CLINICAL REPORTS

Diabetes insipidus as a complication of acute myelomonocytic leukaemia

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Summary

A female patient, aged 44, with diabetes insipidus as a complication of acute myelomonocytic leukaemia (AMML) is described. She presented with bleeding, anaemia, polyuria and polydypsia. She was treated with intranasal vasopressin for diabetes insipidus and responded well to treatment. Chemotherapy was administered for the leukaemia and a full remission was achieved. The patient relapsed a few days before final admission to hospital and died of septicaemia 7 months after initial diagnosis. A short review of the literature related to this subject is also presented.

KEY WORDS: diabetes insipidus, myelomonocytic leukaemia, vasopressin.

Introduction

It is known that the central nervous system may be involved in leukaemia. An unusual manifestation of this involvement is diabetes insipidus, generally attributed to leukaemic infiltration of one or more components of the supraoptico-hypophyseal system. The case of a middle-aged woman with acute myelomonocytic leukaemia is reported, who developed diabetes insipidus during the course of her disease.

Case report

A 44-year-old Greek housewife was admitted as an emergency to our unit on 1 February 1980.

Five weeks before her admission, she had noticed some bleeding of the gums. Three weeks later the patient developed profound menorrhagia and she was transfused with 2 units of blood. She then

developed blurred vision, severe dyspnoea, excessive polydypsia and polyuria.

On admission the patient was markedly dehydrated, pale and extremely weak. Hypertrophy, bleeding of the gums and retinal haemorrhages were noted. There was no lymphadenopathy or hepatosplenomegaly. Investigations showed haemoglobin 3.3 g/dl, white cell count 100×10^9 /litre, platelets 80×10^9 /litre.

Random urinalysis revealed a specific gravity of 1003, negative tests for protein and glucose, and a sediment which showed a very small number of erythrocytes and leucocytes.

Blood urea, electrolytes, creatinine and fasting blood sugar were all within normal limits. Chest and skull X-rays and computerized tomographic brain scan were also normal. Bone marrow aspiration showed 98% blast cells, some of which had the characteristics of monoblasts, and the others typical myeloblasts. Auer bodies were not seen.

A diagnosis of acute myelomonocytic leukaemia (M4 according to FAB classification) (Bennett *et al.*, 1976) was made and blood transfusions and antibiotics were given. During the first 3 days of hospitalization, the urine output ranged between 6 and 8 litres per day with a specific gravity of 1003. A prolonged fluid restriction test was not done because of the patient's poor general condition and extreme thirst.

Intranasal administration of pitressin (vasopressin) at a dose of 0.1 ml (40 units) twice daily resulted in a sharp diminution of the daily urine output to 2-3 litres/day with a specific gravity of 1010. Cerebrospinal fluid revealed no evidence of leukaemia.

On the basis of the above tests, vasopressin insufficiency, (diabetes insipidus), was diagnosed and

the patient was then given intranasal vasopressin, 40 units twice daily, with complete control of the diabetes insipidus.

A combination chemotherapy consisting of cytosine arabinoside, daunorubicin, thioguanine and prednisolone was given and a full remission was achieved. The patient was discharged home on intranasal vasopressin therapy (40 units twice daily).

She continued chemotherapy monthly with 5-day courses consisting of cytosine arabinoside, prednisolone plus daunorubicin and thioguanine on alternate courses. An attempt to discontinue the intranasal vasopressin resulted in a sharp increase of urine output to 6 litres/day. The patient died 7 months after her first admission with septicaemia. Permission for post-mortem was denied.

Discussion

Diabetes insipidus in leukaemia is very rare. Williams, Diamond and Craver (1958) reported only one such case in 1864 patients with leukaemia. Blotner (1958) studying 124 cases of diabetes insipidus found only 2 cases where leukaemia was the aetiological factor. Miller and Campbell (1971) reviewed 20 reported cases of diabetes insipidus in association with leukaemia. Twelve cases were classified as myelocytic, three as lymphocytic, three as monocytic, one as a stem cell and one as haematocytoblastic.

The mechanism responsible for this complication is not clear. The anatomic site responsible for the synthesis and secretion of antidiuretic hormone (ADH) includes the supraoptic and paraventricular nuclei of the hypothalamus, the hypothalamo-hypophyseal tracts and the pituitary gland itself. Leukaemic

infiltration, haemorrhage, and coagulative necrosis due to local leucocyte thrombi (leucostasis) have been found to be the underlying pathological mechanisms of this involvement in patients with leukaemia. Treatment of the leukaemia has not led to improvement in the diabetes insipidus in reported cases.

Although our patient responded well to ADH administration, it has been reported (Laakso, 1964) that 15% of cases of diabetes insipidus are resistant to exogenous ADH. Shurygin (1960) reported two cases where leukaemia cells had infiltrated the renal tubules and suggested that this ineffectiveness was probably due to dysfunction of the renal tubules as a result of leukaemic infiltration. A third such case was reported by Kovacs and Monus (1956), who suggested that the failure of response to pitressin was probably due to decreased sensitivity of the tubular epithelium to ADH.

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(Accepted 11 June 1982)