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Letter to the Editor

Menopause, and not age, is a critical factor associated with a worse response to antiviral therapy in women affected by chronic hepatitis C

We read with great interest the article entitled "Impact of sex on virologic response rates in genotype 1 chronic hepatitis C patients with peg-interferon alpha-2a and ribavirin treatment".[1] It was shown that in women affected by chronic hepatitis C and treated with antiviral therapy, the sustained virological response (SVR) rate decreases with age as a likely consequence of gradual estrogen decline. Moreover, it was reported that among young patients, SVR is higher in females than in males, while in older subjects the opposite occurs.

Although the data reported are interesting, we would like to make some comments. First of all, the choice to select a priori patients with genotype 1 produces a selection bias, as genotype 1 infection is universally known to be associated with resistance to interferon, and thus the population was not representative of all hepatitis C virus (HCV) females. Moreover, we found extremely interesting the clear-cut difference in SVR according to the three age categories chosen (<40 years, 40–50 years, and 50–60 years), with SVR decreasing in females from the first category to the last one. We think that this fits, with astonishing accuracy, the data recently published by our group on the effect of menopause in HCV-positive women.[2] Indeed, the last category described by Yu et al. (age 50–60 years) most likely includes almost only menopausal women. In this regard, our finding applies to all menopausal women, although the effect is most evident in those with genotype 1.

We believe that menopause and not age is the key factor in determining the lack of response to antiviral therapy. We have demonstrated that cytokine dosage and immunohistochemical assessment of tumor necrosis factor alpha (TNF-α) and suppressor of cytokine signaling 3 (SOCS3), dramatically increase in women after the menopause in comparison with women of reproductive age. Our data suggest that the early menopause (estrogen deprivation <5 years) is associated with an up-regulation of hepatic TNF-α and SOCS3 together with a marked increase in circulating interleukin 6 (IL-6), whose levels correlate with higher necro-inflammation; its postmenopausal rise is associated with the progression of fibrosis and with worsened necro-inflammation. The levels of the analyzed cytokines progressively decrease after the menopause and, over time, the hepatic expression of TNF-α becomes comparable to that of women of reproductive age. This also occurs in younger women who undergo surgical menopause.

These modifications are causally linked with the occurrence of resistance to the action of interferon and therefore explain the progressively lower SVR rate in women: menopause and not age is the critical factor.

Conflict of interest: None to declare.

References

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