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Link Between Anthrax Immunization and Hypersensitivity Pneumonitis?

To the Editor:

The recent case report by Timmer et al,¹ in the August 2002 issue of *CHEST*, purports to describe hypersensitivity pneumonitis (HP) caused by anthrax immunization. I must respectfully disagree with the hypothesis that anthrax vaccination caused the chronic pulmonary illness (bronchiolitis obliterans with organizing pneumonia [BOOP] caused by HP) described in this patient, although he most likely did suffer from HP.

IgE-mediated phenomena, such as urticaria that the patient experienced shortly after the immunization, is not a feature of HP. As the authors note, the patient was exposed to a very well-described source of antigen that does cause HP, a cockatiel at home. Indeed, she had evidence of sensitization to birds, *ie*, positive serum precipitins to cockatiel droppings and feathers.

The improvement of the patient after he was treated with corticosteroids, despite the continued presence of the cockatiel, is not strong evidence that the cockatiel did not cause his disease. The relationship between exposure and illness in HP is not linear.

It is important that there be very substantial evidence of cause and effect when a new cause of HP is described, in this instance, anthrax vaccination causing HP. This evidence should include conclusive evidence linking a putative etiologic agent with the disease. This should include repetitive episodes of deterioration after more than one exposure to the responsible agent and the lack of exposure to any known cause of HP. Clearly, these criteria are not satisfied by this case report.²

I believe that the patient had an immediate IgE-mediated adverse event after the anthrax vaccination. During the evaluation of this event, his pre-existing BOOP/HP due to cockatiel exposure became evident. In view of the possible future importance of anthrax immunization in our nation, it is important that we be very sure that a particular adverse event was caused by this immunization before reporting it in the medical literature.

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- 1 Timmer SJ, Amundson DE, Malone JD. Hypersensitivity pneumonitis following anthrax vaccination. *Chest* 2001; 122: 741-745
- 2 Schuyler M, Cormier Y. Diagnosis of hypersensitivity pneumonitis. *Chest* 1997; 111:534-536

To the Editor:

Thank you for your insightful comments. Publication was delayed for nearly a year while a variety of specialists from the National Institutes of Health, Armed Forces Institute of Pathology, and the Air Force and Navy Surgeon General's office reviewed the case to confirm our conclusions. Additionally, our patient's status was reconfirmed with a comprehensive battery of sophisticated testing related to his bird exposure history. The components of the case suggesting that the anthrax vaccination was the most likely cause of his hypersensitivity pneumonitis (HP) and bronchiolitis obliterans with organizing pneumonia (BOOP) are as follows.

First, the subsequent temporal sequence of the development of his symptoms and lung disease was believed to be more typical of an induced lung reaction. Two allergy experts also recognized the initial skin reaction as atypical for HP, and the patient was initially seen in allergy consultation for the skin reaction. An IgE event was postulated at that time.

Second, the high-resolution CT demonstrating well-defined peribronchiolar nodules within the ground-glass opacities, coupled with the transbronchial lung biopsy showing the (probably heterogeneous) fibroblastic plugs indicated a lung reaction that includes a BOOP component. This pattern is more consistent with a chemical induction than with an organic inhalational stimulus, which is more typically associated with ill-defined nodules (rarely) and patchy airspace consolidation, usually in the mid-lung zones.¹

In 1-year follow-up of the patient (off steroids for 8 months), specific immunologic testing results for this particular cockatiel were negative. Moreover, the patient has continued to live with the bird without further symptoms. The clinical heterogeneity of HP, especially with steroid therapy, is certainly recognized. We feel that the temporal and pathologic association has biologic plausibility. This case was also reported to the Vaccine Adverse Event Reporting System and was classified as having "likely correlation" with anthrax vaccination by this expert panel.

Finally, as military physicians, we remain advocates for this safe and effective vaccine, especially in the current world situation. We reported the case to ensure complete disclosure and to enhance management of any further cases.

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