Altered mental status in a case of multiple myeloma not related to a metabolic cause

Sir,

Altered mental status (AMS) in a patient with multiple myeloma (MM) is generally attributed to uremia, hypercalcemia, hyperviscosity and/or increased serum ammonia. We present an unusual case of altered mental status that could not be attributed to metabolic encephalopathy.

Our patient was a 68-year-old African American male who was admitted for AMS. The patient was asymptomatic 1 week prior to admission. On examination, no focal neurologic deficit other than altered sensorium was found. The rest of his physical examination was normal. Routine laboratory analysis revealed elevated BUN of 58 mg/dl (7–25 mg/dl), creatinine of 4.9 mg/dl (0.7–1.4 mg/dl), calcium of 12.1 mg/dl (8.5–10.3 mg/dl), total protein of 9.6 g/dl (6.8–8.1 g/dl), albumin of 3.6 g/dl (3.5–5.0 g/dl), and serum ammonia of 65 mcg/dl (35–65 mcg/dl) with normal liver function tests. A toxicology screen was negative. Intravenous hydration with normal saline was initiated. Magnetic resonance imaging (MRI) of the brain showed chronic microvascular ischaemic changes with no acute infarct. On cerebrospinal fluid (CSF) analysis, he was found to have elevated protein of 172 g/dl (15–45 g/dl), a negative cytology, but abnormal bands of high intensity. Polymerase chain reaction on CSF for herpes simplex was negative. Electroencephalogram (EEG) showed no seizure activity. Though all metabolic parameters normalized by the third day (creatinine of 1.3 mg/dl and calcium of 12.1 mg/dl), there was no improvement in his sensorium. To rule out paraneoplastic syndrome of unknown aetiology, a whole body CT scan was done. It showed a soft tissue mass in the pre-sacral area with multiple diffuse lytic bone lesions. The bone marrow was diagnostic for plasma cell myeloma. Serum immunofixation revealed 5050 mg/dl (700–1600 mg/dl) of monoclonal IgG. The serum viscosity was normal. A repeat lumbar puncture revealed a CSF with negative cytology, but abnormal bands of high intensity in the immunoglobulin region identical to the serum electrophoresis pattern. Four days after the normalization of all his metabolic parameters, there was still no improvement in his sensorium. The patient was started on intravenous dexamethasone for MM. After the first cycle, his sensorium returned to normal.

The most common cause of AMS in a patient with MM and acute renal failure (ARF) is metabolic encephalopathy.
Peripheral CD19+ B cells are increased in children with active steroid-sensitive nephrotic syndrome

Sir,

Pathogenesis of steroid-sensitive nephrotic syndrome (SSNS) is thought to be related mainly to T-cell dysfunction [1]. However, the beneficial use of rituximab in cases of frequently relapsing SSNS provided evidence of B cell involvement [2–4]. Our aim was, thus, to investigate prospectively the levels of the circulating CD19+ B cells in children with a first episode of SSNS in sequential stages (presentation, remission on steroids and remission off steroids).

Twenty-three children (M/F = 13/10, age = 2.5–14 years, median = 4.32 years) with a first episode of SSNS were studied; 23/23 both at presentation (before steroids initiation) and in remission on steroids (40 mg/m^2 on alternate day); 15/23 were tested as well in remission off steroids for at least 6 months. Twenty-five age-matched children who had come to the outpatient haematology clinic in order to be tested for b-thalassaemia trait were found to be negative and served as healthy controls (controls 1). Considering that the presentation of SSNS may be associated with a recent infection, mainly a respiratory tract infection, twenty age-matched children with an upper respiratory tract infection acted as a second control group (controls 2).

The percentages of CD3+ T cells, as a pan T-cell marker, and the percentages of CD19+ and CD20+ B cells were evaluated in all children. The above-mentioned parameters were determined in each sample by flow cytometry using the lysed whole blood method. The duochrome phycoerythrin-cyanin5 (PE-Cy5) conjugated CD3± monoclonal antibody (MoAb) and phycoerythrin (PE) conjugated CD19+ and CD20+ MoAbs purchased from Beckman Coulter were used. The samples were analysed with a EPICS-XL flow cytometer. The results were expressed as percentages (%) of fluorescence-positive cells as well as actual numbers (cells/µL) of the circulating CD19+ and CD20+ B cells, based on the white blood cell count.

Statistical analysis was performed using the Statistical Package for the Social Sciences for Windows (SPSS version 11.5). The paired t-test and independent-samples t-test were used to compare differences between study groups with and without paired data, respectively. Pearson’s coefficient of correlation (r) was used to determine the correlations. A P ≤ 0.05 was considered to be statistically significant.

In 5 of 23 children with a first episode of SSNS, there was a recent history of an upper respiratory tract infection. Remission was achieved in all children within 6–15 days after steroid initiation. During remission, all patients presented normoalbuminaemia and were free of proteinuria and albuminuria. Percentages of CD3± T cells were found to be within normal limits in all patients (at presentation of SSNS, in remission still on steroids and in remission off steroids) compared with the two control groups (P ≥ 0.05). As depicted in Figure 1, the circulating CD19+ B cells were significantly higher at presentation of SSNS (mean percentage = 18.13 ± 5.43, mean actual number = 695.34 ± 258.29) compared with remission on steroids (mean percentage = 13.57 ± 4.22 and P < 0.001), remission off steroids (mean percentage = 13.25 ± 2.32 and P < 0.001, mean actual number = 414.88 ± 140.76 and P < 0.0001), controls 1 (mean = 13.96 ± 3.29 and P = 0.008, mean actual number = 442.75 ± 99.78 and P = 0.009) and controls 2 (mean percentage = 14.18 ± 3.6 and P = 0.01, mean actual number = 508.05 ± 148.9 and P = 0.015). During remission stages, on and off steroids, CD19+ B cells were significantly higher in children with active steroid-sensitive nephrotic syndrome compared with the healthy controls (controls 1).

1 Division of Nephrology
Department of Medicine
2 Department of Pathology
St Luke’s Roosevelt Hospital Center
Columbia University College of Physicians & Surgeons, New York USA
E-mail: gsandhu@chpnet.org

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