C4. MILIARY TUBERCULOSIS AND HAIRY CELL LEUKEMIA IN A PATIENT WITH CHRONIC MYELOID LEUKEMIA.

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The input of tyrosine - kinaze inhibitors (TKI) into the therapeutic arsenal of the chronic myeloid leukemia lead to a dramatic change of the natural course / prognostic of these diseases.

TKI produce both hematological (bone marrow suppression), immunological (immune suppression) and non hematological side effects that are distinct from one drug to another.

The immunosuppressive effects may be caused by imatinib, but are especially due to dasatinib. Treatment induced granulocytopenia and immunosuppression are accountable for several infections, including for miliary tuberculosis.

The development of a myeloproliferative and a lymphoproliferative disorder in the same patient is uncommon. The association between chronic myeloid leukemia (CML) and hairy cell leukemia (HCL) is extremely infrequent. The undercause of this adjunction is not known. The concurrent or sequential association between CML and HCL raises various question marks about their joint pathogenesis: the cytoreductive drug's part, the involvement of a common stem cell with bi-lineage manifestations or merely a chance coincidence of the two.

We are going to portray the clinical case of a 51 years old man that has been diagnosed with chronic myeloid leukemia in 2005. From 2005 until 2012 the patient underwent treatment with Glivec, 400 mg/day and presented a sustained major molecular response.

The treatment with Glivec was interrupted in January 2012 and was substituted with Dasatinib due to sepsis caused by Candida glabrata and coagulase postitive staphylococcus; the antibiotics and antipyretics were inefficient and we were in the presence of a newly installed hepatosplenomegaly with jaundice. The lab works revealed pancytopenia, hepatocytolisis, cholestasis and altered coagulation tests, meaning a disseminated intravascular coagulation (DIC). The computer scan revealed micronodular lesions in the lungs, liver and spleen. We had negative blood cultures.

We arose the suspicion of a disseminated tuberculosis and we begun a trial treatment with antitubercular agents that had as a result the resolution of all clinical symptoms, the regression of the hepatosplenomegaly and the progressive normalization of the bioumoral markers. Subsequently the diagnosis is confirmed by sputum culture.

The treatment with Glivec 400 mg/day is reintroduced and after two months of treatment a progressive splenomegaly emerges accompanied by pancytopenia with lymphocytosis, presenting atypical lymphocytes with cytoplasmatic projections on the blood smear. The diagnosis of hairy cell leukemia is set by marrow biopsy, flowcytometry and molecular analysis of the BRAF mutation. The joint treatment with Glivec and α interferon is followed by the remission of the HCL and the persistence of the major molecular response of the CML.

We argue the part played by the immunosupression caused by TKI, possibly an underclinical expression of HCL, in the manifestation of a miliary tuberculosis, the significance of the CML-HCL association and the optimal treatment course of these morbid couplings.