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Research Article

REACTIVE AIRWAYS DYSFUNCTION SYNDROME (RADS) AFTER HIGH LEVEL IRRITANT EXPOSURES

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ABSTRACT

To identify those agents as being associated with reactive airways dysfunction syndrome (RADS) that should raise awareness of this potential risk in that work environment. A systematic case reporting was undertaken. Patients with occupational asthma were screened and selected against pre-determined diagnostic criteria for RADS. The clinical, functional and occupational evolution was evaluated. Of 19 patients who met Brooks' criteria, 14 male and 5 female with median age was 37.8 years. The proportion of non-atopic and smokers was higher. Most exposures occurred in the workplace was accidental. The reported agents were chlorine, toluene di-isocyanate (TDI), oxides of nitrogen, acetic acid, paint and sulfuric acid. Dyspnoea, cough and wheeze were the commonest symptoms. Symptoms developed within 5 to 24 hours and symptom duration was 5 to 30 months in all subjects. FEV_1% <80% and X-ray report was normal in all cases. With regard to the clinical evolution, there was an improvement and patients who inhaled in the workplace continued working. There is lack of adequate information about RADS that can better explore it. A more structured approach to gathering information on exposure, investigation and outcome is required. A minimum data set for reporting RADS cases is proposed. We suggest that a web-based database of RADS cases be established which would allow continuous update and better analysis of outcome in these individuals.

Key Words: Reactive airways dysfunction syndrome, Irritant- induced asthma, Asthma, Inhalational irritant

INTRODUCTION

Reactive airways dysfunction syndrome (RADS) appears shortly after exposure to the causative agent and is characterized by increased nonallergic airway responsiveness. We consider it different from typical occupational asthma because of its rapid onset, specific relationship to a single environmental exposure, and no apparent preexisting period for sensitization to occur with the apparent lack of an allergic or immunologic etiology. Although the exposure is often unique, the syndrome may be long-lasting.[1] This syndrome can occur after exposure to a variety of toxic gases, including chlorine, ammonia, acids and hydrogen sulphide.[2-6] Over the past three years, we evaluated a number of patients at the saurastra region of Gujarat, India, were observed to have an illness develop after a single excessively high environmental or occupational exposure. We report 19 patients who met Brooks' criteria[1], 14 male and 5 female developed RADS as a consequence to inhalational irritant exposure either at work place or at home. In most instances, the airways hyperreactivity induced by the agents is transient. Exposure to agents can lead to acute or chronic respiratory symptoms. Recent study has described clinical history, spirometry, causative agents and management of RADS.

METHODS

The study conducted at saurastra region of Gujarat, India, between the years 2009 and 2011. During this period, there were approximately 650 cases examined were patients with apparent bronchial asthma, mostly suspected of being occupational or environmental in origin. Among the approximate 160 cases of occupational asthma, there were 22 with suspected RADS. Three of these RADS cases did not have completed past histories or medical information or lacked some of the clinical criteria listed in Table 1. The final population for reporting consisted of 19 subjects who fulfilled the specific criteria listed in Table 1.

A detailed medical and occupational history was obtained, and a physical examination performed by the same examiner in all cases. The history was obtained by an administered questionnaire. [2] In all subjects, baseline pulmonary function studies were performed according to accepted criteria using the spirometer (calibrated daily). [7] The test was considered positive when there was a 20 percent or greater fall in FEV_1, pulmonary function studies were performed until the two best FEV_1 values were within 5 percent. The best FEV_1 was used to calculate percent fall. %. FEV_1/FVC ratios were also available for all subjects. Respiratory function test was recorded before and after treatment of patients with reactive airway disease. Posteroanterior chest x-ray films were obtained.[8]

RESULTS

Of the 19 RADS cases who met Brooks' criteria, fourteen (74%) men and five (26%) women aged 27 to 60 years were evaluated. The mean age in this group was 37.8 years. Of 19 patients, seven patients (36.8%) were smokers with consumption of 13 pack-years, three patients (15.8%) were ex-smokers with consumption 5 pack-years and nine patients (47.3%) were non-smokers. There were three subjects (21.4%) were considered to be atopic as determined by past history. The information obtained from past medical records and discussion with patients indicated no subjects had evidence of preexisting pulmonary disease.

The agents which developed RADS were chlorine (five subjects), toluene di-isocyanate (TDI) (three subjects), oxides of nitrogen (three subjects), acetic acid (two subjects), paint (four subjects) and sulfuric acid (two subjects). Information regarding FEV_1% was available for all subjects with RADS. Among these 19 subjects, 13 subjects (68.4%) had an FEV_1% <60-80% and 6 subjects (31.5%) had an FEV_1% <60%. Eight of the 19 patients (42%) had an FEV_1/FVC ratios <0.6 while 11 patients (58%) had an FEV_1/FVC ratios >0.6. Chest x-ray films at time of evaluation were normal in all persons (Table 2).

Patients received injections of corticosteroids over the next few weeks for these complaints. They treated with short courses of corticosteroids, beta agonist aerosol and inhaler,

anticholinergic or theophylline preparations. A variety of offending agents were incriminated (Table 2).

Table 3 provides temporal information related to patient studies. This information was obtained from the patient's interview and by discussions with persons familiar with the incident. In each case, there was a specific incident where a very high exposure occurred, either by accident or because there was very poor workplace ventilation. In each case, the exposure was characterized toxicologically as being irritant in nature and present in high concentrations. Table 3 lists clinical symptoms and shown dyspnoea, cough and wheeze pre- dominating. Seventy-eight percent of RADS subjects had dyspnoea (n = 15), 57% cough (n = 16), 63% wheeze (n = 12), 42% chest tightness (n = 8), 31% upper respiratory irritation (n = 6), 5% eye irritation (n = 1), 25% mucus production (n = 5), 31% fever (n = 6) and 21% cyanosis (n = 4).

The most frequent location of exposure episode in those with RADS (n = 19) was the workplace (n = 17) with others occurring in the home (n = 2). Time from the beginning of exposure to development of symptoms was 1.5 hour to less than 24 hours in all cases. In six subjects, the duration of exposure lasted 3 hours or less; it lasted four hours or more in another thirteen affected persons (Table 3). Generally, there was some time interval between the end of exposure and when the person first reported RADS symptoms. There were no differences in clinical, physiologic, or prognostic parameters among persons with immediate compared to delayed onset of symptoms. An important consideration of RADS was persistence of symptoms after termination of exposure and treatment of the acute episode. It was documented to be present for one year or more in thirteen cases and less than one year in six.

With regard to the clinical evolution, there was an improvement in 13 of 19 (68%) patients, while the rest remained stable. In the functional follow up, 4 of 19 (21%) showed partial changes, 12 of 17 (63%) improved and 3 of 19 (16%) worsened. Among the patients who inhaled in the workplace, 10 of 19 (53%) continued working in the same job, 2 of 19 (11%) were off sick and 7 of 19 (37%) changed their role.

DISCUSSION

According to the original definition of reactive airway dysfunction syndrome (RADS) the victim's symptoms will develop very quickly, within minutes or hours after a single, high-intensity exposure and the asthma-like symptom (chest tightness, cough or dyspnea) persisted for a longer period and usually non-specific challenge test is positive.[1] The case histories described in this article have similar clinical presentations with each affected person developing an asthma-like illness after an exposure to a high level of an irritant vapor, fume, or smoke.[9] When the subjects were evaluated after the incident, a consistent physiologic alteration was airways hyperreactivity. The incriminated etiologic agents all shared a common toxicologic characteristic of being irritant in nature. In some cases, the agent was present as a gas, such as the case chlorine. In other situations, the toxic inhalant was an aerosol as with the spray painting or the fumigating fog exposure. In two instances, it was due to heating or combustion; one case was fire and smoke inhalation, and one case was due to inhalation of heated acid vapors and fumes during welding.

Mechanisms to explain the development of RADS must focus on the toxic effects of the irritant exposure on the airways. This conclusion is only speculative and not substantiated. Our investigation is retrospective and highly dependent on the recollection of and clinical description given by the subject affected. In several instances, litigation procedures were operative, and the subject's recollection of events might have been biased.

The exact prevalence of nonspecific bronchial hyperreactivity in the general population is not known, but one estimate is 3 percent of presumed normal.[10] Increased nonspecific bronchial reactivity also is reported in cigarette smokers with normal lung.[11] Three subjects were atopic individuals with allergic rhinitis, although these patients did not have lower respiratory symptoms. However, if the airways were previously hyperreactive, then all individuals studied, as well as we can accurately determine, were without respiratory complaints and were not receiving medications. After the exposure, all individuals required medication at some time, including corticosteroids, beta-adrenergic and anticholinergic or theophylline like bronchodilators. RADS is not frequently suspected and thus its diagnosis and treatment can be delayed for months or years. We believe the hyperreactive airway noted in our patients is likely due to an inhalation injury.

The present study documents a clinical syndrome we feel has not previously been well emphasized. RADS might be similar to an asthma syndrome such as "intrinsic asthma," an entity where in most cases, specific etiologic factor is documented. It differs from typical occupational asthma because of the absence of a preceding period for sensitization to occur and the onset of the illness after a single, first time exposure.[12] Instead, there was clinical increased nonspecific bronchial reactivity to a number of irritants. Thus, the typical work-related precipitation of symptoms was absent and individuals reported symptoms both at home and at work.

While our definition of RADS is restsictive and requires the presence of a high level exposure, it is conceivable that a low level chronic exposure could cause a similar type process in some individuals. An important consideration of RADS is once it develops, there may be long-term sequela and chronic airways disease occurring. Further investigations into the role of nonimmunologic environmental and occupational factors in the pathogenesis of asthma syndromes and airways hypes-reactivity seem warranted.

The most commonly reported agents in this article associated with a diagnosis of RADS were chlorine, TDI and oxides of nitrogen. The agents most frequently implicated in RADS were as anticipated although this list is likely to be incomplete as many cases of RADS may go unreported. It is possible that a degree of publication bias exists, so the relative contribution of some agents to the overall burden of RADS may be underestimated. Information on outcomes in relation to exposures needs to be collected formally and in a structured way if better advice and understanding of these conditions is to be gained.

It is proposed that constitute a minimum data set for reporting of RADS cases in the medical literature. A web-based reporting system with a database that could be updated online to permit the reporting and follow-up of cases would be of benefit and would deal to some extent with the issue of publication bias. In summary, a systematic reporting as being associated with RADS has been undertaken.

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Table 1. Clinical criteria for diagnosis of reactive airways disease (RADS) [1]

1. A documented absence of preceding respiratory complaints.
2. The onset of symptoms occurred occurred after a single exposure incident or accident.
3. The exposure was a gas, smoke, fume or vapour which was present in very high concentrations and had irritant quantities to its nature.
4. The onset of symptoms occurred within 24 hours after the exposure and persisted for at least three months.
5. Symptoms simulated asthma with cough, wheezing and dyspnea predominating.
6. Pulmonary function tests may show airflow obstruction.
7. Other types of pulmonary disease were ruled out.

Table 2. Demographic and Spirometric Results in Subjects with RADS

Patients	Age (yr)	Sex	Smoking (pk/yr)	Atopy	Exposure	Laboratory examination			Treatment*
						FEV1 %	FEV1/ FVC	X-ray	
1	53	M	0	-	Notrogen oxide	61.5	0.63	-	CS, BA,AC
2	33	M	0	-	Chlorine	63	0.59	-	CS, BA,AC
3	40	F	7	-	Acetic acid	62	0.57	-	CS, BA
4	45	M	13	-	Paint	65	0.65	-	CS, BA,AC,T
5	60	M	0	-	Toluene di-isocyanate	54	0.57	-	CS, BA,AC
6	52	M	9	+	Notrogen oxide	66	0.67	-	CS, BA,AC
7	45	M	0	-	Floor sealant	64.5	0.6	-	CS, BA,AC,T
8	50	F	4	-	Sulphuric acid	67.5	0.63	-	CS, BA,AC
9	52	M	0	-	Chlorine	64	0.6	-	CS, BA,AC
10	43	M	10	+	Toluene di-isocyanate	57.5	0.53	-	CS, BA
11	39	M	0	-	Notrogen oxide	59	0.51	-	CS, BA,AC
12	47	M	0	-	Chlorine	67	0.69	-	CS, BA,AC
13	46	F	14	-	Fire, Fumigating fog	59.5	0.63	-	CS, BA,AC,T
14	49	F	0	-	Paint	68	0.66	-	CS,AC
15	34	M	12	+	Toluene di-isocyanate	57	0.5	-	CS, BA,AC
16	50	M	5	-	Chlorine	55.5	0.62	-	CS, BA,AC,T
17	27	M	11	-	Chlorine	61	0.61	-	CS, BA,AC
18	36	M	20	-	Acetic acid	63	0.65	-	CS, BA,AC
19	43	F	0	-	Sulphuric acid	62.5	0.63	-	CS, BA,AC

*CS, Corticosteroid; BA, Beta-agonist; AC, Anticholinergic; T, Theophylline.

Table 3. Temporal Relationships

Patient	Length of Exposure (hr)	Time Before Onset of Symptoms (hr)	Duration of Disease (months)	Symptoms				
				Dyspnoea	Cough	Wheeze	Chest tightness	Others
1	1/2	3	26	+	+	**0**	+	+
2	1/2	8	15	+	+	**0**	**0**	+
3	8	12	12	0	+	+	+	+
4	13	20	26	+	+			+
5	2	5	22	+	+	+	**0**	+
6	1	1:30	5	+	+	**0**	**0**	+
7	4:30	5	18	0	+	+	+	+
8	7	13	13	+	+	**0**	+	**0**
9	1	2	17	0	+	+	+	+
10	3	6	24	+	+	**0**	**0**	+
11	2	2	8	0	+	+	**0**	+
12	1:30	2	7	+	+	+	**0**	**0**
13	3	3	24	+	**0**	+	**0**	+
14	10	18	9	+	+	**0**	**0**	+
15	5	7	23	+	+	+	**0**	**0**
16	2:30	4	26	+	+	**0**	+	**0**
17	1	6	17	+	**0**	+	+	+
18	9	13	13	+	+	+	**0**	**0**
19	10	15	10	+	+	**0**	+	+

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