

Reactive airways dysfunction syndrome (RADS): fact or fantasy?

Authors' affiliations:

E.J. Bardana, Jr, Division of Allergy and Clinical Immunology, Oregon Health Sciences University, Portland, Oregon, USA

Correspondence to:

Emil J. Bardana, Jr, MD
Professor of Medicine
Head, Division of Allergy and Clinical Immunology
Oregon Health Sciences University
Portland
OR 97-201-3098
USA

Introduction

Chronic and recurrent asthma-like respiratory symptoms resulting from toxic inhalation exposure have been recognized for many years. As early as 1970, Gandevia (1) and a colleague reported four workers in whom new-onset asthma developed after exposure to excessive concentrations of gases and vapors such as hydrogen sulfide, fumes from overheated plastics, and smoke and fumes from the combustion of a variety of acids. The mechanism of causation was implied in the descriptive name used to refer to the process, "inflammatory bronchospasm."

In 1985, this characteristic, post-chemical-induced, asthma-like condition was formally described by Brooks and Lockey and called reactive airways dysfunction syndrome (RADS) (2). The original abstract described six workers who showed symptomatic and physiologic evidence of bronchoconstriction within hours of inhaling a corrosive gas, fume, vapor, or dust. In most of these cases, symptoms resolved over a period of several weeks (3).

There remains some controversy related to whether RADS represents a true variant of occupational asthma. There is a general consensus that there is sufficient evidence in the literature to support its existence as an entity (4-6). If one divides new onset occupational asthma (OA) into two broad categories of immunologic OA and nonimmunologic OA, RADS constitutes the major nonimmunologic variant (5, 6). While I believe the literature supports its existence, the condition is relatively rare, with between 100 and 150 well-documented cases since 1985 (6, 7).

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Epidemiology

The question of the prevalence of RADS is difficult to answer. Blanc et al. interviewed 323 subjects of a

consecutive sample of 693 toxic inhalational exposures (8). Only 20% of patients had symptoms that persisted 14 days or more. This suggests that RADS is a relatively infrequent disorder. Brooks et al. reported a prevalence of 2% (definite) and 6% (suspected) RADS among patients with suspected occupational and environmental asthma (2). On the other hand, Tarlo and associates have reported much higher prevalence in their studies (9). Similarly, Wheeler et al. reviewed the results of a 10-year occupational medicine program at the University of Washington. Seventy-one patients were determined to have work-related asthma. Among the 71, 18 (25%) were felt to have RADS (10). As can be seen, there is a significant variance depending on the diagnostic criteria applied to make the diagnosis. My own inclination would be in the same range as that reported by Brooks (2).

Diagnosis

The diagnosis of RADS is based on a compatible history and the demonstration of persistent nonspecific bronchial hyperresponsiveness. Clinically, the presentation of RADS is quite different from that of immunologic work-related asthma. In RADS, the exposure is characteristically acute, singular, and extreme in nature, without a latency period. In general, the exposure is brief and often lasts only a few minutes. Often it is attributable to an accident or an unintended circumstance that results in poor ventilation in the presence of high concentrations of an intoxicant. Generally, the intensity of the exposure is such that the affected individual seeks immediate medical attention, and it may necessitate hospitalization.

The criteria for the diagnosis of RADS as defined by an American College of Chest Physicians Consensus Statement (11) were as follows:

- 1) a well-documented absence of preceding respiratory complaints
- 2) onset of symptoms after a single exposure incident or accident
- 3) exposure to a gas, dust, fume, or vapor with irritant properties present in very high concentrations
- 4) onset of symptoms within a 24-h period after the exposure with persistence of symptoms for at least 3 months
- 5) symptoms resembling asthma with cough, wheeze, and dyspnea
- 6) presence of airflow obstruction on pulmonary function

tests and/or the presence of nonspecific bronchial hyperresponsiveness

- 7) other types of pulmonary disease excluded.

There is general consensus regarding these criteria, which could be characterized as major criteria. I would also recommend a number of minor criteria which help strengthen the diagnosis if fulfilled to a greater or lesser extent. These are as follows:

- 1) absence of an atopic state
- 2) absence of significant peripheral or pulmonary eosinophilia
- 3) bronchial hyperreactivity moderate to severe; i.e., positive below 8 mg/ml concentration of methacholine
- 4) histopathology showing minimal lymphocytic inflammation
- 5) reversibility generally less than that seen in immunologically-induced asthma.

Pathology

Histopathologic studies of patients with RADS are very limited at this time. The two cases in Brooks' initial series in which biopsies were performed showed features of nonspecific inflammation (2). The cellular infiltrate consisted primarily of lymphocytes and plasma cells. Deschamps et al. found a mild inflammatory response with sparse lymphocytes and polymorphonuclear cells. There were no eosinophils (12). Gautrin et al. reported a predominance of lymphocytes in bronchoalveolar lavage fluid (BAL) in three of five subjects studied. Histopathologic studies revealed subepithelial thickening with fibrosis, a finding not previously described (13). The authors postulated that these fibrotic changes might be the explanation for the less than expected bronchodilator response in patients with RADS. Electron microscopy showed many deciliated cells with the presence of inclusion bodies.

Prognosis/management

Those patients who survive the brief exposure to the toxicant generally recover completely without significant clinical or physiologic sequelae regardless of the severity of the initial clinical manifestations (14). The treatment of RADS is no different than it would be for most asthmatics. It has been observed that as a class these patients tend to be

less responsive to the β -agonist class of drugs. It has been suggested that inhaled ipratropium and corticosteroids be employed for 1–3 months of therapy.

Summary

Most evidence suggests that RADS is a distinct syndrome and not simply an exacerbation of pre-existing hyperresponsiveness. There is no doubt that much remains to be explained regarding pathogenesis. On the other hand, I urge caution about the claims of "low-level RADS"(15). Here the data are much more anecdotal and leave much to be desired.

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