metabolism was unaffected since factors VII, IX, X, PC and PS were within the normal range. LA was found in one patient and may have been the cause of the PVT. Due to the importance of LA in thrombosis, this raises the question of whether LA could be investigated in children with PVT.

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References

1. Alvarez F, Bernard O, Brunelle F, Hadchouel P, Odievre M, Lagille D. Portal obstruction in children. I. Clinical investigation and hemorrhage risk. J Pediatr 1983; 103:696-702.
2. Cohen J, Edelman R, Chopra S. Portal vein thrombosis: A Review. Am J Med 1992; 92:173-82.
3. Comp PC. Control of coagulation reaction. In: Williams JW, Bentler E, Erlev A, Lichtman MA, eds. Hematology. 14th ed. New York:McGraw Hill, 1990. p. 1304-11.
4. European Concerted Action on Thrombosis. Bulletin ECAT, n.2 Assay procedures, 1985.
5. Boneu B, Bes G, Pelzer H, Sié P, Bocalono H. Thrombin Antithrombin lll complexes and prothrombin fragments 1+2: diagnostic value in clinically suspected deep vein thrombosis. Thromb Haemostas 1991; 65:28-32.
6. Astrup T. Fibrinolysis in the organism. Blood 1956; 11:781.
7. Brandt JT, Triplett DA, Alving B, Scharrer I. Criteria for the diagnosis of the lupus anticoagulants: an update. On behalf of the subcommittee on lupus anticoagulant/antiphospholipid antibody of the scientific and standardisation committee of the ISTH. Thromb Haemostas 1995; 74:1185- 90.
8. Rosendaal FR, Koster T, Vandenbroucke JP, Reitsma PH. High risk of thrombosis in patients homozygous for factor V Leiden (activated protein C resistence). Blood 1995; 85:1504-8.
9. Seixas CA, Hessel G, Ribeiro CC, Arruda VR, Annichino-Bizzacchil JM. Factor V Leiden is not common in children with portal vein thrombosis. Thromb Haemostas 1997; 77:258-61.

Hyperammonemic encephalopathy in multiple myeloma

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We report two cases of hyperammonemic encephalopathy in patients with multiple myeloma. This rare complication, whose pathophysiology remains unknown, is associated with disease progression and so with a very bad prognosis. We believe that this complication should be included in the differential diagnosis of encephalopathy occurring in multiple myeloma.

Hyperammonemia is usually found in chronic liver diseases with portal-systemic shunts and acute fulminant hepatic failure.[1] It has also been described in hematologic malignancies such as acute leukemia,[2] following bone marrow transplantation[3] and in eleven patients with multiple myeloma (MM).[4-10] We report two new cases of hyperammonemic encephalopathy in MM.

Patient #1. IgG λ MM was diagnosed in a 56-year-old woman. Five courses of vincristine, adriamycin and dexamethasone (VAD) resulted in good partial remission. Three months later she presented with a one-week history of alternating lucidity and delirium, lethargy and inappropriate behavior. Serum electrolytes and creatinine were normal. Serum IgG λ spike amounted to 1920 mg/dL. A lumbar puncture and a computed axial tomography were unremarkable. The electroencephalogram presented changes compatible with metabolic encephalopathy. Plasma ammonium concentration was 170 mg/dL (normal < 82 mg/dL). Bilirubin, liver transaminases, coagulation tests, viral hepatitis serology, an abdominal ultrasound and a transjugular liver biopsy showed no alterations. Dietary nitrogen was eliminated and oral lactulose therapy was started, but mental status and plasma ammonium levels did not improve. A bone marrow (BM) aspirate showed 84% plasma cells. Three days after reinstituting chemotherapy (VAD), plasma ammonium decreased to normal and the patient became rapidly asymptomatic. Three months later the patient developed the same symptoms and died of disease progression.

Patient #2. IgA κ MM was diagnosed in a 51-year-old man. Chemotherapy (VAD) and local radiotherapy to the ribs and lumbar spine were started. After 6 courses he presented with disorientation, bradypsychia and myoclonus. Neurological examination and a lumbar puncture were normal. A magnetic resonance imaging scan showed diffuse edema in the brain. The electroencephalogram recorded triphasic waves. Serum electrolytes and renal and liver function were normal. Plasma ammonia level was 233 mg/dL. Serum IgA κ spike amounted to 4000 mg/dL. There were progressive osteolytic lesions and 100% plasma cells in BM aspirate were demonstrated. The clinical manifestations were ascribed to hyperammonemic encephalopathy and treatment with dexamethasone (8 mg/day) was started. Hyperammonemia and the neurologic alterations improved immediately after chemotherapy (VAD) was instituted. One month later the patient again presented with hyperammonemic encephalopathy and died of dis-

ease progression.

Hyperviscosity and hypercalcemia are the usual causes of encephalopathy in MM. Hyperammonaemic encephalopathy is usually described in serious liver dysfunction and is characterized by lethargy, confusion and asterixis, which can progress to coma and death.[1]

Mitchell *et al*.[3] identified this complication in eight of 460 patients who had leukemia or had had a bone marrow transplantation. A few cases have also been reported in MM.[4-10] The etiology of this syndrome has yet to be determined. Matsuzaki *et al.*[6] found that the myeloma cells from a patient with hyperammonaemic encephalopathy secreted ammonia at a high level into the culture medium.

Different treatments (protein restriction, lactulose, neomycin, plasmapheresis, hemodialysis...) have been tried in this syndrome,[4-10] but only chemotherapy has been successful. Nevertheless this complication is associated with disease progression and so with a very bad prognosis. We suggest that hyperammonaemic encephalopathy should be included in the differential diagnosis of disturbances of consciousness in MM.

Keywords

Multiple myeloma, encephalopathy, hyperammonemia

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References

1. Fraser CL, Arieff AI. Hepatic encephalopathy. N Engl J Med 1985; 313:865-73.
2. Watson AJ, Karp JE, Walker WG, Chambers T, Risch VR, Brusilow SW. Transient idiopathic hyperammonaemia in adults. Lancet 1985; 7:1271-4.
3. Mitchell RB, Wagner Je, Karp JE, Watson AJ, Brusilow SW, Prepiorka D, et al. Syndrome of idiopathic hyperammonaemia after high-dose chemotherapy. Review of nine cases. Am J Med 1988; 85:662-7.
4. Fine P, Adler K, Gerstenfeld D. Idiopathic hyperammonemia after high-dose chemotherapy. Am J Med 1989; 86:629.
5. Tsunoda S, Sasaki R, Miwa A, Sakurabayashi I, Miura Y. Coma, hyperviscosity syndrome, hyperammonemia and myelofibrosis in a patient with IgG lambda type multiple myeloma. Jpn J Clin Hematol 1989; 30:361-5.
6. Matsuzaki H, Uchiba M, Yoshimura K, et al. Hyperammonemia in multiple myeloma. Acta Haematol 1990; 84:130-4.
7. Kawano F, Tsukamoto A, Satoh M, Sanada T, Shido T, Miura K, et al. Non-secretory primary plasma cell leukemia with hyperammonemia. Jpn J Clin Hematol 1991; 32:399-403.
8. Caminal L, Castellanos E, Mateos V, Astudillo A, Moreno C, Dieguez MA. Hyperammonaemic encephalopathy as the presenting feature of IgD multiple myeloma. J Intern Med 1991; 233:277-9.
9. Matsuzaki H, Hata H, Sonoki T, Matsuno F, Kuribayashi N, Yoshida M, et al. Serum amino acid disturbance in multiple myeloma with hyperammonemia. Int J Hematol 1995: 61:131-7.
10. Ohmoto A, Kohno M, Yasukawa K, Matsuyama R. Massive ascitis as an initial sign, plasmacytoma of the cervical supine, and hyperammonemic consciousness disturbance in a patient with biclonal type multiple myeloma. Jpn J Clin Hematol 1996; 37:346-51.

High prevalence of anti-HGV/E2 antibodies in HCV-positive patients with non Hodgkin's lymphoma

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We evaluated in a series of 33 HCV positive (both RT-PCR and HCV RIBA 2 assays) B cell non-Hodgkin's lymphomas (NHL) patients the prevalence of active and inactive HGV infection by HGV RNA assays (RT-PCR) and anti HGV antibodies directed against E2 structural protein (immunoenzimatic method), a reliable serologic marker of past HGV infection followed by viral clearance. We found only one patient with HGV positivity at RT-PCR (3%). Twenty-six of 33 patients were positive for anti HGV/E2 antibodies (78.8%) suggesting past infection. If confirmed, our preliminary data seem to suggest a higher incidence of HGV past infection in our group of HCV postive patients with B cell NHL.

A possibile etiologic correlation between hepatits C virus (HCV) and B cell NHL was recently suggested by some authors.[1-5] and the ability of HCV to infect lymphocytes and to determine clonal expansion of such cells has been clearly documented. Another flaviviridae agent, GBV-C/HGV, was recently isolated and described as a possible etiologic agent of non A–E hepatitis. There is a close molecular correlation between HCV and HGV and co-infection with HGV is frequent in HCV positive patients.

The prevalence of HGV infection in B cell lymphomas is not known, although if there are some preliminary data from Italy[6] and Japan.[7] Zignego *et al.*[6] reported a 6% of prevalence of HGV RNA in a series of 150 B cell NHLs: no significant differences in HGV prevalence was found between HCV positive (n = 37) and negative (n = 113) cases. The HGV prevalence in Italian NHL patients was similar to that observed in non A-E hepatitis patients but significantly higher than that in healthy subjects. On the other hand, Nakamura *et al.*[7] found 4 HCV RNA positive cases and one HGV RNA/HCV RNA positive case in a series of 51 B cell NHL patients (2% of prevalence for HGV RNA).

We, therefore, evaluated, in a series of 33 HCV positive (both RT-PCR and HCV RIBA 2 assays) B cell NHL patients, the prevalence of active and inactive