

CORRESPONDENCE

Congenital and Acquired Polycythemias

by Fabian P. Siegel, Prof. Dr. med. Petro E. Petrides in volume 4/2008

Radioactive Phosphorus in Polycythemia Vera Therapy

The article provides a useful overview of diagnosis and therapy of polycythemia rubra vera, among others. However, no mention was made of the therapeutic option of radioactive phosphorus-32. Although this nuclear medical treatment has not been administered to a great extent, it is well tolerated by patients if the indication is defined accordingly. Moreover, it is uncomplicated to administer. I am interested to find out why this therapeutic option was left out from the review article (1, 2).

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Key Role of HIF-2 α

This excellent review article follows on seamlessly from August 2007's "Essential Thrombocythemia." It remains to be seen whether the two other chronic myeloproliferative disorders – chronic myeloid leukemia and myelofibrosis – will also be reviewed so comprehensively.

In figure 2, the authors illustrate the cycle of erythropoiesis via erythropoietin and the central role of HIF-2 α in cellular oxygen sensing. Further to the mutations described by the authors, a mutation of the HIF-2A gene (G1909T) (1) and of the prolyl hydroxylase domain-containing protein 2 (PHD2) in other familial erythrocytoses has been described (2). This is particularly notable because initial clinical studies have started and have been published on the basis of our understanding of the regulation of erythropoietin production. Oral medications are used to inhibit PHD2 and treat anemias. In light of the current discussion about erythropoiesis stimulating factors, molecular insights into the key role of HIF-2 α will enable the deduction of new strategies to stimulate erythropoiesis and therefore potentially new treatment options for anemia (3).

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Testosterone Induced Polycythemias

This excellent review article omitted mentioning polycythemia due to testosterone, which is unfortunately gaining increasing importance. The article mentions the erythropoietic effects of doping with anabolic steroids and the resultant polycythemia, but the authors forgot that testosterone therapy in the treatment of hypogonadism can also lead to polycythemia. This affects mainly elderly men who are being treated for late onset hypogonadism (LOH) and overweight men with hypogonadism. Not only the dosage of testosterone, but also individual pharmacogenetics – due to an androgen receptor polymorphism – have a role in this context (1, 2).

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In Reply:

The use of radioactive isotopes to treat polycythemia vera as described by Schmidt in his letter was first described in 1940. Although they were easy to handle and effective, scientific discussion since has focused on the leukemogenic effect of phosphorus-32 (1). In the first two decades after phosphorus-32 had been introduced, no other therapeutic options existed: hence an increased risk of developing leukemia at a later stage was accepted in return for acute protection from potentially fatal thromboembolic complications. The thinking on this matter has changed since effective substances – such as hydroxyurea, interferon alpha, or anagrelide – have become available for cytoreduction and thus prevention of thromboembolic complications. Since in treating patients with polycythemia vera, the golden rule is "primum nil nocere," we

recommend phosphorus-32 because of the increased leukemia risk only in exceptions, i.e., in patients older than 70 or in patients whose long-term medication cannot be well controlled (2).

Tsamaloukas mentioned new developments in anemia treatment that utilize novel insights into the molecular basis of the regulation of renal erythropoiesis; these are indeed fascinating. Discussing these would have exceeded the scope of our review. However, his wish for a current German language review article of primary myelofibrosis can be fulfilled (3). We thank Nieschlag for mentioning the special scenario of testosterone induced polycythemia in elderly men. The fact that androgens can increase erythropoiesis has been known for a long time (4). The conclusion from these observations is that the blood of patients receiving testosterone substitution should be monitored regularly. However, what is not known is whether androgen induced erythrocytosis is also associated with an increased risk of thromboembolic complications.

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Conflict of interest statement

The authors of all letters and the reply declare that no conflict of interest exists according to the guidelines of the International Committee of Medical Journal Editors.