# Leon's helmet

When we first saw Mr. Leon on the list of patients scheduled during our consultation, we were surprised by his age: 95 years old! The letter sent by his attending physician mentioned massive phlebitis in the left popliteal vein associated with hemoglobin (Hb) at 103 g/L, hyperleukocytosis 14x10$^9$/L with neutropenia at 0.42x10$^9$/L, and the presence of blast cells. The platelet rate was normal. We immediately thought of a form of myelodysplasia or leukemia.

We called Leon - which was his fictitious first name - and we invited him to come to our office. He was a smiling man, with a sharp look, of medium height, who walked alone with confidence and held a biker's helmet in his hand. From the outset, he asked us: why should he come urgently while he was in great shape? Worse, he would miss a ping-pong session in his club! Very surprised we asked him if he was accompanied by someone and to whom the helmet belonged. He explained that it belonged to himself and that he had arrived alone driving "his" moped which was parked in front of the building! We were incredulous, wanting to harmonize the reassuring image of the individual we had in front of us with his disturbing blood results we had in our hands. Before continuing, we asked for a new blood test, and then we continued to fill out his file. The man was a retired lathe miller, the father of a 60-year-old son, and a widower. He lived on his own in an apartment and he was perfectly autonomous i.e., he did his own shopping at the market and cooked for himself. Clinical examination was strictly normal except for a few small skin hematomas. Suddenly he started doing push-ups in front of us wanting to prove his athletic form to us, it was too much. A few minutes later, the laboratory communicated the following results: Hb 99 g/L, white blood cells (WBC) 15,01x10$^9$/L, absolute neutrophil count (ANC) 1,5x10$^9$/L, absolute lymphocyte count (ALC) 2.7x10$^9$/L, reticulocytes 62x10$^9$/L and a 72% rate of blast cells.; the cytogenetics test for *BCR ABL* was negative, and multiparametric flow cytometry of blast cells showed that 87% of the cells expressed CD34+/38+ markers. It was acute undifferentiated leukemia. A molecular biology test showed: *WT1* expression was positive with 6.96/100 copy; *EVI1* expression was negative; absence of *FLT3*-ITD and *NPM1* mutation. Given the context, a myelogram was not performed.

In the meantime, his son had arrived. We announced the "bad news" as well as the possibility, if he wished, to receive simple outpatient treatment. The patient agreed, although he hardly showed an upset look. This is how we started, a first series of azacitidine 75 mg/m$^2$/day, 7 days per month. Chemotherapy resulted in partial remission involving myelodysplasia for 18 months with acceptable toxicity. Two years later, faced with an increase in peripheral blasts cells, we then added all-trans retinoic acid (ATRA) 30 mg/m$^2$/day 10 days per month, for 6 months without noticeable effect, so we stopped it. Three years later, we administered for 6 months, six courses of idarubicin 20 mg/m$^2$/day by mouth (PO), 4 days per month, allowing a reduction in blasts cells at the cost of an increase in transfusion support. Four years later, while the patient showed a correct general condition with an Eastern Cooperative Oncology Group performance status equal to 0, we started treatment with lenalidomide as monotherapy 15 mg PO dispersible tablets (DT)/day for 14 days in a row per month. The answer was correct with Hb 110 g/L, WCB 12x10$^9$/L, platelets 154x10$^9$/L despite the persistence of an impressive peripheral blast rate of about 50%! On the positive side, the transfusion support had been discontinued. In July 2020: Hb 81 g/L, WCB 36x10$^9$/L, platelets 68x10$^9$/L and 95% circulating blasts. At first, we increased the dose of lenalidomide to 20 mg DT/day, to which the patient proved to be unresponsive. Moreover, non-COVID pneumonia is complicated. Five years after initial diagnosis, we started venetoclax monotherapy with 80 mg only three times a week (Monday/Wednesday/Friday). A blood test at day +40 show: Hb 95 g/L, WBC 1.06x10$^9$/L, platelets 87x10$^9$/L, ANC 0.4x10$^9$/L, ALC 0.6x10$^9$/L and 0% blasts! However, in March 2021, while the patient was on 80 mg DT/day, he was admitted to the emergency room with a neurological syndrome combining dizziness and hallucinations. The blood test showed Hb 118 g/L, WCB 1.87x10$^9$/L, ANC 1.38x10$^9$/L, ALC 0.42x10$^9$/L, platelets 73x10$^9$/L and 0% blasts. Tumor lysed syndrome (TLS) was not observed. Venetoclax administration was stopped. The electroencephalogram performed was almost normal. The patient was treated with risperidone, tiapride and rivaroxaban and light monitoring was decided.

Six years later, we commemorated his 100$^{th}$ anniversary in consultation. He was fine, but worried because of an age-related macular degeneration (ARMD) diagnosis... several months later, the blood count amounted to 5% of circulating blasts once more... and, we resumed venetoclax in small doses. Three months later, everything was fine, but he was hospitalized for COVID-related breathing difficulties even though he was vaccinated. He died on Christmas Eve.

Acute myeloid leukemia (AML) commonly affects the elderly, with a median age of 67 years at diagnosis. Elderly patients (≥ 65 years) with AML often respond poorly to induction chemotherapy and demonstrate increased resistance to treatment. Our patient does not fit into the

profile of the classic statistics of the different results published with the molecules used.[1-7] This explains the choice of dosage used during the 6 years of follow-up. A centenarian patient is therefore unique and must be the subject of special care. No treatment should be imposed. As we can see, even at a very advanced age, while respecting the quality of life, it is possible to treat by changing certain paradigms in the care of patients. The new treatments offer a wide range of care. Currently, we have three molecules: azatidine, lenalidomide and venetoclax[1,3,5-7] which are very interesting to use, in the era of molecular-targeted therapies, in particular venetoclax a BCL2 inhibitor[5-7] whose effectiveness is remarkable with very acceptable toxicity but which remains to be evaluated. Recently many papers show impressive results in older patients with the azatidine-venetoclax association.[7] The issue of treatment costs is an unresolved dilemma to date that may in some countries simply prohibit this type of therapeutic approach.

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**Contributions**

All authors wrote and approved the final version of the manuscript. AM-R, MS and MH takes responsibility for the DNA-RNA sequencing date and cytogenetics test. GG takes responsibility for cytology and flow cytometry date.

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