



SCIENTIFIC LETTERS

Diabetes insipidus as an atypical presentation of acute myeloid leukemia[☆]

Diabetes insípida como forma de presentación atípica de leucemia mieloide aguda

Introduction

The association of central diabetes insipidus (CDI) and acute myeloid leukemia (AML) is uncommon, occurring in less than 2% of all patients with DI and less than 1% of patients with AML^{1–4} with a variable time sequence. It may precede or occur at the same time or after clinical evidence of hematological disease.

Studies conducted on such associations report a high prevalence of chromosome 7 monosomy and karyotypic changes in the 3q21q26 region, in addition to normal or high platelet counts.^{4–9} Considered by some authors as a nosological condition in itself,⁸ this set of clinical, laboratory, and karyotypic findings usually has a poor prognosis. It is highly refractory to chemotherapy, with a complete remission rate of LMA with chromosome 7 monosomy (7–) and CDI of 4%, while the complete remission rate of LMA 7– without CDI is 48%.^{7,10}

We report a case where CDI clinically preceded any other symptom or sign of AML and its diagnosis.

A 37-year old with an unremarkable history was admitted to the endocrinology department for urinary frequency, polydipsia, and nocturia of approximately 5 L of water daily. Symptoms had started one week before admission. A system-oriented history was negative except for headache of mixed characteristics and increasing severity for several weeks that had been treated with corticosteroids for the 4 days preceding the patient's attendance at the clinic.

Physical examination revealed no fever, BP of 128/87 mmHg, heart rate of 69 beats per minute, good general condition, and normal hydration. Cardiac and pulmonary auscultation was normal, abdomen was soft and non-tender, and there was no hepatomegaly, splenomegaly, or lymphadenopathy. No focal neurological deficits were found.

Laboratory tests results included glucose 97 mg/dL (71–110), urea 15 mg/dL (16–47), creatinine 0.66 mg/dL

(0.66–1.10), protein 8.15 g/dL (6.6–8.0), albumin 4.37 g/dL (3.40–4.80), aspartato aminotransferase 33 IU/L (10–30), alanine aminotransferase 43 IU/L (7–34), gamma-glutamyltransferase 33 IU/L (6–40), alkaline phosphatase 52 IU/L (20–90), sodium 147 mmol/L (136.6–143.8), potassium 4.1 mmol/L (3.68–4.86), chloride 110 mmol/L (99–109), plasma osmolality 305 mOsm/kg (280–295), urinary osmolality 60 mOsm/kg (500–800), urinary sodium less than 10 mequiv./L, Hb 15.6 g/dL (11.8–14.7), WBC $7.3 \times 10^9/L$ ($4.1–9.9 \times 10^9/L$) with 21.7% blasts, 0.9% metamyelocytes, 24.3% segmented neutrophils, 31.3% lymphocytes, 21.7% monocytes. Hormone study results were normal: TSH 0.98 mU/L (0.4–4.0), free T4 0.93 ng/dL (0.7–1.6), LH 5.2 U/L (follicular phase: 1.1–11.6; ovulation peak: 17–77; luteal phase: 0.1–14.7; menopause: 11.3–39.8), FSH 3.3 U/L (follicular phase: 2.8–14.4; ovulation peak: 5.8–21; luteal phase: 2–10; menopause: 21.7–153), prolactin 11.5 ng/mL (1.9–25.0), progesterone 3.58 ng/mL (follicular phase: 0.2–1.2; luteal phase: 0.95–21.0; menopause: 0.20–1), estradiol 130 pg/mL (follicular phase: 20–100; periovulatory: 40–400; luteal phase: 30–250; menopause: <30), ACTH 44 pg/mL (5–46), cortisol 22 mcg/dL (5–25), androstenedione 4.3 ng/mL (0.5–4.7), DHEAs 314 mcg/dL (35–430), somatotropin 2.2 ng/mL (less than 8.0), and IGF-I 102 ng/mL (94.0–307.0).

In a 6-h water deprivation test (the Miller test), the patient showed a urine output of 3400 mL, with serum sodium elevation from 147 to 158 mmol/L and urinary osmolality of 120 mOsm/kg. Subcutaneous administration of desmopressin 4 mcg induced a progressive decrease in urine output, with normalization of natriemia and a maximum urinary osmolality of 622 mOsm/kg, findings consistent with CDI. Magnetic resonance imaging of the pituitary gland demonstrated the absence of the characteristic hypersignal of the neurohypophysis in T1. After diagnosis of CDI, treatment was started with desmopressin with initial persistence of high urine output, consistent with heavy hyperhydration during the days of chemotherapy administration. Urine output normalized after the chemotherapy cycle was completed, and standard desmopressin doses were subsequently used.

Bone marrow aspiration confirmed AML. Examination of cerebrospinal fluid was negative for infiltration of the central nervous system (CNS). A cytogenetic study showed trilinear dysplasia, 45XX, inv (3) (q21;26), –7, with no rearrangement of the MLL gene, no tandem duplication of the FLT3 gene, and no mutation in the NPM1 gene. Based on the diagnosis of AML subtype M2 of the French-American-British Cooperative Group (FAB) classification, the

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patient started induction chemotherapy with the IDICE scheme (cytarabine, idarubicin, and etoposide), to which she was refractory. Two new rescue cycles were therefore required, after which only a partial response was achieved. Adverse effects included grade 4 hematological toxicity, grade 3 mucositis, systemic candidiasis, and pulmonary aspergillosis. Allogeneic bone marrow transplantation from an unrelated donor was subsequently performed. No graft-versus-host disease occurred, but the patient's course was unfavorable and she died two months later.

Although signs of CNS infiltration are common in acute leukemias, the occurrence of CDI as the initial clinical sign is a rarely reported finding. Some authors² consider CDI as the first CNS involvement by leukemia, even with normal cerebrospinal fluid examination and magnetic resonance imaging of the brain.

Chromosome 7 monosomy and the inversion of chromosome 3q21:q26 in AML represent an endocrine-hematological syndrome which is uncommon, but has been documented in the medical literature and predisposes to the occurrence of CDI. The pathophysiology of CDI secondary to AML is ill-defined. It has been postulated that endocrine changes may be secondary to the infiltration of leukemic cells into the hypothalamic-pituitary axis, bleeding, thrombosis, infection, or the abnormal migration of leukemic myeloblasts to that region. Platelet changes affecting vasopressin transport^{1-3,5,7,8} or dysregulation of transcription factors⁶ with the resultant development of CDI in patients with AML have also been suggested.

AMLs with the previously described genetic characteristics and associated with CDI are conditions which are highly refractory to chemotherapeutic treatment, having poorer response, shorter survival times and worse vital prognosis.

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Metabolic surgery: Report of three cases[☆]

Cirugía metabólica: a propósito de 3 casos

Diabetes mellitus has been treated as a chronic disease, but may now be considered as a condition where remission is possible. In this regard, we would define remission as the achievement of glycemic goals below the diabetic range in the absence of active pharmacological or sur-

gical treatments. A distinction may be made between partial remission (glycosylated hemoglobin [HbA1c] less than 6.5% and fasting blood glucose ranging from 100 to 125 mg/dL) and complete remission (HbA1c in the normal range and fasting blood glucose less than 100 mg/dL for longer than one year without active drug treatment).

For remission of type 2 diabetes mellitus (T2DM) there are two possibilities: metabolic/bariatric surgery or an effort by the patient to implement lifestyle changes consisting of weight loss and physical exercise.¹

Treatment goals for comorbidities (high blood pressure or dyslipidemia) should be the same in a patient who achieves partial or complete remission as in a patient with diabetes,

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