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Hypercoagulability State in Celiac Disease and Hepatitis C Association

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Abstract A concerning pathological and serological aspect that is found in both HCV and celiac disease is the hypercoagulability state which can lead to various complications.

Keywords: *celiac disease, hepatitis C, hypercoagulability state*

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1. Introduction

Is there any connection between celiac disease and hepatitis C? [1]. Celiac disease (CD) is characterized by heterogeneous clinical manifestations of variable severity that can occurat any age [2]. It is worth paying attention to one warning sign that occurs in advanced cases of CD and liver complications in HCV patients, namely the hypercoagulant state.

2. Hipercoagulabity State in CD Patients

In CD patients, the pathogenesis of hypercoagulant state is the result of various interplay between genetic factors (methylenetetrahydrofolate reductase mutations), autoimmunity (thrombophilic autoantibodies), haematological factors (abnormality of platelets and endothelial dysfunction) and vitamin deficiencies (folate, vitamin B12 or vitamin K) [3]. It is well known that vitamin K is necessary for the carboxylation of coagulation factors (II, VII, IX, X), anticoagulation factors (protein C and S), but also for the carboxylation of extrahepatic vitamin K dependent proteins, such as osteocalcin in bone [4], growth arrest specific protein 6 (Gas6) [5] and matrix Gla protein (Mgp) in arterial wall [6,7]. In a case report was noticed that low vitamin K supplies, due to malabsorption or poorly dietary intake of vitamin K, were assigned to a defectively controlled CD [8]. Furthermore, Berthoux et al have identified risk factors for thrombosis, such as deficiency of protein C and S due to vitamin K insufficiency, which could be associated to CD [9].

3. Hipercoagulabity State in HCV Patients

On the contrary,in HCV patients with liver fibrosis, there is an apparent paradox: a manifest decline in procoagulant factorsactivity leading to prolonged common coagulation tests [10,11] coexist with theevidence of hypercoagulabilitycaused by an impaired synthesis of anticoagulant factors, such as protein C and antithrombin III [12,13]. Moreover, it has been assessed that in patients with progressive HCV liver disease the promotion of thrombin formation will lead to the activation of hepatic stellate cells therefore via PAR-1 cleavage, promoting liver fibrosis [14,15]. Other findings strengthen the link between liver fibrosis in HCV patients, activated protein C resistance and acquired protein C deficiency [16,17], these patients being prone to thrombotic events.A study on 3686 patients with newly diagnosed HCV compared the incidence ofvenous thromboembolism in the HCV group and a 14,744 healthy control group, the risk of venous thromboembolism was significantly higher in the HCV group than in the control group [18]. Following the idea of assessing the carboxylating status, the most sensitive marker for vitamin K deficiency is the prothrombin induced by vitamin K absence-II (PIVKA-II), which is a functional marker of coagulation [19]. Kamel et al have found elevated PIVKA-II serum levels in patients with hepatocellular carcinoma, the most significant complication of viral hepatitis, concluding that PIVKA-II could be a sensitive and specific marker for its early detection [20].

4. Conclusion

Accordingly, to ascertain whether hypercoagulant state is actually (and to what extent) established in CD or HCV patients with liver complications, laboratory analyses should go beyond the common coagulation tests. In this regard, vitamin K deficiency has to be assessed by using non-invasive serum markers, e.g. PIVKA-II for liver, different carboxylated / uncarboxylated conformations of osteocalcin for bones and Mgp for vasculature.

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