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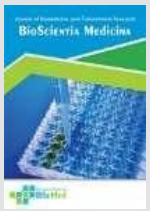

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Central Diabetes Insipidus in Langerhans Cell Histiocytosis: A Case Report

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A B S T R A C T

Background: Diabetes insipidus (DI) is part of a group of hereditary or acquired polyuria and polydipsia diseases. Diabetes insipidus can be caused by central and nephrogenic disorders. This study aimed to describe the etiologies, clinical symptoms, and management of central diabetes insipidus in Langerhans cell histiocytosis. **Case presentation:** A 4 years 4 months old boy came with excessive and frequent micturition since 9 months ago. The patient drinks 4-5 L per day and still feels thirsty. The patient had a history of Langerhans cell histiocytosis (LCH). During laboratory work-up, urine osmolarity decreased, and serum osmolarity and electrolyte were normal. The patient was diagnosed with central diabetes insipidus with Langerhans cell histiocytosis. The treatment given to the patient is desmopressin. **Conclusion:** Langerhans cell histiocytosis may affect any organs of the body. The long-term management of diabetes insipidus in Langerhans cell histiocytosis requires measurement to prevent dehydration and, at the same time to prevent water intoxication. The focus of management is based on the education of the patient about the importance of regulating their fluid intake according to the patient's hydration status.

1. Introduction

Diabetes insipidus (DI) is part of a group of hereditary or acquired polyuria and polydipsia diseases. It is associated with inadequate arginine vasopressin (AVP) or antidiuretic hormone (ADH) secretion or renal response to AVP, resulting in hypotonic polyuria and compensatory underlying polydipsia.[1] Diabetes insipidus (DI) is a form of polyuria–polydipsia syndrome and is characterized by hypotonic polyuria (excessive urination; more than 50 ml/kg body weight/24 hours) and polydipsia (excessive drinking; more than 3 L/day).[2,3]

DI is a rare disease, with a prevalence of 1:25.000. DI can present at any age, and the prevalence is equal among males and females. The age of presentation depends on the etiology. Less than 10% of DI is hereditary. X-linked nephrogenic DI (NDI) accounts for 90% of cases of congenital NDI and occurs with a frequency of 4–8/1 million male live births. Autosomal NDI accounts for approximately 10% of the remaining cases.[1]

Central DI is the most common type of DI. Central DI is most often due to various acquired or hereditary lesions that destroy or damage the neurohypophysis, either by pressure or infiltration. The severity of the resulting hypotonic diuresis is dependent on the extent of the neurohypophyseal damage, resulting in either partial or complete deficiency of AVP secretion. Patients with DI, especially those with underlying osmoreceptor defect syndromes, can also show varying

degrees of dehydration and hyperosmolality other than showing symptoms such as polydipsia and polyuria.[4,5] However, some laboratory and radiological work-up are needed to diagnose central DI. Specific replacement therapy for central diabetes insipidus treatment is usually straightforward and primarily aims at ameliorating symptoms (polyuria and polydipsia) by replacing antidiuretic hormone.[6] Desmopressin, an AVP analogue, is the preferred drug for almost all patients.[7]

Langerhans cell histiocytosis (LCH) is an idiopathic condition characterized by the proliferation of abnormal Langerhans cells (antigen-presenting immune cells).[8] The disease has characteristics of both an abnormal reactive process and a neoplastic process. Langerhans cell histiocytosis is rare. It occurs in 1 to 2 newborns per million per year. The incidence in children aged less than 15 years old is 4 to 5 cases per million per year.[9] The cause of LCH is unknown and continues to be debated; however, most agree that LCH is either a reactive or neoplastic process.

Symptoms and physical exam will depend on organ involvement at the time of presentation. The rash is the most common presentation. Bone involvement occurs in about 78% of patients. Pulmonary lesions occur in 20% of patients, and lymph node involvement in 30%. Langerhans cell histiocytosis also has a predilection for infiltration of the pituitary and causing diabetes insipidus. Treatment varies greatly depending on the involved organs. If the disease is isolated, observation alone may be appropriate. Surgical removal of an isolated area is also a treatment option.[8,9] Involvement of the central nervous system occurs in approximately 5% of patients with LCH. Involvement of the ethmoid, orbital, temporal, or zygomatic bones confers a higher (25%) chance of central nervous system involvement. Central diabetes insipidus caused by involvement of the pituitary gland occurs in approximately 25% of patients overall.

Langerhans cell histiocytosis is a heterogeneous disease characterized by the accumulation of dendritic cells with features similar to epidermal Langerhans cells in various organs.[10] Langerhans cell histiocytosis exhibits a predilection for the hypothalamic-pituitary region, leading to permanent posterior and/or anterior pituitary hormonal deficiencies in a subset of patients.[11] Diabetes insipidus is the most common disease-related consequence that can predate the diagnosis or develop anytime during the course of the disease. This study aimed to describe the etiology, clinical symptoms, and management of central diabetes insipidus in Langerhans cell histiocytosis.

2. Case Presentation

A 4 years 4-month-old boy came to the outpatient clinic of the pediatric department, Dr. M. Djamil General Hospital, with excessive and frequent micturition since 9 months ago. The patient could have micturition approximately 4-5 L, more than 10 times in frequency, especially at night. The colour was yellow, with no redness, cloudy or sandy, and no pain. The patient drinks 4000-5000 cc per day and still feels thirsty. His appetite was normal. The patient eats 2-3 times per day and could take on a full meal. Colour dan consistency of feces was normal. The patient's weight at this time was 17 kg, and the body weight increased by only 0,5 kg in half a year. The patient had a history of Langerhans cell histiocytosis and had chemotherapy two years ago. The patient was diagnosed with Langerhans cell histiocytosis based on the results of nails and skin biopsy. Bone marrow puncture results according to the Langerhans cell histiocytosis.

Based on physical examination, the patient looked moderately ill, and compos mentis, vital signs were normal and well nourished. Examination of chest, abdomen, genital, and extremities was normal. Patients diagnosed with suspect diabetes insipidus central, differential diagnosis with the syndrome of inappropriate antidiuretic hormone secretion, cerebral salt wasting, and history of Langerhans Cell Histiocytosis post-chemotherapy. The patient received treatment with regular meals of 1400 kcal and chemotherapy evaluation. A laboratory finding of osmolarity was calcium 9,0 mg/dL, urine osmolarity

65 mOsmol/kgH_2O, and serum osmolarity 280 mOsmol/kgH_2O. Electrolyte laboratory findings were normal. The patient received therapy minirim 3x ½ tab (tablet 0,2 mg).

3. Discussion

Diabetes insipidus (DI) is part of a group of hereditary or acquired polyuria and polydipsia diseases.[1,2] It is associated with inadequate arginine vasopressin (AVP) or antidiuretic hormone (ADH) secretion or renal response to AVP, resulting in hypotonic polyuria and compensatory underlying polydipsia.[5] DI can present at any age, and the prevalence is equal among males and females.

This patient had a history of Langerhans cell histiocytosis and had chemotherapy before. Central diabetes insipidus is the common endocrine manifestation in Langerhans cell histiocytosis (LCH). It may result when the hypothalamic-pituitary axis is involved with consequent impairment of antidiuretic hormone secretion from the posterior pituitary gland.[10] The condition typically presents with polydipsia, polyuria, and nocturia. LCH may affect any organs of the body. The studies have shown a 5 to approximately 20% prevalence of LCH in their series of patients with different causes of CDI. However, these percentages may change over time due to the last classification of LCH as an inflammatory myeloid neoplasm. Furthermore, CDI is the most frequent CNS manifestation of LCH, occurring in 10-50% of all patients.[10,12]

Polyuria and polydipsia in DI and primary polydipsia do not necessarily differ in their specific manifestations, even though the underlying impairment of the urinary concentrating mechanism is different in the two conditions. In a day patient could urinate 4000-5000 cc and drink 4000-5000 cc per day. Young children may present with severe dehydration, vomiting, constipation, fever, irritability, sleep disturbances, retardation of growth, and failure to thrive. Mental retardation can be caused by repeated and unrecognized dehydration.[13,14]

In this case, there were no symptoms like severe dehydration because the patient drank equal to the urination. There are no symptoms like vomiting, constipation, fever, irritability, sleep disturbances, retardation of growth, and failure to thrive. Polyuria in children is defined as the excretion of urinary volumes of >150 ml/kg/day in neonates, >100-110 ml/kg/day in children <2 years of age, and >50 ml/kg/day in older children.[15]

Untreated central and nephrogenic diabetes insipidus may lead to hyperosmolar dehydration. The general goals of treatment of all forms of diabetes insipidus are, therefore, a correction of any preexisting water deficits and a reduction in ongoing excessive urinary water losses. The patient's condition is not in hyperosmolar dehydration, so water deficit correction was not essential. Specific replacement therapy for central diabetes insipidus treatment is usually straightforward and primarily aims at ameliorating symptoms (polyuria and polydipsia) by replacing antidiuretic hormone.[15] Desmopressin, an AVP analogue, is the preferred drug for almost all patients. This patient, when the diagnosis is upright to CDI, gets the therapy desmopressin-like minirin (doses 0,025-1,2 mg/body weight/day in 1-3 dose oral).

The treatment monitoring can be accomplished most efficaciously by a fixed daily fluid intake regardless of the patient's thirst, which can be adjusted in response to changes in body weight. The success of the fluid prescription should be monitored periodically by measuring serum sodium concentration.[15] If treated accordingly, central diabetes insipidus is associated with a fairly normal quality of life, particularly when oral or nasal desmopressin is prescribed.

4. Conclusion

Langerhans cell histiocytosis may affect any organs of the body. The long-term management of diabetes insipidus in Langerhans cell histiocytosis requires measurement to prevent dehydration and, at the same time to prevent water intoxication. The focus of management is based on the education of the patient

about the importance of regulating their fluid intake according to the patient's hydration status.

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