

IgG2 Deficiency Tied to Severe H1N1 Disease

BY BRUCE JANCIN

KEYSTONE, COLO. — The explanation for pregnancy as a risk factor for severe pandemic 2009 H1N1 influenza infection may lie in a newly described association between the severity of H1N1 disease and the presence of IgG2 subclass deficiency.

This finding by Australian investigators, if confirmed, may not only shed new light on the pathogenesis of severe H1N1 infection but also prove to have important therapeutic implications, Dr. Gwen Huitt observed at a meeting on allergy and respiratory diseases.

Early in the pandemic, pregnant women were identified as one of the groups at particularly high risk for severe infection requiring ICU admission. Other high-risk groups included children less than 2 years of age, the obese, and individuals with chronic lung, heart, or kidney disease. The mechanisms underlying this increased risk have been unclear, said Dr. Huitt, professor of medicine at the University of Colorado and director of the adult infectious disease care unit at National Jewish Health, both in Denver.

Investigators in Melbourne decided to assess total IgG and IgG subclasses in a consecutive series of patients requiring ICU admission for pandemic flu. The impetus for their study came when they noted IgG2 subclass deficiency in a pregnant woman admitted to the ICU for severe H1N1 disease.

The study population consisted of 39 patients hospitalized for H1N1 infection and 17 healthy pregnant controls. A total of 19 patients had severe infection, meaning they required mechanical ventilation and ICU admission. Twenty others had moderate H1N1 disease, defined by hospitalization without ICU care. A total of 7 of the 19 patients with severe infection were pregnant, as were 2 of 20 with moderate infection.

Fifteen of the 19 patients with severe H1N1 infection had low IgG2, with a mean value of 1.8 g/L, as did 5 of the 20 with moderate infection. Furthermore, 10 of the 17 healthy pregnant controls had mildly low IgG2, although their diminished levels were nonetheless significantly higher than those of the pregnant women hospitalized for H1N1 infection.

Severe H1N1 infection was also associated with low total IgG, anemia, and hypoalbuminemia, although multivariate analysis revealed that the associations were significant only for low mean IgG2 and hypoalbuminemia.

Follow-up of 15 surviving H1N1-infected, IgG2-deficient patients showed that 11 remained IgG2-deficient at 90 days, well after recovery from their acute disease episode. In contrast, hypoalbuminemia typically resolved within 30 days (Clin. Infect. Dis. 2010;50:672-8).

The investigators argued that long-term follow-up may be warranted in patients sick enough to require hospitalization for H1N1 infection, since the late implications of lingering IgG2 deficiency in this population are unclear. For ex-

ample, it is not known whether such patients will have a diminished immunologic response to influenza vaccination.

In terms of the potential therapeutic implications of the Australian findings, the investigators noted that administration of convalescent blood products during the 1918 H1N1 flu pandemic resulted in a survival benefit. Inspired by that experience, the Australians have given pooled immunoglobulins to several IgG2-deficient

patients with severe H1N1 infection, although they are unclear whether the immunoglobulins had an effect because they weren't given under a study protocol.

Dr. Huitt said the Australian study raises an intriguing hypothesis: "The question is, was this virus selective in choosing those who may be living with a slightly low IgG2, and then overwhelming the immune system's ability to fight the cascade induced by that infection?"

"This is something that needs a lot more work," Dr. Huitt said at the meeting, which was sponsored by the National Jewish Medical and Research Center.

IgG2 subclass deficiency is typically asymptomatic. ■

Disclosures: The study was funded by the National Health and Medical Research Council of Australia. Dr. Huitt reported having no relevant financial conflicts.



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