

INFLUENCE OF ETHINILESTRADIOL ON C1S INHIBITOR: A NEW ETIOPATHOGENETIC MECHANISM OF ANGIOEDEMA. CASE REPORT

L. Bettoni MD (1)

The deficiency of the inhibitor of the first complementary component (C1s-inh) is an important cause of angioedema. Two types of deficiency have been described: hereditary (deficiency of quantity or quality) and acquired (associated to lymphoproliferative diseases or to antibodies anti C1s-inh).

The more frequent causes of angioedema are not associated to deficiency of C1s-inh: immunologic or extra-immunologic pathogenetic mechanisms are recognized. Drugs (penicillins, oral contraceptives, AINS and others), foods (milk, eggs) and hymenoptera venom are the major etiologic agents of angioedema (1).

The case of our patient shows the action of estrogens on the levels of C1s-inh and, in accord to other studies (2-3), can represent a new etiopathogenetic mechanism of angioedema.

O.P. is a young barman of 26th. She came to our observation in December 2003 for recurrent episodes of angioedema of the face associated to diffuse paresthesia to the upper limbs.

She presented familiarity for NIDDM and for mild allergopathic diseases (allergic rhinitis).

In the first years of her life she complained of contact dermatitis due to nickel, disappeared after the puberty. She had a good digestive and alvine function. No smoke, nor alcoholic.

In December 2003, after a gynecologic examination, she began oral contraceptive with Levonorgestrel 0,1 mg and Ethynil estradiol 0,02 mg. The fifth day of therapy she complained of a vaste oedematous reaction on the face. The adverse event has been spontaneously resolved in a few hours. The day after, she took another pill and in 30 minutes she complained of a new, strong angioedema episode associated to paresthesia of the upper limbs.

The reaction was slowly resolved in an emergency unit by anti-histamines and steroids i.v.

No systemic signs were recorded.

The patient, so, came to our observation and we diagnosed a possible allergic reaction to estrogens, in accord to the characteristic of the angioedema and the reports of the Literature (4).

In Day-hospital she underwent to a tolerance test with an oral contraceptive containing only a progestinic, precautionally different from Levonorgestrel: the Desogestrel.

Placebo preceded the drug administration that was diluted 1:100, then 1:10 and, at the end, indiluted. The interval between the doses was 30 minutes. No reaction was recorded and, after four hours from the last administration, the patient went home.

We perform serologic and immuno-allergologic tests: only a mild reduction of C1s-inh was registered (0,13 ??? normal value 0,15-??). The absence of previous episodes of angioedema and the normal value of the other complement components (in particular C4) excluded with more certainty the diagnosis of hereditary angioedema. Actually, after six months of oral progestinic contraceptive, the patient feel well, no other episodes of angioedema have been reported, and the C1s-inh is normal (0,20??).

This case can suggest a possible mechanism of interaction between estrogens drugs and C1s-inh levels. In our opinion the possible pathogenetic event is the formation of antibodies anti C1s-inh, estrogens dependent. This observation is based on the known action of estrogens in the formation of auto-antibodies: female sex and oral estrogens contraceptive are, in fact, two of the most important risk factors in the formation of immunologic diseases mediated by auto-antibodies (i.e. LES).

A large number of patient must be surely observed but perhaps a new etiopathogenetic mechanism of angioedema will be disclosed.

References

- (1) Errigo E. - Malattie allergiche, 3° ed., vol. 1, 1999, 349-352.
- (2) Andre C., Andre F., Veyseyre-Balter C., Rousset H. - Acquired angioneurotic edema induced by hormonal contraception. *Presse Med.* 2003 may 24;32(18):831-5.
- (3) Van der Klooster J.-M., Schelfhout L.-J., Grootendorst A.-F., Zweers P.-G. - Recurrent attacks of angioedema ascribed to the use of estrogen preparations and a pregnancy (hereditary angioedema type 3). *Ned Tijdschr Geneesdk.* 2002 aug 24;146(34):1599-602.
- (4) Binkley K.-E., Davis A.-E. 3rd - Estrogen-dependent inherited angioedema. *Transfus Apheresis Sci.* 2003 dec; 29(3):215-9. Review.

(1) Servizio Immunotrasfusionale - Ospedale di Gavardo - via Gosa 73 25085 - Gavardo (BS)