nephrogenic diabetes insipidus (3), but the authors did not fully evaluate the pathogenesis of severe hypokalemia in their patient. It is known that amphotericin B-treated patients develop renal tubular damage, which produces increases in fractional excretion of sodium and potassium, and requires a large amount of ion supplementation (4). I think that hypokalemia should be profoundly associated with the renal tubular damage in their patient, though other signs of tubular damage were not manifested. It is evident that the withdrawal of amphotericin B rapidly reverses urinary concentrating ability.

Arginine vasopressin (AVP) binds to its V₁ receptors and generates cyclic AMP in renal collecting duct cells (5). Aquaporin-2 (AQP-2) is an AVP-regulated water channel, located in renal collecting duct cells. AVP increases water permeability through the AQP-2 water channel (5). Because of decrease in AVP V₁ receptor binding to its ligand, the renal response to AVP is blunted in nephrogenic diabetes insipidus. Chronic administration of amphotericin B decreases the expression of AQP-2 protein in the outer and inner medulla of rat kidney (6). This finding confirms the reduced production of cyclic AMP in response to AVP in renal collecting duct, associated with amphotericin B-induced tubular damage. Occasionally, acute renal failure is also a serious complication of amphotericin B therapy, and it seems related to drug-induced renal vasoconstriction in addition to direct tubular action (7). We should understand the etiology, symptoms and signs associated with nephrotoxicity and nephrogenic diabetes insipidus, as well as intervention to prevent nephrotoxicity in patients receiving amphotericin B.

See also p 458.

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References