To the editor:

Congenital JAK2V617F polycythemia vera: where does the genotype-phenotype diversity end?

A previously healthy 7-month-old girl was admitted to her local hospital with tonsillitis. Full blood count showed polycythemia (Hb 190 g/L) along with an elevated platelet (946 × 109/L). Due to the long-term risks of malignant transformation and thromboembolism, she underwent an uneventful sibling (JAK2V617F-negative) allogeneic bone marrow transplantation. Complete donor chimerism and undetectable JAK2V617F mutation have been observed from day +14 to present. She remains clinically well and in molecular remission after hematopoietic stem cell replacement.

Although polycythemia vera (PV) is extremely rare in young children, to the best of our knowledge this is the first report of prenatal JAK2V617F PV and further highlights the genotype-phenotype diversity that is seen among this group of JAK2V617F-positive myeloproliferative neoplasms. The frequency of the mutation in pediatric PV has been variably reported in the literature but our observation proves that it can occur at all ages. The absence of the mutation in either parent or the oral mucosa of the child shows that this was most likely an acquired somatic event that occurred in utero. The JAK2V617F mutation is thought to be acquired in both familial and sporadic MD. In a study of 22 families with PV, the mutation in either parent or the oral mucosa of the child shows that this was most likely an acquired somatic event that occurred in utero. The JAK2V617F mutation is thought to be acquired in both familial and sporadic MD.

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To the editor:

Hepatitis C virus (HCV) infection, monoclonal immunoglobulin specific for HCV core protein, and plasma-cell malignancy

Hepatitis C virus (HCV) infection can lead to B-cell malignancy via direct infection and transformation of B lymphocytes, or via indirect transformation by chronic antigen-driven stimulation. Both mechanisms may occur simultaneously, as we previously reported in a case of HCV infection followed by plasma-cell leukemia (PCL), where blasts were infected with HCV and the monoclonal immunoglobulin (Ig) they produced was directed against the core protein of the virus. Approximately 10% of HCV-positive patients responding to viral infection with poly- or oligoclonal Ig develop a monoclonal Ig, the specificity of which is usually unknown. The present study aimed at evaluating the link between chronic HCV-antigen–driven stimulation and plasma-cell transformation by determining the specificity of monoclonal Ig developed in the context of HCV infection.

Over a period of 13 months beginning in January 2002, sera from patients consulting or hospitalized at the Centre Hospitalier Universitaire of Nantes that the Biochemistry Laboratory declared positive for monoclonal Ig were systematically tested for the presence of HCV RNA and anti-HCV Ig. Among the 700 patients studied, 10 (1.4%) were found positive for HCV; 2 of these 10 patients were also positive for human immunodeficiency virus. Only 3 of 10 patients were infected with HCV genotype 1, the predominant genotype in western France; 7 of 10 patients were infected with genotypes 2 (5 patients), 3, or 5 (Table 1), suggesting contamination from blood products before 1980. Purification of the monoclonal Ig was achieved for 7 of 10 patients. Using immunoblotting, the purified monoclonal Ig (2 IgG, 1 IgA, 1 IgM) of 4 patients, all with genotype 2, recognized the C22-3 fragment of HCV-core protein; 2 (IgG) recognized NS-4 and 1 did not recognize HCV (Table 1, Figure 1). Among the 4 patients with anti-HCV core monoclonal Ig, 2 presented with mixed (type II) cryoglobulinemia (patients 12 and 20) and one was diagnosed with multiple myeloma (patient 21). Anti-HCV treatment resulted in the disappearance of the monoclonal Ig (patients 8, 9, and 10).

Altogether, for all but one patient presenting with monoclonal Ig in the context of HCV infection, the monoclonal Ig was directed against the virus. Taking into account the first reported case, 2 of 5 patients who responded to HCV infection with anti-HCV core monoclonal Ig developed multiple myeloma or PCL, implying that a monoclonal Ig response directed against HCV core may distinguish patients with increased risk of plasma-cell malignancy. Efforts should be made to identify such patients, as associated antiviral therapy should help eradicate the malignant, HCV-driven plasma-cell clone.

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