Conclusion

La réaction de Jarisch-Herxheimer, bien connue pour d'autres localisations de la tuberculose telles que la tuberculose ganglionnaire, la pleurésie, la méningite et le tuberculome intracrânien, est possible au cours de la tuberculose intraoculaire. Elle peut survenir, au cours de différentes formes d'uvéites et en particulier au cours de la choroïdite pseudo-serpigineuse. Cette réaction doit être reconnue par les ophtalmologistes pour éviter de la prendre pour une erreur diagnostique ou une résistance au traitement antituberculeux.

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Antiviral therapy for hepatitis C virus infection, cryoglobulinemic glomerulonephritis and low-grade malignant lymphoma: a challenge?

R. Ennaifer, M. Sabbah, R. Hefaiedh, H. Romdhane, M. Cheikh, N. Belhadj
Service de Gastroentérologie. Hôpital Mongi Slim La Marsa
Université de Tunis El Manar, Faculté de Médecine de Tunis

Hepatitis C virus (HCV) is a hepatotropic and also lymphotropic virus that chronically infects over 170 million people worldwide and is the leading indication for liver transplantation [1]. HCV frequently causes extrahepatic manifestations, the most common and severe of which is mixed cryoglobulinemia (MC), a systemic vasculitis that cause glomerulonephritis in one third of patients, ranging from asymptomatic proteinuria to nephritic syndrome with variable progression to chronic renal insufficiency [2]. Moreover, HCV infection could be responsible not only for chronic liver disease and cryoglobulinemia, as its role in the development of B cell non Hodgkin lymphoma is now admitted [3]. Indeed, HCV MC is considered as a B cell lymphoproliferative disorder. Treatment of HCV related cryoglobulinemia is difficult and must be adapted to the severity of the disease: it can be directed to eradicate HCV, limit or suppress B lymphocyte proliferation and ameliorate symptoms [4]. On the other hand, antiviral therapy can lead to remission of HCV related low grade non Hodgkin lymphoma [5]. Nevertheless, use of combination therapy with pegylated interferon (Peg IFN) and ribavirin (RBV) is poorly tolerated in patient with worsening kidney function and therefore is challenging.

Therefore, we report a case of an association between HCV infection, B cell non Hodgkin lymphoma and mixed cryoglobulinemia treated with antiviral therapy.

Case-report

A 74 years-old man was admitted in our department for the management of lower limb oedema, ascites and loss of weight. Physical examination disclosed mild ascites and oedema. Abdominal ultrasound disclosed isolated ascites without signs of portal hypertension or liver dysmorphy. Ascitis fluid examination showed a paucicellular transudative liquid. Laboratory tests objectified inflammatory anemia, hypoprotidemia (50g/L) and hypoalbuminemia (21g/L). Cholesterol level, prothrombin time, factor V and platelets count were normal. Renal laboratory tests were perturbed: glomerular filtration rate was decreased to 42 ml/mn and urine protein level was raised (up to 7g/24hours) leading to the diagnosis of impure nephrotic syndrome. Hepatitis C antibodies were positive (genotype1b, fibrotest: A1-A2 F4 and high serum HCV RNA level). Cryoglobulinemia was positive (mixed, type II) and renal biopsy showed a membranoproliferative glomerulonephritis. Upper gastrointestinal endoscopy, initially looking for esophageal varices showed erythematous gastritis and histological examination confirmed a low grade MALT lymphoma with a positivity of Helicobacter Pylori (HP) and CD20 and CD3 in immunohistochemical examination. No extension was found in computed tomography, bone marrow biopsy, colonoscopy and cavum exploration.

The final diagnosis of a nephrotic syndrome linked to cryoglobulinemic glomerulonephritis associated with gastric lymphoma classified IE of Ann Arbor in a patient with chronic hepatitis C was retained. For the lymphoma, we started with cures of therapy for HP, leading to eradication after 3 cures (the last one involved levofloxacin) and complete remission of the lymphoma. As the kidney damage was increasing, and despite the age, we decided to treat the patient with Peg IFN alpha 2b 1µg/kg/weekly plus RBV 400mg/day as a first line therapy, hoping that HCV eradication may lead to a sustained clinical improvement. Under antiviral therapy, ascites disappeared, urine level of protein decreased (reaching 3g/24hours) and renal tests normalized. RNA serum level of HVC was negative at 12 and 24 weeks. However combination therapy was stopped after eight months because of severe anemia resistant to erythropoietin. Follow up after six month showed no relapse for HCV RNA serum level and no worsening in kidney disease.

Conclusion

This report confirms previous observations on the striking association between cryoglobulinemia, B cell non Hodgkin lymphoma and HCV infection. HCV should be considered as a potential oncogenic virus although its mechanism of action has to be clarified. The mechanism could involve mixed cryoglobulinemia which may be responsible for activating and expanding memory B cells. Combination therapy with Peg INF and RBV may be useful for control of viral replication and cryogobulinemia and thus, for prevention of lymphoma. However, in the presence of cryoglobulinemic glomerulonphritis with kidney damage, tolerance of antiviral therapy remains a challenge.

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