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LETTER TO THE EDITOR

Hodgkin lymphoma in a sickle cell anaemia child treated with hydroxyurea

L. Couronné · P. Schneider · M. de Montalembert · C. Dumesnil · A. Lahary · J. P. Vannier

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Dear Editor,
Hydroxyurea (HU) is a chemotherapeutic agent used in adults and children severely affected with sickle cell anaemia (SCA). Current indications are: recurrent painful crises, more than two acute chest syndromes, early chronic organ damage (respiratory, renal, hepatic, myocardial insufficiencies), association with an auto-immune disease or Hb level below 6 g/dL [4, 5].

HU is the only drug that has been proven to modify the disease at short- or middle-term with an acceptable short-term toxicity [1]. However, few data are available about the potential risk of carcinogenesis. We report the case of a Hodgkin lymphoma that occurred after 4 years of HU therapy.

Our patient was diagnosed at the age of 12 months as compound heterozygote for HbS and β^0-thalassaemia. When he was 13 years old, he presented pulmonary arterial hypertension leading to prescribe nocturnal oxygen therapy. At the same time, our patient developed severe anaemia (6.0 g/dL Hb), thrombocytosis (706.10^9/L platelets) and hyperleukocytosis (28.10^9/L white blood cells).

At the age of 14 years and given the cardiovascular and haematological consequences of the disease, HU therapy was started at an initial dose of 17 mg/kg daily. Six months after the initiation of HU, all the haematological parameters improved, and 1 year later, pulmonary pressure decreased allowing a reduction of oxygen therapy.

Four years after the initiation of HU treatment, our patient presented a Hodgkin lymphoma stage IIAa. He was enrolled in MDH 03 protocol (running French protocol) and received so far four courses of vinblastine, bleomycin, etoposide and prednisone (VBVP). He is currently in complete remission and a 20-Gy involved fields radiotherapy is planned.

Only few reports of malignancies appeared during HU therapy have been published. Among 225 children with SCA, one case of acute lymphoblastic leukaemia occurred in a girl treated for 1.5 months with hydroxyurea [6]. Moschovi et al. reported a SCA boy who developed Hodgkin lymphoma 6 months after HU treatment [7]. Three other single reports described haematological cases (acute myeloblastic leukaemia) occurring after 6 years [9] and, in two cases, 8 years of therapy [2]. In Schultz' study, three SCA patients with cancer had been exposed to HU including a 14-year-old boy with acute lymphoblastic leukaemia diagnosed 3 months after initiating therapy, a 39-year-old man with fatal testicular seminoma and a 47-year-old woman with two types of breast cancer and malignant histiocytosis [8]. With the present report, nine malignancies have been so far reported.

In vitro, DNA damage cannot be fully repaired in the presence of HU, leading to the accumulation of somatic mutations and chromosomal damages. In contrast, using a VDJ assay, no study shows a significant increased number of VDJ mutations in SCA children with long HU exposure [3, 10].

It is impossible to affirm a causative association between HU and cancers, but it is important to record all the cases. The indications for HU treatment must remain cautious.

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The safety of long-term administration, particularly with respect to leukaemogenesis, should now be evaluated in a long-term follow-up of cohorts of children.

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