COMMENT & CRITIQUE

Depression and beta-thalassemia: a genetic link?

To the Editor:

Beta-thalassemia is one of the most prevalent monogenic illnesses in the world. It is caused by mutations in the beta chain of the hemoglobin molecule. Genetic studies suggest an important genetic factor in the etiology of depressive disorders. Several candidate genes, most notably the gene situated on chromosome 11, proximal to the genes involved in beta-thalassemia, are potentially involved in the development of depressive disorders in predisposed individuals (1). In reporting a case in which recurrent depression and thalassemia minor (heterozygous beta-thalassemia) occurred simultaneously in several members of a family, one can suggest the existence of a genetic link between these two disorders. The patient gave her consent for this report to be published.

Ms A, a 38-year-old Caucasian woman, native from Belgium, had an 8-year history of recurrent major depressive disorder without psychotic symptoms (DSM-IV). She was hospitalized three times for depressive episodes. The patient had a family history of recurrent major depression involving two generations (father and two paternal uncles). A mild anemia was diagnosed during her first hospitalization at the age of 30 as thalassemia minor following DNA analysis. The four family members (including the patient) and her son aged 15 had thalassemia minor. They all fulfilled the Research Diagnosis Criteria for recurrent major depression except her son who was in good mental health. Other family members had no psychiatric or somatic diseases.

Depression in Ms A is unlikely to be attributable to psychosocial consequences of thalassemia minor as the disease had little clinical effect on her and other members of her family.

Depression is the most frequent psychiatric disorder in the community, and its lifetime prevalence in men and women is 13 and 21%, respectively (2). Several linkage studies suggest that genetic components may contribute to the development of depressive disorders (1). However, the identification of these genetic factors encounters several obstacles: the complex interactions between physiological, psychological and environmental elements; the clinical heterogeneity of depressive disorders; and the presence of phenocopies (3).

Several studies reveal, however, that by the sequencing of chromosome 11, a possible genetic susceptibility for depression can be located on the short arm of this chromosome near the gene involved in beta-thalassemia (11p15). In fact, one of the human tryptophan hydroxylase genes (TPH1), the rate-limiting enzyme in serotonin biosynthesis, is implicated in depressive disorders and can be found on the short arm of chromosome 11 (11p14-p15.3) (4).

No study has yet been done to examine the prevalence of beta-thalassemia in patients with depressive disorders, but an estimate based on the prevalence of each disorder (13–21% depression and <1% beta-thalassemia northern European populations) suggests that the possibility of observing both disorders in multiple individuals in two families is rare, thus providing tentative support for a possible genetic link between the two disorders.

A review of literature revealed no reports of possible genetic relationship between thalassemia minor and depressive disorders. To our knowledge, our case study is the first report that discusses a possible association between these two disorders.

In conclusion, genetic studies have described the existence of a genetic susceptibility factor for depressive disorders on the short arm of chromosome 11, near to the gene involved in beta-thalassemia. We have described a case report so as to highlight a possible genetic link between these two pathologies. A known genetic disease (beta-thalassemia) can help to confirm the presence, on the short arm of chromosome 11, of a genetic susceptibility factor for depression. Linkage studies should be performed in families with a strong association of both diseases in order to improve our understanding of the physiopathology of depressive disorders, along with possible therapeutic implications.

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Acta Neuropsychiatrica 2007: 19:134

DOI: 10.1111/j.1601-5215.2006.00180.x

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