



Case of T-cell Prolymphocytic Leukemia Successfully Treated with Fludarabine, Mitoxantrone and Cyclofosfamide



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Context

T-cell prolymphocytic leukemia (T-PLL) is an extremely rare mature T-cell neoplasm, associated with an aggressive clinical course, poor response to conventional chemotherapy and a dismal prognosis. Current therapeutic strategies conventionally employ anti-CD52 antibody alemtuzumab as the most active agent.

Alemtuzumab, originally marketed for use in cancer (Mabcampath®), is currently licensed and formulated for the treatment of relapsing multiple sclerosis (Lemtrada®), causing a lack of drug availability, with potential grave consequences on T-PLL patients' prognosis.

Design

We present the case of a 68-year old male patient, diagnosed with T-PLL in December 2020, who underwent four cycles of fludarabine 25 mg/m², mitoxantrone 8 mg/m² and cyclofosfamide 200 mg/m², and achieved complete remission (CR), according to the criteria established by the T-PLL International Study Group.

Case presentation

A 68-year old Caucasian male, with a medical history relevant for arterial hypertension, dyslipidemia, type 2 diabetes mellitus and benign prostatic hyperplasia, presented to our center with fatigue and weakness for several months and a history of persistent, progressive lymphocytosis for the past 18 months.

A computer tomography scan revealed bilateral cervical, axillary and intraabdominal lymph nodes measuring approximately 3 cm each, an enlarged spleen of 180 mm in length and mild hepatomegaly measuring 177 mm on midclavicular line. The patient also associated bilateral pleural effusion, mild pericarditis and moderately large ascitis.

Laboratory studies revealed leukocytosis (282 × 10⁹/L) and an absolute lymphocyte count of 255 × 10⁹/L, with no anemia or thrombocytopenia.

The metabolic profile was normal except for an elevated lactate dehydrogenase of 974 U/L. Coagulation tests showed decreased fibrinogen levels of 193 mg/dl and increased levels of D-dimers, 767 mcg/dL.

Peripheral blood smear revealed polymorphic, atypical mature lymphocytes and a few smudge cells. Blasts were not identified.

Hepatitis panel, HIV serology and human T lymphotropic virus (HTLV)-1 serology were negative, apart from a positive hepatitis B-core antibody.

A hepatitis B viral load was performed, and was negative.

The bone marrow aspirate showed 86-88% polymorphic lymphoid cells, while the flow cytometry analysis indicated T cells, positive for CD2, surface and cytoplasmic CD3, CD5, CD7, CD44, with heterogenous expression of CD99, 70% of them being CD4+CD8+, and 30% CD4+CD8-. The abnormal T-cell population did not express CD1a, nuclear TdT or CD56.

The core biopsy revealed a markedly hypercellular marrow (80%), with a lymphoid infiltrate made up of small/medium-sized cells, some with cerebriform nuclei, some with prominent nucleoli, with weakly positive immunohistochemistry staining for CD52, CD2+, CD3+, CD5+, CD7+, CD99+/-, TdT-, CD1a-, FOXP3-. Cytogenetics revealed no abnormalities.

Diagnostic and therapeutic thoracentesis was performed. The cytology revealed 90% lymphocytes with the same immunophenotype and the same CD4+CD8+ and CD4+CD8- populations ratio, which was consistent with the diagnosis of T-PLL.

Upon diagnosis, he underwent four cycles of fludarabine 25 mg/m², mitoxantrone 8 mg/m² and cyclofosfamide 200 mg/m², and achieved complete remission (CR), according to the criteria established by the T-PLL International Study Group (complete hematological recovery, circulating lymphocyte count <4 × 10⁹/L, T-PLL cells <5% of mononuclear cells in the marrow, regression of the long-axis lymph nodes diameters to <1 cm, spleen <13 cm in craniocaudal length, absence of constitutional symptoms and remission of any other specific site involvement, in this case polyserositis).

Conclusions

The patient presented in this case study was treated with conventional chemotherapy alone and achieved CR of T-PLL, maintaining the treatment response to date (3 months after completion of the therapy). Despite this, alemtuzumab remains a crucial element in the arsenal of treatment for T-PLL, and its lack of availability poses a serious challenge for clinicians.

References

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