Imperial Journal of Interdisciplinary Research (IJIR)
Vol-2, Issue-7, 2016
ISSN: 2454-1362, http://www.onlinejournal.in

Reactive Airway Dysfunction Syndrome (RADS) following accidental exposure to Dimethyl Sulphate (DMS)–first case reported in Sri Lanka

P. A. J. N. Wickramaratne[1], Anula Wijesundara[2] &
A. M. A. L. R. Alagiyawanna[3]
[1]MBBS, DCCM, Registrar in Emergency Medicine, National Hospital of Sri Lanka
[2]MBBS, MD, FRCP, Consultant Physician, Sri Jayawardenapura General Hospital, Sri Lanka
[3]MBBS, Registrar in Oncology, National Cancer Institute, Sri Lanka

Abstract: *DMS exposure by inhalation damages pharynx, larynx and lower airways. We report a case related to DMS exposure leading to RADS. A 37 year old man admitted to Emergency Department with dry cough, severe burning sensation of throat, mild dyspnoea, photophobia and hoarseness following accidental exposure to DMS vapor. His temperature was 38.1^{0}C and had pharyngeal redness, B/L conjunctivitis, excessive cholinergic activity. Fluid therapy and Oxygen were initiated. he became progressively drowsy and respiratory signs & symptoms got exacerbated. Basal haziness of right lung and vascular prominence of lung hilum was evident on chest x-ray (CXR). Patient clinically improved over next two weeks. But his respiratory symptoms persisted for further 6 months. Owing to above criteria this was interpreted as RADS following exposure to DMS vapor.*

1. Introduction

DMS is an oily liquid without a color. It has an onion-like odor and easily vaporize at room temperature. This methylation agent is used in organic synthesis. It also uses as a solvent, stabilizer, sulfonation agent or catalyst. Final products of DMS are surfactants, pesticides, dyes, perfumes and flavors. We also encounter it in some pharmaceuticals and water treatment units. It's use as a war gas is also well evident. Due to the aforesaid qualities, exposure to DMS has been mainly reported at workplaces via inhalation or skin contact. Acute exposure to DMS vapor will cause inhalation injury to the upper and lower air-passages. Effects could be short or long-lasting. Literature on human DMS poisoning is scarce [1]. There have been no case reports related to the DMS exposure in Sri Lanka to date and here we report the first such case in Sri Lanka.

2. Case Report

A 37 years old previously healthy man presented to the Emergency Treatment Unit (ETU) of Sri Jayawardenapura General Hospital, Sri Lanka following an unexpected exposure to the DMS vapor. He was working in a perfume industry and while trying to test a sample from a DMS contained bottle, was broken and exposed to the vapor. He had no symptoms initially and had not taken medical advice until 2 hours. His past medical history is free of asthma and atopy. On admission to ETU, he was awake and alert. His main complains were dyspnoea, dry cough, hoarseness and photophobia. His vitals were: BP 115/85mmHg, PR 94/ min, RR 28/min and temperature 38^{0}C. On examination, pharynx was inflamed and there were features of conjunctivitis and cholinergic symptoms such as diaphoresis, coryza, miosis and lacrimation. Lungs were full of rhonchi. Further examination of the throat shows marked oedema and pallor of the soft palate and larynx, uvula was edematous, elongated and appeared white in color. The first Arterial blood gas analysis showed O2 saturation of 88% in room air, PaO2 of 53 mmHg, and PCo2 of 30.1 mmHg. He responded to 6 liters/minute of oxygen through face mask and SaO_2 improved to 96%. During the ETU stay, he became progressively drowsy and respiratory symptoms deteriorated. Basal haziness of right lung and prominence of vasculature in lung hilum was evident in the CXR (figure 2).
Patient was transferred to the Intensive Care Unit (ICU). Indirect laryngoscopy showed mild swelling of the glottis and oedema of vocal cords. Intravenous steroids (hydrocortisone) was started. Atropine infusion was maintained and titrated to the heart rate and cholinergic symptoms. O_2 via face mask and fluid therapy with normal saline was continued for the first 24 hours. WBC was 20480/ mm3 and CRP was 20 fold elevated. Initial hemo-concentration, neutrophil leukocytosis and 20-fold rise in CRP were obvious in investigation results.

Conjunctivitis, hoarseness and exertional dyspnea were prominent over the second day of admission. Patient had mild fever, bilateral coarse crackles in both lung fields, tachycardia, burning sensation of throat, mouth and retro-sternal region. Para cardiac haziness was evident in CXR and intravenous (IV) co-amoxciclav and metraniadazole were initiated. Patient could not take anything orally due to severe pharyngeal irritation that provoked cough. A nasogastric (NG) tube was inserted and feeding started. Sputum full report revealed >25 pus cells, 25 epithelial cells and Gram positive cocci, but culture was sterile.

On fourth day of admission patient clinically improved and transferred to the ward. However, his wheezing, hoarseness of voice and conjunctivitis persisted. After 1 week, CRP became normal. But the conjunctival congestion and hyperemia persisted (Figure 1). However, Ophthalmologist could not find any corneal abrasions. IV methyl prednisolone started on the second day. Bronchoscopy performed on day 14 showed signs of chemical burns in pharynx, larynx, vocal cords with oedema. IV methyl prednisolone dose was increased from 10mg to 12mg daily based on above findings. Supportive care given with oxygen, fluids and nebulization. Patient was improved and discharged on the 16th day of admission. Inhaled steroids and bronchodilators were prescribed on discharge.

Patient was followed up at outpatient clinic 2 weekly for the first month and monthly thereafter. High resolution CT scan of the chest performed at one month showed mild bronchiectasis (figure 4). Lung function tests showed restrictive pattern. Burn scars on pharynx, larynx and vocal cord oedema were less on repeat fiber-optic laryngoscopy (figure 3). Patient was persistently having wheezing, exertional dyspnea and thick scanty white sputum for 3 months. This led to the diagnosis of RADS resulting from exposure to DMS vapor inhalation. Methylprednisolone therapy was continued for 4 months. Hoarseness lasted for 5 months. Laryngeal edema was noticed even in the laryngoscopy performed at 4 months.

3. Discussion

RADS is a form of an occupational asthma evident by sudden onset of asthma following a single exposure to susceptible vapor, fume, or smoke.

The diagnosis is mainly on clinical grounds and exclusion of other possibilities as there is no gold standard method available. It is likely when a person develops acute asthma like symptoms without previous history of broncho-spasms within 24 hours of exposure to an irritant agent. Clinical examination of such victims may show features of acute severe asthma such as accessory muscle usage, hyper inflated lung fields and diffuse rhonchi. Lung function test are not diagnostic but may yield important supportive evidence, mainly obstructive pattern or a significant bronchodilator reversibility response. Although not specific, a positive methacholine test would give strong evidence to support the diagnosis. Our patient had restrictive type lung function tests and CT showed features of mild bronchiectasis which was quite different from previously reported cases. Diagnostic criteria for the RADS include; absence of previous respiratory disease, sudden onset of symptoms following a single exposure or accident, exposure to a very high concentrations of susceptible agents, symptoms within 24 hours after an exposure, persistence of symptoms more than three months, predominance of asthma like symptoms such as cough, wheezing and dyspnea, obstructive pattern on lung functions tests and exclusion of other pulmonary conditions [15].

Chemicals that are causing RADS is highly variable. Systemic review by Shakeri MS et al. shows large information gaps in identifying the causative agents. Choline is the most commonly reported agent followed by toluene di-isocyanite (TDI) and nitrogen oxides. Other important agents are ammonia, detergents, formaldehyde, polyurathane and sulphar dioxide. In our patient, the culprit was Dimethyl sulphate. [8]

RADS is closely related to irritant -induced asthma both are forms of asthma which resulted from non-immunologic provocation of bronchial hyper responsiveness. Irritant induced asthma was first described during first world war combatants in early 20th century. [10]

Classical example for an exposure related chronic cough is "world trade center cough" described among fire fighters during the collapse of world trade center. This group was exposed to various dust, chemicals and fumes during the recue battle. Prezant DJ et al. evaluated 332 firefighters who exposed during collapse and concluded that exposure to material generated during collapse of the world trade center was associated with bronchial hyper responsiveness and development of cough [12]. Our patient inhaled saturated vapor of DMS for a very short period and had cough and respiratory symptoms for 6 months which prevented him going for work for 3 months.

There are several hypotheses on pathogenesis of RADS. One relates it to the extensive inflammation following short-term exposure which might then alter receptor thresholds of airways leading to non-specific bronchial hyperactivity. Some think it directly damage bronchial mucosa leading to local release of mediators which causes smooth muscle hyper-responsiveness and broncho-spasms [16].

What are the pathologic features of RADS? Bronchial biopsy data at the time of exposure are

limited. Lemiere C et al. report that these histopathologic abnormalities due to exposure are partially reversible [13].

Our patient developed symptoms after a very short contact period with the high concentrated vapor. Patient opened a half filled large bottle containing DMS which was fully saturated with DMS vapor. Other person next to our client had only minor contact and only had eye symptoms for few hours. Initial signs of acute toxicity are inflammation of eyes, nose, oropharynx, and airways as in our patient. Other reported ones are the edema of airways, mucosal necrosis and non-cardiac pulmonary edema. Involvement of Central nervous system, Liver, renal impairment and heart failure also can occur. In our patient, there was no liver derangement and WBC and CRP became normal within one week. Bronchoscopic findings can be utilized as a diagnostic tool and patient follow up . According to the Rippy et al. delayed toxicity with DMS can occur without any prior warning. Symptoms may be delayed up to 6 – 24 h. This might lead to unnoticed exposure to lethal quantities of DMS [17]. In our patient, symptoms started within 2 hours, and became more obvious after 12 h. However, currently there is no consensus regarding the definitive 'threshold limit value' for the DMS exposure.

RADS is managed with minimal available evidence. In most cases, patients had been treated with intravenous or oral corticosteroids and high-dose inhaled corticosteroids. Bronchial hyper-reactivity need to be monitored closely. Based on the clinical response, inhaled corticosteroids can be tapered off. The response to treatment and time to resolve the symptoms may vary from months to years [14].

In our patient, it took 5 months to regain an acceptable level pulmonary function with steroids and 13 months for a complete improvement.

4. Conclusion

This report emphasizes the importance of protective measures specially in chemical workers. In case of an accidental exposure to DMS, immediate evacuation of victim from the site to fresh air is highly important. It is advised that the contaminated area should be cleaned up using a vacuum device with closed disposal container to minimize dust generation. In addition, defining 'threshold limit values' for inhalational agents and clear criteria for compensation regarding such exposures should be implemented at national level.

5. Acknowledgement

The Authors would like to acknowledge all the doctors, nursing staff and other staff of the ETU, ICU and general medical ward of General hospital, Sri Jayawardenapura for their invaluable contributions to patient management. And also, the patient and her family members, for their support and consent for publishing this case report.

6. References

[1]. Aghabiklooei A, Zamani, Nasim; S, Hamidreza, Rezaei N. Indian Journal of Occupational and Environmental Medicine, Vol. 14, No. 3, 2010, pp. 104-106

[2]. U.S. Environmental protection agency. Integrated risk information system (IRIS) on dimethyl sulfate. National center for environmental assessment, office of research and development. Washington, DC: 1999.

[3]. U.S. Department of Health and Human Services. Hazardous Substances Data Bank. National Library of Medicine, National Toxicology Information Program. Bethesda, MD: 1993.

[4]. Lung Injuries Including Reactive Airways Dysfunction Syndrome (RADS) Available from: [last accessed on 2010 Jul 20]

[5]. Hannu T, Riihimäki V, Piirilä R. Reactive airway dysfunction syndrome (RADS) in a chemistry teacher induced by fumes of mixed iodine compounds. Ind Health. 2009; 47:681–4.

[6]. Khalid I, Godfrey AM, Ouellette DR. Chemical pneumonitis and subsequent reactive airways dysfunction syndrome after a single exposure to a household product: A case report. J Med Case Reports. 2009; 3:112.

[7]. W. Michael Alberts, MD, FCCP; and Guillermo A. do Pico, MD, FCCP. Reactive Airways Dysfunction Syndrome. journal.publications.chestnet.org 1996; 109:1618-26)6

[8]. Shakeri MS, Dick FD, Ayres JG. Which agents cause reactive airways dysfunction syndrome (RADS)? A systematic review. Occup Med (Lond) 2008; 58:205–11. doi: 10.1093/occmed/kqn013. PubMed PMID: 18308694. [PubMed]

[9]. Franzblau A, Sahakian N. Asthma following household exposure to hydrofluoric acid. Am J Ind Med.2003; 44:321–4. doi: 10.1002/ajim.10274. PubMed PMID: 12929153. [PubMed]

[10]. Gautrin D, Bernstein IL, Brooks SM, Henneberger PK. Reactive airways dysfunction syndrome and irritant-induced asthma. In: Bernstein IL, Chan-Yeung M, Malo J-L, Bernstein DI, editors. Asthma in the workplace. 3rd ed. New York: Taylor & Francis; 2006. pp. 581–630.

[11]. Brooks SM, Fox RW, Giovinco-Barbas J, et al: Irritant-induced asthma: role of allergic diathesis in pathogenesis. Am Rev Respir Dis 147(suppl): A378, 1993.

[12]. Prezant DJ, Weiden M, Banauch GI, McGuinness G, Rom WN, Aldrich TK, et al. Cough and bronchial responsiveness in firefighters at the World Trade Center site. N Engl J Med. 2002; 347:806–15. doi: 10.1056/NEJMoa021300. PubMed PMID: 12226151. [PubMed]

[13]. Lemiere C, Malo J-L, Boutet M. Reactive airways dysfunction syndrome due to chlorine: sequential bronchial biopsies and functional assessment. Eur. Resp. J. 1997;10:241–244.doi:10.1183/09031936.97.10010241. [PubMed] [Cross Ref]

[14]. Malo JL, Cartier A, Boulet LP, L'Archeveque J, Saint-Denis F, Bherer L, Courteau JP. Bronchial hyperresponsiveness can improve while spirometry plateaus two to three years after repeated exposure to chlorine causing respiratory symptoms. Am J Respir Crit Care Med. 1994; 150:1142. [PubMed]

[15]. Chan-Yeung M, Alberts WM, Balmes JR, et al: Assessment of Asthma in the Workplace. Chest 108:1084-1117, 1995.

[16]. Alberts WM, Brooks SM: Reactive airways dysfunction syndrome. Curr Opin Pulm Med 2:104-110, 1996.

[17]. Rippey JC, Stallwood MI. Nine cases odf accidental exposure to dimethyle sulfate- a potential chemical weapon. Emerg Med J. 2005; 22:878–9. [PMC free article] [PubMed]

Figure-1

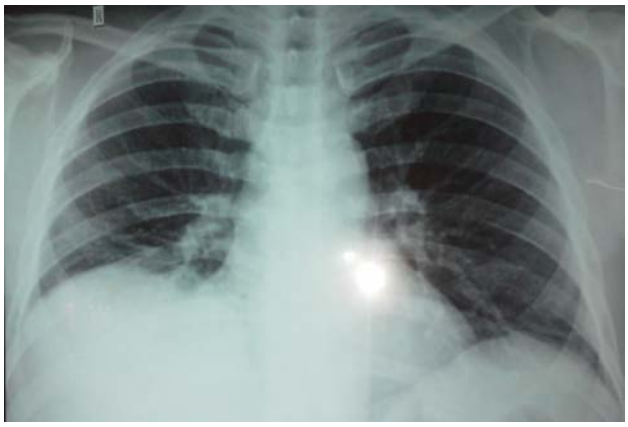

Figure-2

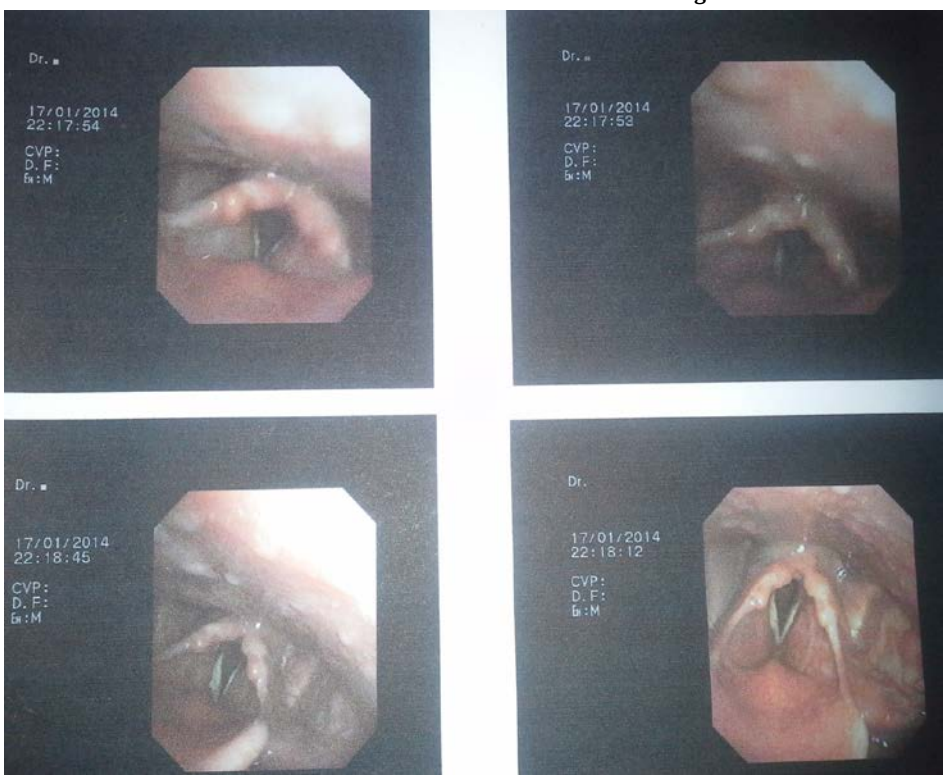

Figure-3

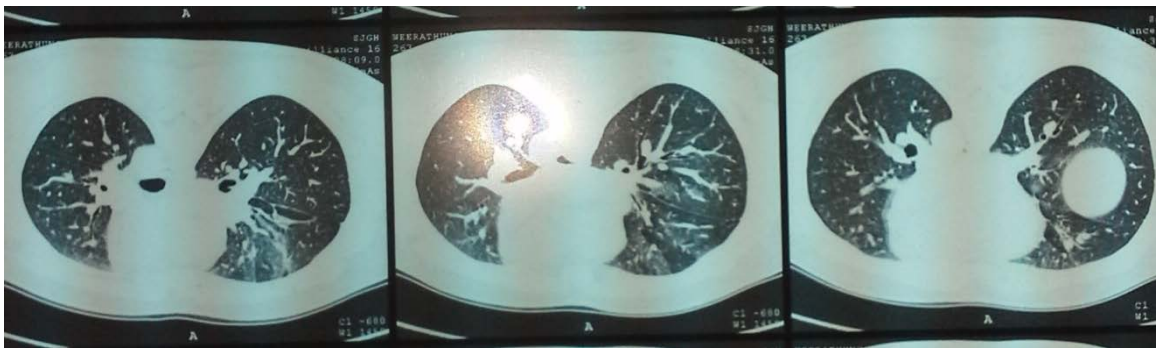

Figure-4