Polyarteritis nodosa and mixed cryoglobulinaemia related to hepatitis B and C virus coinfection

P Garcia de La Peña Lefebvre, L Mouthon, P Cohen, F Lhote, L Guillevin

Abstract

Objective—To determine the responsibility of hepatitis B virus (HBV) and hepatitis C virus (HCV) and therapeutic implications in a patient who developed systemic vasculitis.

Case report—The case of a 38 year old woman who had a past history of addiction to intravenous drugs and developed systemic vasculitis after infection by HBV and HCV is described. The clinical and laboratory findings substantiated not only the diagnosis of polyarteritis nodosa (PAN) but also that of mixed cryoglobulinaemia with a monoclonal IgM component.

Conclusion—Because cryoglobulins are rarely found in HBV related PAN but often associated with HCV infection, and in light of the histological findings, cryoglobulinaemia was interpreted as being secondary to HCV infection. This example of a highly complex situation emphasises the need to gather all relevant clinical, biological, histological, and complementary data so that the best treatment for overlapping of distinct vasculitides can be selected.

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The relation between viruses and vasculitis is now well established: hepatitis B virus (HBV) is considered to be responsible for a minority of cases of polyarteritis nodosa (PAN), and hepatitis C virus (HCV) for more than 80% of mixed cryoglobulinaemias (MC). Because of similar risk factors and routes of infection, several viruses can be acquired simultaneously and cause different diseases, and the optimal therapeutic strategy must be carefully considered.

Herein we describe a patient who developed systemic vasculitis after HBV and HCV coinfection and discuss the responsibility of each virus and the therapeutic implications.

Case report

In January 1995 a 38 year old woman developed arthralgias and myalgias, and lost weight. She had a past history of alcoholic dependence that required specific treatment. She had also had a depression one year earlier. She had no prior history of hepatitis but had been addicted to intravenous drugs since 1984. She had no permanent employment and her two children were healthy. Six months before the first symptoms of vasculitis, she had a short term sexual relationship with a man known to be infected with replicating HBV.

On admission, the physical examination was unremarkable. Blood analyses showed white blood cell count 14×10⁹/l, with 10×10⁹/l, neutrophils; erythrocyte sedimentation rate 100 mm/1st h; alkaline aminotransferase 149 U/l (normal <37); aspartate aminotransferase 249 U/l (normal <50); glutamyltransferase 300 IU/l (normal <50); total bilirubin <17 µmol/l; proteins 59 g/l (normal 62–78); albumin 19 g/l (normal 38–48); γ globulin 4.12 g/l (normal 1–2.5); β globulin 11.9 g/l (normal 4–6.5); γ globulins 16.8 g/l (normal 7–16); IgG 17.5 g/l (normal 6.8–12.7); IgA 2.07 g/l (normal 0.84–2.69); IgM 1.9 g/l (normal 0.7–1.99).

Renal function and parameters were normal. Antinuclear antibodies and antineutrophil cytoplasmic antibodies were negative. Complement fraction C4 was low, 0.08 g/l (normal 12–28); C3 was normal, 1.12 g/l (normal 0.75–1.4); CH₅₀ was normal, 95%; properdin 415 mg/l (normal 200–600 mg/l). Type II cryoglobulinaemia with a monoclonal IgM component was detected and found to be 127 mg/l. Anti-HCV antibodies were found by an immunoenzymatic method and confirmed by a RIBA III test. An HCV-RNA search was positive. Hepatitis B surface antigen (HBsAg) and hepatitis B e antigen (HBeAg) were present without evidence of the corresponding antibodies. HBV DNA was detected by hybridisation test. HIV-1 and HIV-2 serologies were negative, hepatitis A virus (HAV) antigens and antibodies were absent. Abdominal ultrasonography detected homogeneous hepatomegaly without evidence of splenomegaly or abdominal lymph nodes.

A deltoid muscle biopsy showed vasculitis of small and medium sized arteries and venules with leucocytoclasia and lymphocyte infiltrates, but no fibrinoid necrosis. No immunofluorescent study was performed. A hepatic biopsy showed chronic hepatitis (Knodell scale = 11).

Ten days after admission to hospital she developed paraesthesias of both hands; several days later, abdominal pain, weakness, and paraesthesias in the left foot appeared. Electromyography detected axonal neuropathy. An abdominal angiogram showed multiple microaneurysms of mensenteric, renal, splenic, and hepatic arteries, with multiple stenoses and visceral infarcts. HBV related PAN was diagnosed, even though MC could also be considered owing to the muscle biopsy findings.

In April 1995, treatment was started according to the protocol described elsewhere. She received a daily methylprednisolone pulse for three days, followed by oral prednisone (50 mg/day), which was rapidly tapered within 14 days.
days. Thirteen plasma exchanges were performed within one month. After stopping steroids, treatment with interferon alpha-2b (3 MU, three times a week) was prescribed for two months.

Her condition improved after the second plasma exchange; one month later the abdominal pain disappeared and motor nerve palsy progressively regressed while paraesthesias persisted. Six weeks later, anti-HBe antibodies were detected, and cryoglobulinaemia became undetectable.

Three years later, the patient has only minor left foot paraesthesias. Liver function is normal. Anti-HBs and anti-HBe antibodies, cryoglobulins, and HCV serology remain positive, but HCV-RNA replication is undetectable.

Discussion

The association of two virus related vasculitides in one patient is rare. The first studies on MC showed a high incidence of HBV markers, but this concept has changed since the discovery of serological markers for HCV infections. MC had chronic HBV infections, whereas others found 17% HBV related cryoglobulinaemia. The clinical and laboratory findings substantiated the diagnosis of PAN but also that of MC with a monoclonal IgM component. Because cryoglobulins are rarely found in HBV related PAN but frequently associated with HCV infection, and in light of the histological findings in our patient, we interpreted cryoglobulinaemia as being secondary to HCV infection. Indeed interpretation of the histological findings is the crucial point. According to the American College of Rheumatology classification, PAN can be diagnosed, but the Chapel Hill nomenclature would exclude this diagnosis. This example of a highly complex situation emphasises the need to gather all relevant clinical, biological, histological, and complementary data so as to select the best treatment for overlapping of distinct vasculitides.

Although it is difficult to establish definitively the diagnosis between HBV related PAN or HCV related MC, the response to treatment may help to interpret clinical data further. Despite the fact that some symptoms or biological and histological findings overlap, we considered a diagnosis of PAN in our patient to correspond best to all the data collected. The rapid onset of clinical manifestations, biological evidence for a recent HBV infection, and the short time between the probable sexual contamination and the occurrence of vasculitis suggested that HBV was responsible. Diagnostic difficulties came, on the one hand, from the presence of multiple microaneurysms and arterial stenoses on the angiogram, which suggests classical PAN, and on the other, from the biopsy results which included vasculitis of small sized arteries, which tends to suggest MC. In this patient with demonstrated coinfection, clinical and virological evolution supported the hypothesis that clinical manifestations might have been secondary to PAN and not MC. The recovery from all symptoms and the absence of relapse once HBV replication had stopped is also suggestive of the diagnosis of HBV related PAN. However, although complete remission and absence of relapse is rarely seen in MC, HCV related MC may also respond fairly well to interferon. The absence of HCV replication three years after recovery from vasculitis also supports recovery from MC. PAN may also be secondary to HCV infection, as there are several reports of vasculitis affecting abdominal organs in HCV associated cryoglobulinaemic vasculitis.


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