To the editor:

Coenzyme Q is effective on anemia in a patient with sideroblastic anemia and mitochondrial myopathy

In a few cases, sideroblastic anemias seem to be associated with mitochondrial dysfunction. Indeed, mitochondrial dysfunction could result in apoptosis and ineffective hematopoeisis, and iron deposition within mitochondria of developing erythroblasts with ringed sideroblasts. We report here a patient with sideroblastic anemia and mitochondrial myopathy in whom long-term red blood cell transfusion therapy was stopped and improvement of muscle strength was observed under coenzyme Q10 therapy (CoQ10).

A 38-year-old man with no family medical history was diagnosed at 6 years of age with a presumptive diagnosis of aplastic anemia, refractory to corticosteroids, intravenous immunoglobulins, erythropoietin, and cyclosporine. Diagnosis of sideroblastic anemia was finally established at 16 years of age, and the patient required red blood cell transfusions every 3 weeks. When he was 29 years old, he complained of progressive development of cramps upon exertion and loss of strength. Hypogonadism was found, probably related to iron overload. Treatment with norethandrolone was given during one year, then danazol, with poor effectiveness. One year later, a bilateral ptosis, gracile aspect of muscle masses, and proximal muscle weakness were noted. Serum creatine phosphokinase level was within normal range, but aldolase level was increased at 12.4 U/L (normal, 0.0-7.6 U/L). Venous lactate level was 4.97 mM (normal, 0.60-1.4 mM). Serum ferritin level was 2642 µg/L (normal, < 350 µg/L) despite infusion of desferrioxamine. Electromyogram study was typical with a myogenic process. Muscle biopsy showed a typical pattern of mitochondrial myopathy with many ragged red fibers and total diffuse negative staining for cytochrome oxidase activity. Study of the respiratory chains showed a deficiency in complex I, III, and IV on both muscle and lymphocytes studies. Study of lymphocytes, muscle, and fibroblast mitochondrial DNA (mtDNA) was performed. No mtDNA point mutations could be identified using the Surveyor nuclease and large rearrangements and quantitative mtDNA anomalies have been excluded by long-range PCR (using a fragment of 15.5 kb) and quantitative PCR, respectively. However, the patient showed multiple mtDNA deletions in muscle by long-range PCR using a fragment of 8.3 kb. Measurement of CoQ10 concentration in muscle was not possible. Cardiac failure developed at the age of 31 years with an ejection fraction of left ventricule at 17%, requiring treatment with ramipril and carvedilol. At this time, CoQ10 was given during one year, then danazol, with poor effectiveness. Tenon (AP-HP), 4 rue de la Chine, 75020 Paris, France; e-mail: claude.bachmeyer@tnn.aphp.fr.

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References


To the editor:

**CD21**

**low** B cells in common variable immunodeficiency do not show defects in receptor editing, but resemble tissue-like memory B cells

We read with great interest the article by Isnardi et al1 wherein the authors showed very similar phenotypic and genotypic features of CD21**low** B cells to anergic mouse B cells—reminiscent of anergic B cells in mouse models—the authors propose that CD21**low** B cells represent anergic human B cells. Moreover, they showed that the majority of highly HEP2-reactive CD21**low**-B-cell clones express kappa (κ) light chains and suggested that the receptor editing using lambda (λ) light chains might not be induced in those clones serving as a mechanism to silence autoreactive B cells. We would like to suggest a different interpretation of the origin of CD21**low** B cells.

Anergy in CD21**low** B cells in patients with common variable immunodeficiency (CVID) is not complete. In the original model of hen egg lysozyme–transgenic mice,2 anergy in B cells represents a mechanism of central tolerance caused by B cell receptor (BCR)–induced hyporesponsiveness, which is associated with down-regulated BCR, poor calcium response, defective up-regulation of CD86, failure of antibody production, and impaired proliferation.3,4 Although poor Ca**2+** response and impaired proliferation are both features that CD21**low** B cells share with anergic mouse B cells, CD21**low** B cells of CVID patients have not down-regulated their surface BCR (Figure 1A-B) and are able to up-regulate activation markers like CD86 (unpublished data) as well as ICOS-L, TACI, and Fas surface expression upon BCR stimulation.5 Even more importantly, CD21**low** B cells produce higher levels of IgM than naive B cells after stimulation in vitro.6 In addition, a comparison of gene-expression profiles of mouse anergic B cells3,4 and human CD21**low** B cells7 showed only little overlap: only 3 (11.5%) of 26 genes describing the signature of anergic mouse B cells were identically expressed in CD21**low** B cells. In contrast, these cells closely resemble2 the recently characterized tissue memory-like B cells in tonsils8 and circulating “exhausted” CD21low B cells in HIV patients, suggesting rather a mechanism of activation-driven peripheral exhaustion underlying this anergic phenotype.6 This would also better explain the accumulation of CD21**low** B cells in the bronchoalveolar fluid of CVID patients or the synovial fluid of rheumatoid arthritis patients.2

In addition, in our cohort of CVID patients we cannot confirm a defect in secondary editing and λ light chain usage. We actually found that CD21**low** B cells preferentially express λ-chains compared with the naive B cells of CVID patients, which was also the case in 1 of the 3 CVID samples shown in Figure 2D of Isnardi and colleagues’ article.1 In our experience the κ/λ ratio in CD21**+** naive B cells (1.24 ± 0.03; n = 4) of CVID patients was within the normal range (1.0-2.1), whereas CD21**low** B cells showed a

![Figure 1. IgM surface expression and light chain usage in CD21low B cells.](image-url)

Figure 1. IgM surface expression and light chain usage in CD21low B cells. (A) Representative FACS plots for the expression of indicated B-cell markers in B cells of CVID patients (n = 10). CD19-IgM+ B cells were gated on CD21low and CD21**+** naive B cells, according to CD38 and CD21 expression, and IgM surface expression was analyzed as the mean fluorescence intensity (MFI) in CD21**+** and CD21low B-cell subpopulations, respectively. (B) The diagram shows no significant difference in the cell-surface expression of IgM between CD21**+** and CD21low B cells in CVID. (C) Representative FACS plots demonstrate the expression of IgM and λ light chain on CD21 low and naive B cells of CVID patients (n = 4); (D) The diagram shows a significantly decreased usage of κ-light chains in CD21low B cells of CVID patients compared with naive B cells of the same individuals.
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