Concurrent Management of Multiple Sclerosis and Hairy Cell Leukemia with Cladribine

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Background

Cladribine, a synthetic purine nucleoside analog, was originally developed as a treatment for hematological malignancies, including hairy cell leukemia (HCL)[1]. Recently, an oral formulation of cladribine has been approved for the treatment of multiple sclerosis (MS)[2,3] representing a selective high-efficacy, oral form of immune reconstitution therapy (IRT). Its mechanism of action appears to involve semi-selective and relatively long-lasting depletion of B and T lymphocytes, with a particularly significant and sustained reduction in memory B cells. This lymphocyte-depleting effect may address both autoimmune and neoplastic processes.

Case presentation

We describe the case of a 53-year-old man who presented to our clinic in February 2018 with a two-week history of paresthesias starting in the feet and progressively ascending to the umbilical region, accompanied by gait disturbance and dysesthesias. Past medical history was unremarkable for neurological disorders, except for known β-thalassemia trait. Neurological examination showed no motor weakness. Bilateral hypoesthesia extended from the thighs downward, accompanied by dysesthesias and paresthesias. Gait was cautious but independent.

Cervicodorsal MRI demonstrated multiple T2/FLAIR lesions, including an intramedullary lesion at D9–10 with contrast enhancement. Brain MRI revealed multiple bilateral supratentorial T2/FLAIR hyperintensities consistent with demyelinating disease. Cerebrospinal fluid analysis revealed no oligoclonal bands. Somatosensory evoked potentials of the lower limbs were bilaterally abnormal.

A diagnosis of MS was established, and high-dose intravenous corticosteroids induced marked clinical improvement. In March 2018, the patient started interferon-β therapy. In June 2019, due to persistent adverse effects, treatment was switched to dimethyl fumarate (240 mg twice daily). In 2020 the patient remained clinically and radiologically stable without adverse events.

In October 2020, follow-up cervical MRI noted bone marrow reconversion, prompted further investigation (*Figure 1*). Blood tests showed chronic anemia and moderate leukopenia with lymphopenia. Hematology consultation led to supportive vitamin-B therapy and follow up. In December 2021, further hematological deterioration with thrombocytopenia prompted bone-marrow biopsy, which diagnosed HCL, BRAF-positive.

Dimethyl fumarate was discontinued and the patient received subcutaneous cladribine at 0.14 mg/kg/day for 5 days in February 2022, together with antibiotic prophylaxis and subsequent epoetin and filgrastim. In September 2022, new bone-marrow biopsy confirmed complete remission of the leukemic infiltrate.

Given documented efficacy in both MS and HCL [1,2,3] we decided to transition to oral cladribine for MS (two annual courses administered May–June 2023 and May–June 2024; 3.5 mg/kg cumulative dose over 2 years). Neurological examinations and MRI scans have remained stable. Hematologically, the patient undergoes laboratory and clinical follow-up every 6 months (including abdominal ultrasound and annual chest X-ray), with ongoing remission.

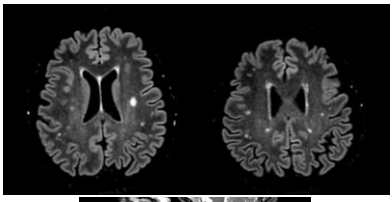

Figure 1

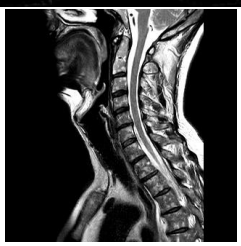

Figure 2

Discussion

This case highlights the unique opportunity to manage two distinct diseases—MS and HCL—with a single agent, cladribine. Originally developed for hematologic malignancies, cladribine is a purine nucleoside analogue with potent and selective lymphocyte-depleting effects that target both dividing and resting B and T cells [1,2,3]. In MS, cladribine tablets represent an IRT, administered in two short annual courses that achieve long-term disease control by reduction, repopulation, and reconstitution of lymphocytes [2,3,4]. In HCL, cladribine remains the first-line standard of care, inducing durable complete remissions in the majority of patients by targeting the BRAFV600E-driven malignant B-cell clone[1]. The drug's high specificity for lymphoid cells allows effective eradication of leukemic cells while sparing innate immunity. Our patient's course illustrates how oral cladribine enabled concurrent, sustained control of both MS and HCL, simplifying treatment and minimizing cumulative immunosuppression (Figure 2). This dual efficacy is supported by early case reports of cladribine successfully treating HCL with concomitant MS[5]. Moreover, during follow-up the patient experienced no serious infections, a finding consistent with post-marketing data showing that cladribine induces transient, selective lymphocyte depletion while generally preserving innate immune competence, resulting in a favorable safety profile[4,6].

This case underscores the relevance of personalized therapy and careful immunologic monitoring when immune-mediated diseases coexist with hematologic malignancy.

Conclusions

In this case, cladribine achieved sustained and concurrent control of both multiple sclerosis and hairy cell leukemia, allowing therapeutic simplification and long-term clinical stability.

Its convenient oral dosing schedule, limited to two short annual courses, and the low monitoring burden make cladribine a highly manageable option for patients who require durable efficacy without continuous immunosuppression.

1. Troussard X, Maître E, Paillassa J. Hairy cell leukemia 2024: Update on diagnosis, risk-stratification, and treatment-Annual updates in hematological malignancies. Am J Hematol. 2024 Apr;99(4):679-696
2. Sipe JC. Cladribine for multiple sclerosis: review and current status. Expert Rev Neurother. 2005;5(6):721–727
3. Giovannoni G, Mathews J. Cladribine Tablets for Relapsing-Remitting Multiple Sclerosis: A Clinician's Review.Neurol Ther. 2022 Jun;11(2):571-595
4. Giovannoni G, Boyko A, Correale, J, Edan G, Freedman M S, Montalban X, Rammohan K, Stefoski D, Yamout B, Leist T, Aydemir A, Borsi L, Verdun di Cantogno E. (2023). Long-term follow-up of patients with relapsing multiple sclerosis from the CLARITY/CLARITY Extension cohort of CLASSIC-MS: An ambispective study. Multiple sclerosis (Houndmills, Basingstoke, England), 29(6), 719–730
5. Hilbe W, Berger T, Konwalinka G, Thaler J. Cladribine treatment of a patient with hairy cell leukemia and concomitant multiple sclerosis. Acta Haematol. 1999;102(2):99-100
6. Buttari F, Dolcetti E, Rizzo FR, Rizzi C, Lauritano G, Borrelli A, Azzolini F, Fantozzi R,Assogna F, Conte A, Centonze D. Cladribine tablets in the new multiple sclerosis era. Ther Adv Neurol Disord. 2025 Jun 19;18:17562864251342855