Letter to the Editor

Questionable Role of the Angiotensin II Receptor Subtype 1 Autoantibody in the Pathogenesis of Preeclampsia

To the Editor:

Other than its critical role in cardiovascular and fluid homeostasis, several lines of evidence connect the renin–angiotensin system with hypertensive pregnancy disorders. Recent findings further support the key role of the renin–angiotensin system in the etiology of pregnancy-related hypertensive disorders, since Wallukat et al. identified an agonistic autoimmune antibody against the angiotensin II receptor subtype 1 (AT1-AA) as being detectable in preeclamptic patients but not in women with healthy pregnancies or in those with essential hypertension.

Although there was a clear rationale for assuming that AT1-AA could be one of the circulating factors causing the maternal syndrome and the preeclamptic phenotype, we identified the AT1-AA also in normotensive pregnancies with intrauterine growth restriction and in pregnant women without clinical signs of maternal or fetal compromise and, thus, excluded the AT1-AA as a specific marker for preeclampsia. Because the AT1-AA-positive pregnancies were characterized by an increased uterine placental resistance presenting with abnormal Doppler findings of the uterine arteries, the AT1-AA should be regarded as a consequence of an impairment placental development rather than mediating the preeclamptic phenotype.

In one of the last issues, however, Hypertension published 2 articles implicating that the AT1-AA may still keep causative properties in the development of preeclampsia and postpartum cardiovascular diseases. Hubel et al. documented the persistence of the AT1-AA months after preeclampsia in 17% of the affected women, which leads to the speculation that the AT1-AA could be the link to the long-term cardiometabolic risk after preeclampsia. The second article described repetitively the occurrence of the antibody in maternal circulation in women with preeclampsia, but could also demonstrate the AT1-AA first in fetal circulation. The latter one is not surprising, because antibodies of the IgG class usually cross the placenta. Because both publications still implicate a causative role for the AT1-AA in the manifestation of preeclampsia, we would like to add further evidence against their conclusion other than our published findings that the AT1-AA does not correlate with confirmed markers of preeclampsia as sFlt1. In a case report, we previously described a high maternal sFlt1 level and proteinuric hypertension in a pregnancy with virus-induced hydrops of fetus and placenta, a clinical situation also described by other authors. We demonstrated that the resolution of the hydrops after intravascular transfusion was associated with the disappearance of the preeclamptic symptoms and a dramatic fall of the circulating sFlt1 level. In an additional study, we measured the AT1-AA activity in many of the hydrops and preeclamptic symptoms and after resolution of hydrops and normalizing maternal situation. At both time points, we measured high AT1-AA antibody activity in the maternal circulation (Figure). This clearly implicates that the AT1-AA is not the key in determining the preeclamptic phenotype, because the disappearance of clinical symptoms did not require the loss of the autoantibody. This conclusion has been further supported, because we could repeat the findings in a second pregnancy with successfully treated virus-induced hydrops with preeclamptic properties (Figure).

We take these findings as an additional strong proof that the AT1-AA may keep cardiovascular modulatory properties but is not causative for the preeclamptic phenotype.

Disclosures

None.

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Hypertension. published online May 14, 2007;
Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2007 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/early/2007/05/14/HYPERTENSIONAHA.107.091421.citation

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