TWO CASES OF HEMOCHROMATOSIS ASSOCIATED WITH SEVERE DEPRESSIVE EPISODES
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ABSTRACT

Hemochromatosis is a severe autosomal recessive disorder caused by iron overload and primarily affects liver function, pancreas or heart. Although hypophysis iron deposits may also be involved, the association between psychiatric disease and hemochromatosis is less common. We present two patients, a female aged 76, and a male aged 49, in whom depression in combination with increased ferritin levels and transferrin saturation lead to the diagnosis of hemochromatosis. In both cases interdisciplinary treatment with antidepressants, psychotherapy and phlebotomy was successful. Although, the exact pathophysiology of this association between hemochromatosis and depression remains to be elucidated, physicians should be aware of this co-morbidity.

Key words: Hemochromatosis, ferritin level, transferrin saturation, depression, association, case report

INTRODUCTION

Hemochromatosis is a disorder of iron metabolism which is characterized by increased intestinal absorption of iron. As a consequence total body iron may supersede normal values of 6 to 8 g 10 times¹. Due to this overload iron may deposit in organs such as liver, heart, pancreas, glands, skin or brain. Severe complications are liver cirrhosis, arrhythmia, lethargy, diabetes or hypogonadism. Recently, Parkinson’s disease and Alzheimer’s disease were reported be associated with iron overload ²-³. Hemochromatosis is – in most cases - an autosomal recessive disease more common in men, the HFE gene (hereditary hemochromatosis protein) being responsible in 90 % of the cases. In general, 30 % of homocygote men develop clinical symptoms ⁴. Apart from clinical signs and laboratory (elevation of ferritin or transferrin saturation, hepatic iron load) genetic investigations should nowadays be done ⁵-⁶. Therapeutically, drugs such as desferoxamine or proton pump inhibitors may be helpful but longterm phlebotomy or erythrophoresis may be unavoidable ⁷-⁸.
The association between iron overload and mood disorders is by far less established compared to associations such as liver cirrhosis or arrhythmia on the one side and depression on the other side. Recently, Serata et al. reported a case of bipolar disorder which subsided completely after repeated phlebotomy. The subsequent case reports show that hematocromatosis and depressive disorders may be associated and discusses clinical implications.

**CASE REPORT**

**Case 1**

A 76-year old female slim patient (BMI 20 kg/m2) was referred to the department of psychiatry due to a depressive episode. Several repeated episodes had been recorded for years so that recurrent depressive disorder (ICD 10 F33.1) was ascertained. Moreover social factors such as a severe disease of her husband and the disability of her grandson deteriorated the depressive syndrome. Apart from depression she suffered from a mild cognitive impairment (ICD 10 F06.7), a slight lack of folic acid (ICD 10 E33.8) and arterial hypertension (ICD 10 I10.00). She presented with a depressive syndrome having a depressed mood and worries, psychomotoric retardation, anhedonia, anxiety, loss of appetite as well as suicidal ideation. She was integrated in a standard multifunctional program on the wards. The already initialised administration of venlafaxine (up to 150 mg sid) was continued and lorazepam (up to 0.5 mg tid) was added temporarily. After 4 weeks time the treatment was changed due to sufficient response (nortriptyline (50 mg bid) and mirtazapine was started (30 mg hs) to further sleep. She went quite well but negative thoughts and worries did not halt. After additional prescription of olanzapine (2.5 mg bid) she recovered almost completely and was discharged in mentally good condition after 7 weeks.

The physical examination on admission revealed severe perlèche and showed increased iron (29.5 SI) concentrations and transferrin saturation (56.09 SI). The presumed diagnosis of hemochromatosis could be confirmed genetically (C289Y allel, homocygote) and phlebotomy was started in cooperation with the department of internal medicine. Fortunately, no clinically relevant organic affections could be detected. When she left the department she was in good health and subsequent out-patient dates were arranged with the department of internal medicine for continuous phlebotomy.

**Case 2**

A 49-year old strenuous stout man of business (BMI 26 kg/m2) was referred the department of psychiatry due to increasing depressive mood and impaired sleep for months. He had continuously to deal with complex situations in his enterprise and complained of progressive lack of resilience. Leading psychopathology was a depressed and instable mood, withdrawal from contacts, loss of interests and rumination (ICD 10 F32.1). He also reported occasional alcohol intake. Mirtazapine (15 to 30 mg hs) was administered and soon sleep quality improved. Mood and anhedonia improved with a latency of a few weeks.
Due to suspicious iron metabolism values (increased ferritin and transferring saturation) the patient had been referred to the department of internal medicine during his stay in the psychiatric clinic. Liver sonography confirmed the steatosis with slight fibrosis and moreover, hemochromatosis was ascertained genetically (compound heterocgyote alleles C282Y / H83D). The patient was informed about the syndrome and regular phlebotomy was initiated. After discharge from the psychiatric ward, the patient was referred to an out-patient clinic for psychotherapy as had difficulties to cope with the work-related offences and the diagnosis of hemochromatosis.

DISCUSSION

The two cases impressively demonstrate the clinical association between hemochromatosis and depressive episode. Although we diagnosed a depressive episode in both patients, we are aware of the fact that organic components (ICD 10 F 06.3) or even adjustment disorder (ICD 10 F43.2) with regard to hemochromatosis may contribute to the combined syndrome. So far, the exact mechanism is not known, and several metabolic sequelae of hemochromatosis may – apart from the psychological aspects – be a link between iron metabolism and depression. First, liver impairment itself similar to Wilson’s disease may affect the brain 12. Moreover, indirect mechanisms such as inflammatory reactivity or endocrinological disorders (gonads, hypophysis, thyroid gland) may affect fronto-temporal areas and neurotransmitter release 13. We should keep in mind that hypercortisolemia is discussed a trigger factor of depression. Mitochondrial function, possibly involved in Alzheimer’s disease, may play a possible role in the aetiology of hemochromatosis associated depression 14.

In conclusion, two clinical case reports impressively demonstrate the association of hemochromatosis and depression. Therefore, physicians should be aware of this comorbidity. In case of steatosis or pathological liver tests and depression it is wise to consider screening tests for hemochromatosis. Further research is needed to elucidate the underlying pathophysiological mechanism.

REFERENCES


