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Letter to the Editor

More on the relationship between cystic fibrosis and venous thrombosis

To the Editor:
We have read the interesting letter by Sipahi *et al.* (1) entitled "Cerebral infarct associated with prothrombin gene G 20210 A variant in a Turkish child with cystic fibrosis: an unusual coexistence". We would like to add our personal experience and a comment on this matter.

FE was an Italian female born in 1962 in whom cystic fibrosis was diagnosed during the first year of life. Chronic pulmonary involvement was present, as was pancreatic insufficiency, which was treated with pancreatic enzyme supplement.

At the age of 15 the patient became chronically colonized by *Pseudomonas aeuriginosa*, and the age of 23 by *Burkholderia cepacia*. She developed a pro-gressive impaired pulmonary function with extensive bronchiectasis. Chronic pulmonary infections raised important problems concerning antibiotic treatment. This led to the insertion of a central line in the right atrium via jugular and superior cava vein in September 1997 when she was 35. One month later painful swelling of the right shoulder was diagnosed as thrombosis of the right succlavia, of the right internal jugular and of the superior cava veins. The patient received continuous i.v. infusion of sodium heparin for 5 consecutive days and an oral anticoagulant (Coumadin) was started simultaneously. INR was maintained between 2 and 3. The patient died 16 months later of respiratory failure.

Before starting anticoagulant treatment the patient was referred to our centre for hemorrhagic and thrombotic diseases in order to asses the prothrombotic risk. Protein C biological activity was 66% (n.v. 64–128), Protein C antigen 70% (n.v. 67–100), Protein S free 55% (n.v. 59–163) and Protein S total 70% (n.v. 59–160), Antithrombin III was 120% (n.v. 80–140). Factor V G1691A and methylenetetrahydrofolate reductase (MTHFR) C677T gene point mutations were absent, while Factor II G20210A gene mutation was present in the heterozygous state.

In our opinion the coexistence of cystic fibrosis and Factor II gene mutation is due to the relatively high incidence of this mutation in the normal population (2%). In adults the relationship between inherited thrombotic conditions and acquired risk factors such as pregnancy, puerperium, surgery, oral contraceptives, etc. in venous thrombosis is well known. There are other acquired thrombotic risk factors which are peculiar mainly to children and young adults. In an international retrospective study on thrombosis in children carried out by the European Society of Pediatric Hematology and Immunology (ESPHI), the incidence of inherited prothrombotic risk in patients with venous thrombosis was 27.4%. In 80% of these cases an acquired risk was also present, made up of an underlying disease (congenital heart defects, oncologic or renal diseases, prematurity, etc.) and a trigger event (infection or CVL).

Cystic fibrosis is a very peculiar disease, since an acquired prothrombotic condition is often present because of low levels of Protein C and Protein S due to poor vitamin K absorption, and to some degree of liver failure. In addition, the presence of an inherited prothrombotic risk along with chronic and/or acute inflammatory episodes and CVL tremendously increase the possibility of a venous thrombotic event.

From a practical point of view, patients with chronic diseases complicated by several inflammatory episodes who require CVL should be examined for congenital prothrombotic risk. In the case of positivity, low molecular weight heparin should be administered, since maintaining INR within the normal range is difficult given the interference of some antibiotics with oral anticoagulants.

Reference

1. Sipahi T, Duru F, Çiftçi E, Şahin F, Akar N. Cerebral infarct associated with prothrombin gene G20210 A variant in a Turkish child with cystic fibrosis: an unusual coexistence. Eur J Haematol 1999;**62**:281–283.

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