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INCLUSION BODY MYOSITIS AND CHRONIC LYMPHOCYTIC LEUKEMIA: A CASE SERIES

Sporadic inclusion body myositis (IBM) is distinguished from other inflammatory myopathies based on clinical and histopathologic features, including slowly progressive weakness in middle or later age, with a predilection for finger flexors, wrist flexors, and quadriceps muscles. We report 4 patients with IBM and chronic lymphocytic leukemia (CLL). Only one such patient has been reported previously.¹

Case reports. *Case 1.* A 74-year-old woman developed B-cell CLL (immunophenotype CD19+, CD20+, CD23+, CD43+, CD5+, CD38+). She did not receive treatment. At age 78, she developed difficulty swallowing, rising from chairs, and walking. Examination at age 80 revealed the following Medical Research Council (MRC) strength (right/left): shoulder abduction 4+/4+, wrist flexion 4+/3- (weaker than wrist extension 5/4), finger flexion 4/4, flexor pollicis longus 4-/1, finger extension 4/4-, hip flexion 4-/4-, and knee extension 3-/3. There was atrophy of quadriceps and ventral forearms. Serum creatine kinase (CK) was 114 U/L.

Muscle biopsy revealed endomysial inflammatory cell infiltrates invading non-necrotic muscle fibers and fibers containing rimmed vacuoles (figure). TAR DNA-binding protein 43 (TDP-43) deposits were present in 18% of myofibers. Inflammatory cells consisted of non-leukemic CD3+ T cells and prominent collections of CD19+ B cells.

Case 2. A 63-year-old man developed B-cell CLL (immunophenotype CD20+, CD23+, CD5+) and progressive leg weakness. Muscle biopsy at age 65 showed extensive endomysial inflammation and rimmed vacuoles (figure). Treatment with prednisone 60 mg daily tapered over 1 year was ineffective. Physical examination at age 67 showed the following MRC grades (right/left): shoulder abduction 4+/4+, wrist flexion 4/4, wrist extension 4/4, finger flexion 3/3, finger extension 4+/4+, hip flexion 4/4, and knee extension 3-/3-.

Case 3. A 45-year-old man developed T-cell large granular lymphocytic type CLL (immunophenotype positive CD3, CD8, and CD57) and difficulty climbing stairs, rising from chairs, and buttoning shirts. His CLL was treated with methotrexate and prednisone. Examination at

age 54 revealed the following MRC grades (right/left): shoulder abduction 5/5-, wrist flexion 3+/3+, wrist extension 4+/4+, finger flexion 1/1, finger extension 3+/3, hip flexion 3-/3-, and knee extension 4+/4+. There was atrophy of the ventral forearms. Serum CK was 347 U/L. Muscle biopsy showed endomysial inflammatory cell infiltrates invading non-necrotic muscle cells and fibers containing rimmed vacuoles (figure). Inflammatory cells were nonleukemic CD4- and CD8-positive T cells.

Case 4. A 57-year-old man developed T-cell large granular lymphocytic leukemia CLL (immunophenotype positive CD2, CD3, CD7, CD8, CD57, CD11c and negative CD4, CD56, CD16) and difficulty climbing stairs, rising from chairs, and swallowing. Laboratory studies showed CK of 605 U/L. Muscle biopsy revealed marked endomysial mononuclear inflammatory cell infiltrate invading non-necrotic muscle fibers (figure). Rimmed vacuoles were not appreciated. Inflammatory cells included CD4- and CD8-positive T cells with a subset of CD57-positive T cells. Serum anti-cN1A autoantibody testing was positive.² Treatment with prednisone 100 mg every other day for 6 months resulted in reduction in CK to 149 U/L, but muscle strength continued to worsen. Examination at age 68 showed the following MRC grades (right/left): shoulder abduction 5/5, wrist flexion 4+/4+, wrist extension 5/5, finger flexion 4/4, finger extension 4+/4+, hip flexion 4-/4-, and knee extension 5/5.

Discussion. We describe 4 patients with both IBM and CLL. All patients developed symptoms of IBM prior to onset of any treatment for CLL. Patients 1, 2, and 3 met European Neuromuscular Center (ENMC) 2000 criteria³ for definite IBM and patient 4 met ENMC 2000 criteria for probable IBM. Patient 4 had positive blood anti-cN1A autoantibody testing for IBM, while patients 1-3 did not undergo such testing. There is one prior published case of IBM with CLL: a woman who was diagnosed with CD8+ T-cell CLL at 72 years of age and IBM 1 year later.¹

CLL has been associated with autoimmunity: B-cell CLL with Coombs-positive hemolytic anemia and autoimmune thrombocytopenia,⁴ and T-cell large granular lymphocytic leukemia with rheumatoid arthritis and Sjögren syndrome.⁵ Among 62 patients enrolled in an IBM blood collection cohort at our institution (47 of

(A–C) Case 1 with (A) trichrome staining demonstrating endomysial inflammation with rimmed vacuoles (arrow, and enlarged in inset), (B) marked CD3+ T-cell infiltrates, and (C) CD19+ B-cell infiltrates. (D–F) Case 2 with (D) endomysial inflammation, (D, E) rimmed vacuoles, and (F) CD20+ B-cell infiltrates. (G) Case 3 with hematoxylin & eosin staining showing endomysial inflammation, invasion of non-necrotic myofibers (arrow), and rimmed vacuoles (arrowhead and enlarged in inset). (H, I) Case 4 with (H) invasion of non-necrotic myofibers and (I) a CD3+ T-cell infiltrate.

whom were described in reference 2), 4 (6.4%) have CLL. This rate is significantly higher than the 1 per 200 (0.5%) prevalence of CLL in the general population⁶ ($p = 0.01$, Fisher exact test). Nevertheless, case series by their nature do not test whether associations between 2 features (in this case, 2 diagnoses IBM and CLL) are due to chance, confounding, or causality. The current case series suggests the possibility of an association between IBM and CLL that is not due to chance, a possibility that can be tested through case-control studies.

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