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Case Report Open Access

Severe Neurological Signs Due to Hyponatremia in Patient with Acute Myeloid Leukemia; Ethiological Factors and Therapeutic Approach

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Abstract

28-year-old male patient with acute promyelocytic leukemia developed pneumonia subsequent to chemotherapy. *Geotrichum capitatum* was isolated from sputum. Patient was admitted to intensive care unit due to respiratuar distress. Linezolid, imipenem, caspofungin and parenteral nutrition therapy (PNT) were initiated. Caspofungin was changed to voriconazole due to widespread reticulonodular and consolidated areas in chest computed tomography. During follow-up at intensive care unit, confusion, hyperkinesia, agitation and rigidity developed due to severe hyponatremia (113 mEq/L). Blood and urine osmolality with hyponatremia indicated inappropriate ADH syndrome. Linezolid and TPN were discontinued and isotonic solution was administered. Hyponatremia and clinical symptoms associated with penumonia recovered after 15 days of follow-up under voriconazole therapy that was administered for one month.

Keywords: Acute myeloid leukemia; Hyponatremia; *Geotrichum capitatum*; Inappropriate ADH syndrome

Introduction

Electrolyte imbalance is commonly seen in patients with acute leukemia. The most common cause of electrolyte abnormality is hypokalemia. But severe hyponatremia is infrequent. Metabolic studies defined disturbances as early increase of urinary sodium excretion, negative water clearance, and higher urine osmolality [1,2]. Central diabetes insipidus (CDI) develops in patients with acute myeloid leukemia (AML) because of infiltration of leukemic cells into the neurohypophysis or another reasons [3].

It is postulated that different etiologies cause this syndrome. In this case report, a patient who had acute myeloid leukemia (AML) and developed hyponatremia with all symptoms of inappropriate SIADH is being evaluated with probable causes and pathogenetic mechanisms of hyponatremia and CDI that is more likely to cause hyponatremia and related severe neurologic symptoms.

Case

28 year-old male patient was diagnosed with Acute Promyeloid Leukemia that includes translocation 15:17 that was detcted by FISH method and remission-induction chemotherapy (idarubicin and vesanoid) was initiated. Subsequent to second induction chemotherapy, profound neutropenia developed. Teicoplanin and imipenem were administered due to patient's complaints including fever >38°C, increased cough, phlegm, dyspnea. Chest computed tomography (CT) was revealed widespread reticulo-nodular increased density, ground-glass attenuation, and patch consolidations (Figure 1). Upper abdominal CT (Figure 2) revealed that multiple hypodense lesions in liver and spleen accordance with the fungal infection. Specimens including blood, urine, sputum, feces were cultured for microbiologic examination. Trimethoprim-sulfamethoxazole and caspofungin were added to treatment due to worsening clinical symptoms. Patients was followed up for two days at intensive care unit. Caspofungin was changed to voriconazole due to pneumonia caused by *Aspergillus spp. Geotrichum capitatum* was isolated from sputum and susceptible to voriconazole. Patient had recovered after ten days of treatment and control chest CT at first month of follow-up was normal (Figure 3). Laboratorial findings were Na with113 mmol/L, plasma osmolality with 235 mOsm/kg H_2O (normal range: 285-295), and urine osmolarity with 398 mOsm/kg H_2O. Antidiuretic hormone (ADH) could not be measured because of technical inconvenience. These results was consistent with inappropriate ADH syndrome and patient was consultated with nephrology. Isotonic solutions were administered. Serum Na decreased to 112 mmol/L and serum sale was added to isotonic solution (500cc) that was infused as adjusted to 25 cc/hour. There was no definitive signs in brain MRI for diagnosis. Lumbar puncture to evaluate the cerbrospinal fluid could not be implemented due to incooperation with patient.

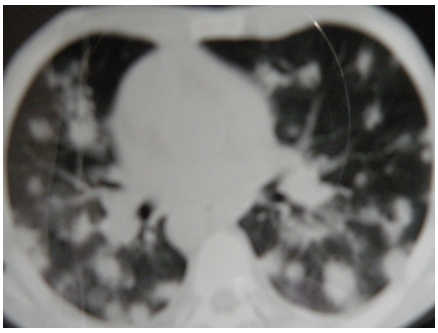

Figure 1: Chest CT scan (sagittal section) shows widespread reticulonodular and consolidated areas.

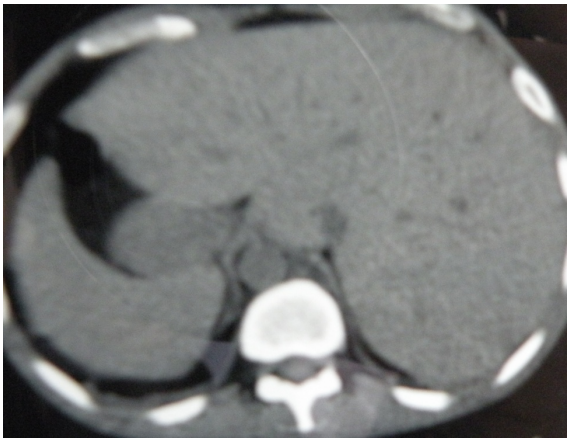

Figure 2: Upper abdominal CT reveals multiple hypodense lesions in the liver and spleen in accordance with the fungal infection.

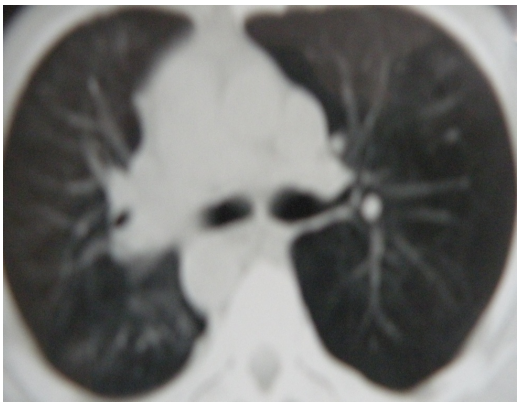

Figure 3: Control CT after one month of voriconazole treatment, resolution of lung infection was onitored.

Hyponatremia may occur due to inappropriate ADH syndrome and be a component of this syndrome due to the parenteral solutions, drugs, pulmonary infection or a combination of these factors. Parenteral nutrition and linezolid therapy were discontinued. Gliotic subcortical ischemic foci in the brain was captured by magnetic resonance imagination (Figure 4), central pontine myelosis was not reported. The patient was disoriented, agitated, anxious, depressed, fatigue, apathetic, confused in this period. There were also hyperkinesia, rigidity and confusion in examination. Sodium treatment was continued for about 10 days and Na level gradually increased to normal values (135 mEq/L). Patient gradually regained consciousness within 5 days. ROM (Range of motion), standing and strengthening exercises were worked out by the physiotherapy and rehabilitation physician. Voriconazole therapy was continued for 2 months. The patient was discharged with the request of patient and his parents. Exremity rigidity was observed minimal in controls, because of uncompleted physical therapy in this period and it had recovered after 2 months.

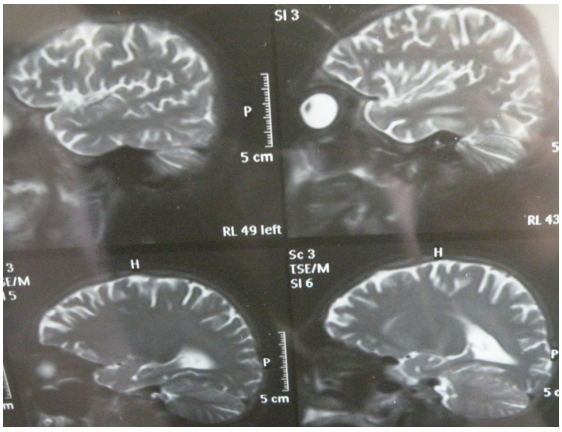

Figure 4: Cranial MRI shows Gliotic subcortical ischemic foci.

Discussion

Anorexia, nausea, vomiting, weakness, confusion, and coma generally develop in patients with hyponatremia associated with inappropriate ADH syndrome. Urine and blood osmolality should be measured for the diagnosis. Essential treatment is fluid restriction. In case whom acute neurological symptoms appear (Na level 110 mEq/L), hypertonic solutions should be initiated. Furosemide and saline infusions are recommended as well. Due to hormones and cytokines secreted by the tumor, neuropathy and myopathy may occur. Hyponatremia can appear with signs and symptoms regarding central nervous system, such as hallucinations, disorientation and hypokinesia, dyskinesia in the extremities. Disatrophy developed in muscle as much as patient could not walk. Hyponatremia may occur due to malignancies, drugs, lung infections, etc. Hyponatremia may be a part of paraneoplastic syndrome in the course of malignancy with inappropriate ADH syndrome (SIADH). However, there are a few studies about hyponatremia and SIADH in patients with acute leukemia [4]. Although the reason of hyponatremia remains unclear in our case, pneumonia caused by *Geotrichum capitatum*, or medication (eg.linezolid) may be considered.

Geotrichum capitatum, a fungus causing systemic infections in immunosuppressed patients. *G. capitatum* infections most frequently occur (80%) in patients with acute leukemia [5,6]. MIC is the lowest with a value of anti-fungal drug, voriconazole [7]. Therefore, this drug was initiated as soon as possible and the response was achieved in our patient.

Retrospective immunohistochemical analysis of blast cells was reported to be positive for antidiuretic hormone (ADH) protein, which clearly demonstrated that the tumor cells produced ADH [8]. To measure serum ADH level is needed for accurate diagnosis. It could not be measured due to technical inconvenience. This diagnosis was supported with blood and urine osmolalities and patient was treated on the assumption of inappropriate ADH syndrome. Clinical symptoms and causes of hyponatremia in patient with acute leukemia are presented and discussed in line with literature.

Consequently, hyponatremia should be taken in to consideration in patients with hyperkinesia, rigidity and confusion under acute leukemia chemotherapy.

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