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Reactive airways dysfunction syndromes: a case report

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Reactive airways dysfunction syndrome (RADS) has been known since 1985 when Brooks and colleagues described ten patients who developed asthmatic symptoms after a single exposure to high levels of an irritating gas, fume or smoke. We report herein a case of RADS from an incident of smoke inhalation. The patient was a 29 year old Thai male working as a labourer in a chemical storage room at Klong Toey Port. He had been well until 1992 when a major fire accurred at the port. Chemicals that burned included methyl bromide and fomaldehyde. He received 15% second degree burns and smoke inhalation. He was admitted to the Burn Unit, Chulalongkorn Hospital. During admission he experienced acute asthmatic attacks and given a bronchodilator and corticorteroids. He was then documented as having bronchial hyperresponsiveness by methacholine inhalation challenge.

Key words : *RADS, Bronchial hyperresponsiveness, Occupational asthma.*

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นับตั้งแต่ปี ค.ศ. 1985 ที่ Brook และคณะได้รายงานผู้ป่วยจำนวน 10 ราย ที่มีอาการหอบหืดที่เกิดจากการได้รับสัมผัสโดยการสูดหายใจด้วย ก๊าซพิษ ฟูม หรือควันไฟ และได้ตั้งชื่อว่ากลุ่มอาการหลอดลมตอบสนองผิดปกติ เราได้พบผู้ป่วยหนึ่งรายที่มีลักษณะอาการเข้าได้กับกลุ่มอาการหลอดลมตอบสนองผิดปกติดังกล่าว โดยผู้ป่วยเป็นชายอายุ 29 ปี ทำงานเป็นกรรมกรในโกดังเก็บของที่ท่าเรือคลองเตย และได้รับอุบัติเหตุจากไฟไหม้โกดังเก็บสารเคมีจำพวก methyl bromide และ fomaldehyde ผู้ป่วยมีบาดแผลไฟไหม้ และสูดควันไฟจากสารเคมีดังกล่าวเข้าไป ได้รับไว้รักษาตัวในโรงพยาบาล ผู้ป่วยมีอาการหอบหืดเกิดขึ้นในขณะอยู่ในโรงพยาบาล และมีอาการต่อเนื่องต้องได้รับการรักษาด้วยยาขยายหลอดลมและ corticosteroid มาโดยตลอด โดยที่ผู้ป่วยไม่เคยมีอาการของโรคหอบหืดมาก่อนเลย

In 1985, the chracterisic post- irritant injury asthma-like syndrome was described by Brooks and his colleques who named the condition " Reactive Airways Dysfunction Syndrome (RADS)".[1] It referred to irritant-induced asthma initiated by a single exposure to a high concentration of irritating gas, fumes or smoke.[2,3] In most instances, the exposure was the result of an accident occurring in the workplace or in a situation where there was poor ventilation in the area. The subjects usually had no apparent preexisting respiratory illnesses. Asthmatic symptoms developed within a few hours after exposure and persisted for many years. A pulmonary function test might be normal or show evidence of airflow obstruction. All patients had airways hyperreactivity documented by a positive test of methacholine inhalation challenge.[4]

Over the past several years, a lot of accidents in the workplace, especially fires, have occurred in Thailand. However, there had been no case reports of RADS in this country before. We had occasion to care for a patient who was a victim in the major fire at Klong Toey Port several years ago. Following that incident of chemical smoke inhalation, he developed asthmatic symptoms which were consistent with the reactive airways dysfunction syndrome.

A case report

A 29-year-old Thai male was referred to the Chest Unit, Chulalongkorn Hospital because of dry cough and intermittent breathlessness with wheezing for two years. He was a nonsmoker and he had no previous history of respiratory disease. He worked as a labourer in the storehouse at Klong Toey Port. He was well until late in 1992 when there was a major fire incident at the storehouse which had many kinds of chemical substances such as methylbromide and formaldehyde. He was a fire victim with burned skin and smoke inhalation. He was admitted to the Burn Unit, Chulalongkorn Hospital. Physical exammination revealed that he had 15 percent of second degree burns on both arms and trunk. He was concious but with respiratory distress and a respiratory rate of 28/min, pulse rate 120/min, blood pressure 130/90 mmHg and body temperature 37.8°C. Chest examination revealed rhonchi and crackles in both lungs. Other examinations were within normal limits.

A complete blood count showed Hct 45%, WBC 12500/cu mm., with neutrophil 85% and lymphocytes 15%. Arterial blood gases were pH 7.52, $P_{a}O_{2}$ 102 mmHg (on mask with bag 10 LPM) $P_{a}CO_{2}$ 28 mmHg. The chest roentgenogram was quite normal.

At that time he was diagnosed with15% second degree burns and smoke inhalation. He was treated with cloxacillin, dexamethasone, and a nebulized bronchodilator and he displayed clinical improvement. He was discharged with Salbutamol MDI after three weeks of hospitalization.

During two years of irregular follow-ups he still had dyspnea on exertion and intermittent wheezing with dry cough. The symptoms were improved by a bronchodilator but sometimes they were severe enough to cause a visit to the emergency room.

At the Chest Clinic, his physical examination revealed normal chest findings. He also had been reviewed for history of allergic disease and there was no atopy in his family. Skin testing for common aeroallergens such as house dust, mites or cockroach as showed negative results. Eosinophil was not found

in his sputum examination. A spirometry was quite normal with FVC 4.51 L (112%), FEV_1 3.25 L, % FEV_1 /FVC 70%, PEFR 8 LPS.

A methacholine inhalation challenge (MIC) was performed using the method as previously described.[5] It was positve with the PC_{20} of 0.5 mg/ml. He was then diagnosed as having RADS or irritant-induced asthma. He was administered inhaled budesonide 400 μg twice daily with β_2 agonist when needed.

He still had some breathlessness during exertion but less occurrances of acute asthmatic attack. Six months after the administration of inhaled corticorterords, MIC was performed again and some improvement was found with the PC_{20} of 1.5 mg/ml (three doubling concentration increasing) a shown in Figure 1.

Discussion

This is the first known case of RADS in Thailand. The diagnosis is definite based on a history of asthmatic symptoms beginning shortly after exposure to a high level of toxic substance fire smoke and demonstration of persistent nonspecific bronchial hyperresponsiveness (BHR) measured by the methacholine inhalation challenge.

RADS was first reported by Brooks and colleagues in 1985 to describe 10 previously healthy subjects who developed symptoms of asthma and nonspecific bronchial hyperresponsiveness after exposure to high levels of an irritant vapor, fume or smoke.[1]

The diagnosis of RADS is based on asthmatic symptom and the demonstration of persistent nonspecific BHR. The criteria for the diagnosis of

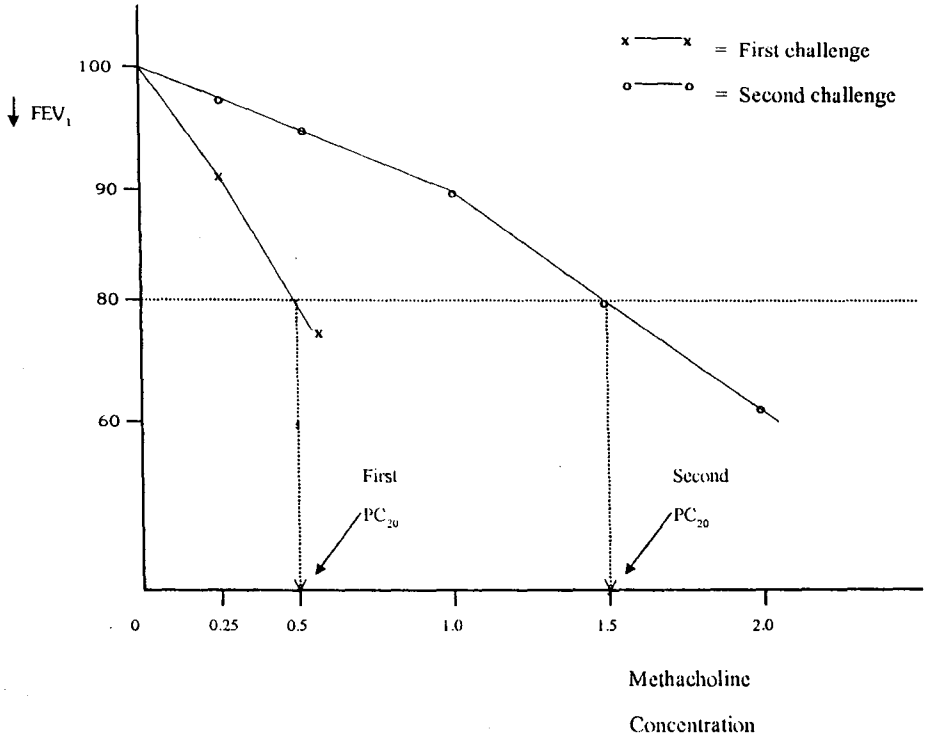

Figure 1. Showing the PC_{20} from Methacholine Inhalation Challenge.

RADS is shown in Table 1. It stresses on a documented absense of earlier respiratory disease and the onset of symptoms occurring shortly (within hours) after a single exposure to a high level of an irritant aerosol or gas. It also stresses that the asthmatic symptoms and nonspecific BHR would persist for at least 3 months, usually longer, and may not end. However, Bardana[6] has recently proposed new diagnostic criteria for the diagnosis of RADS that includes a requirement for histologic study showing minimal lymphocytic inflammation without eosinophilia, as shown in Table 2.

Table 1. Original criteria for the diagnosis of RADS.

Criteria
A documented absence of preceding respiratory complaints
The onset of symptoms occurred after a single specific exposure incident or accident
The exposure was to a gas , smoke , fume, or vapor that was present in very high concentrations and had irritant qualities to its nature
The onset of symptoms occurred within 24 h after the exposure and persisted for at least 3 months
Symptoms simulated asthma with cough, wheezing , and dyspnea predominating
Pulmonary function tests may show airflow obstruction
Methacholine challenge testing was positive
Other types of pulmonary diseases were ruled out

Table 2. Criteria for the diagnosis of RADS.

Criteria
Total absence of preceding respiratory disease in a nonatopic person
Documented exposure to excessive concentrations of corrosive or irritating gas, vapor, fumes, or dust
Abrupt onset of symptoms within minutes or hours (always within 24 h), requiring medical care
Persistence of asthma-like symptoms such as chest tightness, cough, or dyspnea
Normal or reversible airflow pattern on spirometry ;reversibility is generally less than that seen in immunologically induced occupational asthma
Presence of moderate to severe bronchial hyperreactivity on methacholine challenge
Histopathologic study showing minimal lymphocytic inflammation without eosinophilia

The common ethiologic agents causing RADS are been gases such as chlorine , sulfur dioxide and phosgen.[7-10] Metal fumes such as zinc oxide, often used in welding, have also commonly caused RADS in welders.[11] Smoke inhalation by fire victims and fire fighters have also frequently been reported in the literature.[12-15] Because toxic inhalation exposure is often encountered in the workplace, this syndrome is classified as a form of occupational asthma. There are two types of occupational asthma that are distinguished by whether they appear after a latency period.[16] The first, with a latency period, encompasses all instances of immunologic asthma and includes most high and some low molecular weight agents. The other type, without latency, is best illustrated by irritant-induced asthma or RADS. Some agents, such as toluene diisocyanate (TDI) may cause both types of occupational asthma, depending on the exposure conditions.[17] The pathogenesis of RADS is not clear and it was first speculated that it was due to airway inflammation. Alberts and Brooks[18] have speculated that the high-level irritant exposure causes massive epithelial damage and destruction that was followed by the activation of nonadrenergic, noncholinergic (NANC) pathways via axon reflexes and the onset of neurogenic inflammation. Nonspecific macrophage activation and mast cell degranulation may also occur with the release of proinflammatory chemotactic and toxic mediators which enhance the recruitment of inflammatory cells to the site of injury and the subsequent profound inflammatory response is thus sustained. Following the epithelial injury and inflammation, the recovery phase begins with resolution of the inflammation, epithelial cell repair, and improvement in vascular integrity. However, the healing process causes persistent bronchial hyperresponsiveness.

Four major hypotheses have been proposed to explain the persistent BHR in patients with RADS.[4] The first is that following the extensive inflammation, subsequent reepithelialization and neural innervation may result in an altered receptor threshold in the airways. The second hypothesis is that damage to the bronchial mucosa may lead to increased airway permeability which allows the inhaled material easier access to irritant receptors. The third is that inflammatory reactions in the airway may result in a massive release of mediators that alter smooth muscle responsiveness for a long period of time. The forth hypothesis is that airways inflammation persists.

The histopathologic findings of patients with RADS shows some evidence of airway inflammation but there is disagreement in various reports which may be due to the type and extent of the exposure, and the period of time from the initial exposure to the treatment employed, the diagnosis and biopsy.

The treatment of patients with RADS is no different from that of other asthmatics. In addition to relieving symptoms with inhaled bronchodilators, treatment should be directed at reducing the level of nonspecific BHR by corticosteroids. However, the patients with RADS are significantly less responsive to inhaled β_2 agonist than are patients with conventional asthma. Some suggest using inhaled ipratropium and corticorteroids for the first 3 months of therapy.

The long-term expected outcome for patients with RADS has not been well documented. Some have a regression of symptoms, some remaine in stable

condition, and some progress with frequent asthmatic attacks.

Our patient had asthmatic symptoms for more than three years with inappropriate treatment. However, after prolonged administration of inhaled corticosteroids, he improved with fewer asthmatic attacks and there was significant improvement of BHR.

In conclusion, we report the first known case with RADS in Thailand. He developed asthmatic symptoms following a single exposure to fire smoke with high concentrations of toxic chemical substances such as formaldehyde, and methylbromide during a fire at the chemical storehouse at Klong Toey Port. He had symptoms for more than three years, before he was documented with RADS with persistent BHR (PC_{20} 0.5 mg/ml of methacholine). After the diagnosis, he was administered inhaled corticorteriods and ipratropium bromide in combination with β_2 agonist with marked improvement. Methacholine inhalation challenge was performed again after 6 months and it was found that the BHR was significantly improved with three doubling concentration increasing. We planned to administer inhaled steroids for two year to make the airway reactivety became normal and planned to follow the patient as long as possible.

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