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Biological Evolution in a Homozygous Adult with Sickle Cell Disease on Hydroxyurea: A Case Report

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Abstract **Case Report**

Sickle cell disease is an autosomal recessive genetic disorder and one of the most common haemoglobinopathies in Morocco. It is characterised by the polymerisation of haemoglobin S, resulting in a change in the spatial conformation of sickle cell haemoglobin, and consequently in its function. Hydroxyurea is the only product with proven efficacy in preventing the complications of sickle cell anaemia and has been approved by the "Food and Drug Administration". The effects of hydroxyurea are essentially linked to the increase in HbF by inhibiting the polymerisation of haemoglobin S, which is the pathophysiological basis of sickle cell disease. It reduces the frequency of painful attacks in most patients, acute chest syndromes and transfusion requirements in sickle cell patients with a severe form of the disease and prolongs their life expectancy. This was a 40-year-old male patient from a marriage in which the diagnosis of homozygous sickle cell anaemia SS was made following an electrophoresis that showed no trace of foetal haemoglobin, and the patient was put on antibiotics and folic acid without transfusion. The patient was subsequently started on hydroxyurea, 1 x 500 mg tablet twice daily. After 14 years on hydroxyurea, he had no vasoocclusive attacks or acute chest syndrome, and his haemoglobin electrophoresis was as follows: hbF: 42.5% hbS: 54.3% and hbA2: 3.2%. Haemoglobin electrophoresis is a major biochemical examination for monitoring the evolution of haemoglobin S and haemoglobin F fractions in our patient treated with hydroxyurea, a molecule that occupies a privileged place in the management of severe forms of sickle cell disease and gives the best results in the prevention of vaso-occlusive crises and acute thoracic syndromes.

Keywords: Sickle cell disease- Hydroxyurea- haemoglobin S- Haemoglobin electrophoresis.

1. INTRODUCTION

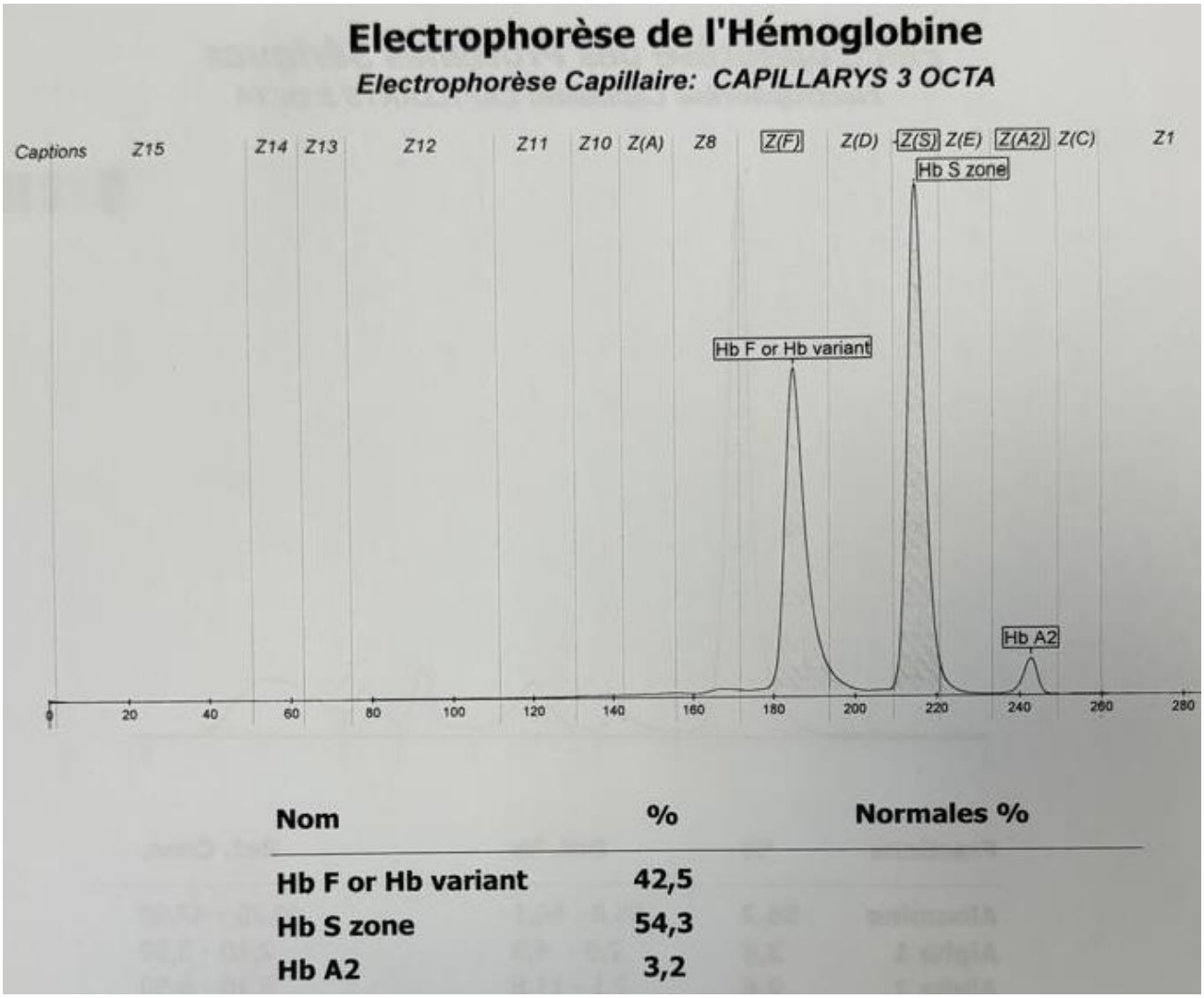
Sickle cell disease is an autosomal recessive genetic disorder, and is one of the most common haemoglobinopathies in Morocco, characterised by polymerisation of haemoglobin S leading to a change in the spatial conformation of sickle cell haemoglobin and consequently its function, and characterised by great variability in clinical and biological expression depending on modulating genetic and environmental factors. l´hydroxyurée est le seul produit dont l´efficacité a été prouvée pour prévenir les complications de la drépanocytose et approuvé par la « *Food and Drug Administration* ». Les effets de l'hydroxyurée sont essentiellement liés à l'augmentation de l'HbF par l'inhibition de la polymérisation de l'hémoglobine S qui constitue la base physiopathologique de la drépanocytose et permet de diminuer la fréquence des crises douloureuses chez la plupart des patients, des syndromes thoraciques aigus et des besoins transfusionnels chez les patients drépanocytaires atteints d'une forme sévère et allonge leur espérance de vie [1-5].

The aim of this study is to describe the evolution of sickle cell disease under hydroxyurea treatment and the value of haemoglobin electrophoresis in therapeutic monitoring in an adult Moroccan patient at the Avicenne military hospital in Marrakech.

2. CASE REPORT

The patient was male, aged 40, the product of a consanguineous marriage and the father of three children. The history of the disease began at the age of 26, when he first came to the clinic with fever associated with jaundice, The diagnosis of homozygous sickle cell anaemia SS was made following electrophoresis, which showed no trace of foetal haemoglobin. The patient was put on antibiotics and folic acid without transfusion.

The patient was subsequently put on hydroxyurea at a dose of 1 x 500 mg tablet twice daily. After 14 years on hydroxyurea, he had no vasoocclusive attacks or acute chest syndrome, and his haemoglobin electrophoresis was as follows: hbF: 42.5% hbS: 54.3% and hbA2: 3.2%.



3. DISCUSSION

Hydroxyurea is an antimetabolite that inhibits DNA synthesis. Its beneficial effect is usually accompanied by an increase in HbF, which has a mitigating effect on the severity of sickle cell disease [6]. Hydroxyurea appears to be the best tolerated molecule for reactivating HbF synthesis [7]. Indeed, we noted a 42.5% increase in HbF in our patient on hydroxyurea. This effect appears to be frequent and stable over time [8]. This is in line with the results of several studies around the world, such as that of F. Mellouli *et al*., carried out in Tunisia in 2007, which reported a significant increase in foetal haemoglobin of between 3% and 30% after using hydroxyurea for 6 years and 9 months [9].

Prevention of vaso-occlusive crises is the main indication for hydroxyurea in severe forms of sickle cell disease [10]. Its beneficial effect varies from 73% [6] to over 90% of cases [12]. Our patient was a good responder thanks to good compliance with treatment and did not present any vasoocclusive crisis.

Prevention of recurrence of acute chest syndrome is the second classic indication for hydroxyurea in sickle cell disease. It significantly reduces the number of ATS events [11,12] and improves patients' longevity and quality of life [13, 14]; our patient did not suffer any acute chest syndrome events.

The most frequently reported adverse events were moderate neutropenia and thrombocytopenia, which resolved with a reduction in dose. There is one published case of persistent pancytopenia [15] and one of opportunistic infection [16]. Our patient had anaemia of 9.8 g/dl and thrombocytopenia of 67,000/ul.

The mutagenic and carcinogenic risks initially feared appear to be extremely low. A 2007 publication reported 2 cases of oligo/azoospermia which were not

reversible on discontinuation of treatment [17]. These uncertainties lead us to believe that hydroxyurea should for the time being be reserved for the most symptomatic forms of the disease. Our patient was on hydroxyurea for 9 years and had three children during this period.

IV. CONCLUSION

Haemoglobin electrophoresis is a major biochemical examination for monitoring the evolution of haemoglobin S and haemoglobin F fractions in our patient treated with hydroxyurea, a molecule that occupies a privileged place in the management of severe forms of sickle cell disease and gives the best results in the prevention of vaso-occlusive crises and acute thoracic syndromes.

REFERENCES

1. Dahmani, F., Benkirane, S., Kouzih, J., Woumki, A., Mamad, H., & Masrar, A. (2016). Etude de l'hémogramme dans la drépanocytose homozygote: à propos de 87 patients. *The Pan African Medical Journal*, *25*.
2. Mukinayi, B. M., Cibeyibeyi, G. K., Tumba, G. D., & Gulbis, B. (2021). Drépanocytose en République Démocratique du Congo: quels sont les obstacles à un traitement par hydroxyurée?. *Pan African Medical Journal*, *38*(1).
3. (RAKOTOSON, Marie Georgine. *Déterminants de la réponse à l'Hydroxyurée au cours du traitement de la drépanocytose*. 2016. Thèse de doctorat. Paris Est.)
4. Charache, S., Terrin, M. L., Moore, R. D., Dover, G. J., Barton, F. B., Eckert, S. V., ... & Investigators of the Multicenter Study of Hydroxyurea in Sickle Cell Anemia. (1995). Effect of hydroxyurea on the frequency of painful crises in sickle cell anemia. *New England Journal of Medicine*, *332*(20), 1317-1322.
5. Steinberg, M. H., Barton, F., Castro, O., Pegelow, C. H., Ballas, S. K., Kutlar, A., ... & Terrin, M. (2003). Effect of hydroxyurea on mortality and morbidity in adult sickle cell anemia: risks and benefits up to 9 years of treatment. *Jama*, *289*(13), 1645-1651.
6. Ferster, A., Vermylen, C., Cornu, G., Buyse, M., Corazza, F., Devalck, C., ... & Sariban, E. (1996). Hydroxyurea for treatment of severe sickle cell anemia: a pediatric clinical trial. *Blood*, *88*(6), 1960-1964.
7. Montalembert, M. D., & Tshilolo, L. (2007). Les progrès thérapeutiques dans la prise en charge de la drépanocytose sont-ils applicables en Afrique subsaharienne?. *Médecine tropicale*, *67*(6), 612-616.
8. Zimmerman, S. A., Schultz, W. H., Davis, J. S., Pickens, C. V., Mortier, N. A., Howard, T. A., & Ware, R. E. (2004). Sustained long-term hematologic efficacy of hydroxyurea at maximum tolerated dose in children with sickle cell disease. *Blood*, *103*(6), 2039-2045.
9. Mellouli, F., & Bejaoui, M. (2008). L'utilisation de l'hydroxyurée dans les formes séveres de la drépanocytose: étude de 47 cas pédiatriques tunisiens. *Archives de pédiatrie*, *15*(1), 24-28.
10. Amrolia, P. J., Almeida, A., Davies, S. C., & Roberts, I. A. (2003). Therapeutic challenges in childhood sickle cell disease Part 2: a problem-orientated approach. *British Journal of Haematology*, *120*(5), 737-743.
11. Olivieri, N. F., & Vichinsky, E. P. (1998). Hydroxyurea in children with sickle cell disease: impact on splenic function and compliance with therapy. *Journal of pediatric hematology/oncology*, *20*(1), 26-31.
12. Hankins, J. S., Ware, R. E., Rogers, Z. R., Wynn, L. W., Lane, P. A., Scott, J. P., & Wang, W. C. (2005). Long-term hydroxyurea therapy for infants with sickle cell anemia: the HUSOFT extension study. *Blood*, *106*(7), 2269-2275.
13. Weiner, D. L., & Brugnara, C. (2003). Hydroxyurea and sickle cell disease: a chance for every patient. *Jama*, *289*(13), 1692-1694.
14. Steinberg, M. H., Barton, F., Castro, O., Pegelow, C. H., Ballas, S. K., Kutlar, A., ... & Terrin, M. (2003). Effect of hydroxyurea on mortality and morbidity in adult sickle cell anemia: risks and benefits up to 9 years of treatment. *Jama*, *289*(13), 1645-1651.
15. Vichinsky, E. P., & Lubin, B. H. (1994). A cautionary note regarding hydroxyurea in sickle cell disease. *Blood*, *83*(4), 1124-1128.
16. Venigalla, P., Motwani, B., Nallari, A., Allen, S., Agarwal, M., Alva, M., ... & Feldman, L. (2002). A patient on hydroxyurea for sickle cell disease who developed an opportunistic infection. *Blood, The Journal of the American Society of Hematology*, *100*(1), 363-364.
17. Grigg, A. (2007). Effect of hydroxyurea on sperm count, motility and morphology in adult men with sickle cell or myeloproliferative disease. *Internal Medicine Journal*, *37*(3), 190-192.