Catamenial Anaphylaxis

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Each month, we present highlights from the Ask the Expert section of the American Academy of Allergy Asthma and Immunology (AAAAI) Web site written by Phil Lieberman, MD. For more questions and answers, visit www.aaaai.org/ask-the-expert.aspx.

Menses-related exacerbations in conditions seen by allergist/immunologists are not uncommon features of diseases we treat. Such exacerbations can be seen in asthma, urticaria, angioedema, and anaphylactic events. There are many potential mechanisms that underlie these exacerbations. One condition in particular serves as a paradigm for menses-related diseases. This is catamenial anaphylaxis, also called progesterone-related anaphylaxis and/or urticaria. Several inquiries to the Ask the Expert section of the AAAAI Web site have been received over the past few years regarding this condition. Two recent inquiries are characteristic examples. The responses to these deal with both the diagnosis and potential therapies. These 2 inquiries and the responses to them are seen below.

AUTOIMMUNE PROGESTERONE URTICARIA

Question:

I am seeing an 18-year-old woman for a second opinion on allergy to progesterone. She has polycystic ovarian syndrome and develops urticaria and vomiting mid cycle every month. Her symptoms resolve when she starts menstruating. Her gynecologist treated her with Lupron (Abb Vie, North Chicago, IL), which successfully suppressed the allergic problem but made her menopausal. She was seen by another allergist and had a positive skin test to progesterone. Her history and the results of testing are fairly convincing for IgE-mediated allergy to progesterone. The question was raised as to whether she can be desensitized to progesterone, and I could not find a protocol that would fit this situation. I would appreciate any help you can offer.

Response:

There are a number of references in the older literature of attempts to desensitize patients to progesterone, as discussed in a review of this condition published in 1995.[1] These attempts have met with various success, which produced, according to this reference, temporary improvement, complete improvement, and failure to induce improvement. More recently, however, 2 publications[2,3] have dealt with the issue of progesterone desensitization, and you will find a protocol for this procedure within these publications.

I mention, parenthetically, that there are other options for treatment that you might consider. The principle behind such therapy is suppression of menses as has been previously tried in your patient by using Lupron. Alternatively, one can treat with birth control pills, but there have been anecdotal reports of a reaction to the progesterone contained in such pills. You can review a discussion in this regard on the Ask the Expert section of the AAAAI Web site (www.aaaai.org/ask-the-expert.aspx) by typing "progesterone" into the search box. Also, danazol has been used successfully.[4]

Thank you again for your inquiry and hope this response is helpful to you.

REFERENCES

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4. Shahar E, Bergman R, Pollack S. Autoimmune progesterone dermatitis: effective prophylactic treatment with danazol. Int J Dermatol 1997;36:708-11.

POSSIBLE PROGESTERONE-RELATED URTICARIA AND/OR ANAPHYLAXIS

Question:

I saw a 31-year-old woman with episodic angioedema, urticaria, and shortness of breath due to upper airway obstruction secondary to tongue and/or throat angioedema over the past 1 to 2 years. She was required to use epinephrine on multiple occasions for her symptoms. The patient's symptoms seem to occur within approximately 1 week before menstruation. However, she states that she had a break from these symptoms approximately 3 times before menstruation over the past year. Her symptoms do not seem to be due to drug, food, or latex hypersensitivity reactions. Also, her tryptase and immunoglobulin levels were within the normal limits. Her antinuclear antibody and rheumatoid factor screen results were negative. I am considering the diagnosis of progesterone-induced anaphylaxis. To complicate matters, she does not have any children and recently saw a fertility specialist for the first time to help her conceive.

I discussed her case with her fertility specialist, and he is going to hold off on any medical treatment to stimulate and/or augment ovulation until progesterone-induced anaphylaxis is ruled out. Her intradermal testing to progesterone is negative, and her serum-specific IgE and IgG levels to progesterone were undetectable. She tells me that having a baby is extremely important for her. I was wondering what your thoughts are on her going ahead with medical treatment to help her conceive.

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Response:

First of all, you have done "due diligence" in evaluating your patient, and your consideration of progesterone-related anaphylactic events is certainly cogent. The fact that she does not demonstrate specific IgE against progesterone does not necessarily rule out this diagnosis because one of the first well-documented instances of progesterone-related anaphylaxis occurred in a patient without demonstrable IgE antiprogesterone,[1] which highlights even more so the conundrum of whether or not to proceed with fertility treatment.

Unfortunately, there is no "correct" or "incorrect" decision in this regard. But I would attempt to better establish the diagnosis at this time before pursuing the issue of fertility treatment. To discern whether or not the symptoms are truly progesterone related, a 3 to 4-month trial of the suppression of progesterone secretion, probably best done by using leuprolide or a related drug, can be done. For a review of this treatment and other therapies, please see the article by Snyder and Krishnaswamy.[2] If such suppression does prevent attacks, I believe that this offers strong confirmation that the episodes are truly progesterone-dependent. A failure of leuprolide to prevent episodes would allow you, with a fair degree of confidence, to rule out progesterone-related events. This would make one feel more comfortable about institution of fertility treatments. I would delay the decision regarding fertility treatment until evidence from this trial better establishes the diagnosis.

Finally, there are more detailed discussions of the condition of progesterone-induced anaphylaxis in previous entries to the Ask the Expert section of the AAAAI Web site (www.aaaai.org/ask-the-expert.aspx). They may be helpful to you in putting your patient's case into perspective. You can access them by going to the Web site and typing "progesterone" into the search box.

Thank you again for your inquiry and hope this response is helpful to you.

REFERENCES

1. Meggs WJ, Pescovitz OH, Metcalfe D, Loriaux DL, Cutler G Jr, Kaliner M. Progesterone sensitivity as a cause of recurrent anaphylaxis. N Engl J Med 1984; 311:1236-8.
2. Snyder JL, Krishnaswamy G. Autoimmune progesterone dermatitis and its manifestation as anaphylaxis: a case report and literature review. Ann Allergy Asthma Immunol 2003;90:469-77.