oustanding efficacy of the type II reagent. We are currently exploring alternative mechanisms that explain such activity.

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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) and white cell count (19.7 × 109/L). Oxygen saturations, arterial blood gases, chest x-ray, abdominal ultrasound, and P50 were normal. Serum erythropoietin was low. No mutations were identified in exons 7 and 8 of the EPO receptor gene, the von Hippel-Lindau tumor suppressor gene and the Prolyl hydroxylase domain 2 gene. Bone marrow examination showed hypercellularity, megakaryocytic hyperplasia, and the JAK2V617F mutation was identified in her peripheral blood or the Guthrie card taken at 2 days of age. Both parents and other genetic abnormalities, possibly inherited, precede the acquisition of JAK2V617F mutation to develop into PV. There is no known familial history of myeloproliferative disorders (MPDs). The JAK2V617F mutation was not detected in the peripheral blood or the oral mucosa of either parent or in the oral mucosa of the patient.

She was treated with regular venesection to maintain her hematocrit less than 45%. Aspirin (45 mg once daily) was started when her platelet count rose above 1500 × 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.1 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 MPD. In a study of 22 families with PV, the mutation was present in variable amounts in affected members and absent in unaffected members.2 Analysis of another single large family with PV showed the presence of JAK2V617F in affected family members but not in an obligate carrier.3 This suggests that other genetic abnormalities, possibly inherited, precede the acquisition of the JAK2V617F mutation. Inheritance of as yet unknown germline mutations may have predisposed toward the acquisition in utero of the somatic JAK2V617F mutation in our particular case, but such events also may have influenced the relatively rapid evolution to the polycythemic phenotype in this infant compared with the estimated time it takes for a JAK2V617F mutation to develop into clinical PV in adult patients.

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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, all sera from patients consulting or hospitalized at the Centre Hospitalier Universitaire de 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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