Chronic lymphocytic leukemia with Dermatomyositis: A therapeutic challenge

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To the Editor,

Chronic lymphocytic leukemia (CLL) is an indolent B-cell malignancy that is often complicated by autoimmune abnormalities like autoimmune hemolytic anemia and immune thrombocytopenia. Non-hematological autoimmunity occurs in 1-2% of patients with CLL[1]. Dermatomyositis (DM) is an immune-mediated, inflammatory muscle disease that is reported to be associated with CLL and causes significant clinical dilemma owing to its rarity. We report a case of CLL diagnosed concurrently with DM, treated with chemo-immunotherapy.

A 60-year-old man presented with progressive skin rash over the root of neck, knuckles of both hands, and trunk along with symptoms suggestive of proximal muscle weakness predominantly involving lower limbs for four months. He was bedridden for the preceding two months. On examination, he had erythematous, irregularly shaped plaques with crusting over the neck, upper chest (shawl sign) (Figure 1 a, b) bilateral knuckle and periumbilical area without any mucosal lesions. Central nervous system (CNS) examination showed bilaterally symmetrical proximal muscle weakness (grade 3/5), predominantly involving lower limbs. Rest of CNS and other systemic examination was unremarkable. He had a hemoglobin of 11g/dL and leukocytosis with an absolute lymphocyte count of 13224/mm³. Peripheral blood smear examination and flow cytometry were compatible with the diagnosis of CLL. Fluorescent in situ hybridization panel for CLL showed 13q deletion. His creatine kinase level was elevated; 2092 U/l (reference range; 10-225 U/l), and so was serum lactate dehydrogenase (557 U/l, reference range; 200-420 U/l). The autoimmune panel, nerve conduction, and electromyographic studies were negative. Skin biopsy showed focal vacuolar interphase colloid bodies, papillary dermal edema and dilated capillaries in the upper dermis with elastotic degeneration suggestive of DM (Figure 1: c,d). The diagnosis of CLL (clinical Rai stage-0) with DM was made. He was started on prednisolone 1mg/kg and methotrexate (
15mg/weekly) by a dermatologist, however, the rashes were gradually progressive. Due to his uncontrolled rashes after two months of steroid and methotrexate and recent-onset marked fatigue, he was put on CLL therapy with BR (Bendamustine at 90mg/m² and rituximab at 375mg/m² q 28days) regimen. He was benefitted from rashes, weakness, and fatigue. He attained complete hematological and clinical remission after six cycles of BR and remains in follow up and disease free from the last 18 months.

Among 15 reported cases of CLL with inflammatory myositis (IM) in the last two decades, only six were associated with DM [2]. It is not known whether this association is coincidental or causal or merely a patient selection bias. DM is usually diagnosed concurrently (5 out of 6 reported cases) or after (one out of six) a diagnosis of CLL and follow a parallel course suggesting a pathogenic link between the two entities [2]. Tumor antigens triggering the autoimmune process either by mimicking endothelial antigens or via bystander stimulation and imbalance of T cell subsets in CLL are the most reported hypothesis[3,4]. In general, the treatment of autoimmune complications in CLL has been the same as when the disease occurs spontaneously, but the question of whether and how to treat CLL itself persists. No treatment plan for 5 out of 6 cases of CLL with DM has been reported, and one received methotrexate with cyclophosphamide. The skin rash in DM does not mean malignant skin involvement; therefore, DM treatment should be initiated separately as in our case. However, DM with associated malignancy responds poorly compared with idiopathic one[5]. Long term outcomes of CLL with DM are unknown, and so is the data regarding the use of chemo-immunotherapy in such patients; albeit, rituximab has shown efficacy in DM[6]. It is prudent for the overworked clinician not to overlook neurological or musculoskeletal symptoms in CLL patients, and a keen search for hematological malignancy is justified in known cases of Inflammatory myopathies.

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References

Fig. 1a Pretreatment erythematous, irregular and crusting plaque like skin rash (shawl sign), 1b Resolved skin rash after therapy, 1c and d Skin biopsy showing focal vacuolar interphase, colloid bodies, papillary dermal edema and dilated capillaries in upper dermis with elastotic degeneration.