568 Letters to Editor

large nerve fibers is also seen<sup>[9]</sup>. Skin biopsy could be suggested as a second line confirmatory exam for CIPA.

It should be noted that rule out of the common disorders by the strongest possible evidences should be considered as the first step in diagnosis. Although the clinical manifestations of the presented cases are compatible with CIPA, having a confirmatory paraclinic data is also needed, especially because of lack of suggestive family history and rare prevalence of this syndrome. For definite diagnosis of CIPA, genetic analysis of the NTRK gene, as the most powerful confirmatory laboratory test. could be recommended in suspicious cases.

## References

- 1. Daneshjou K, Jafarieh H, Raieskarami SR. Congenital insensitivity to pain and anhydrosis (CIPA) syndrome; a report of 4 cases. *Iran J Pediatr* 2012;22(3):412-6.
- 2. Ali N, Sharma S, Sharma S, et al. Congenital insensitivity to pain with anhidrosis (HSAN type IV), extremely rare syndrome that can be easily missed by bone and joint surgeons: a case report. *Iran J Pediatr* 2012;22(4):559-563.
- 3. Sayyahfar S, Chavoshzadeh Z, Khaledi M, et al. Congenital insensitivity to pain with anhidrosis presenting with palmoplantar keratoderma. *Ped Dermatol* 2012; in press.
- Axelrod FB, Gold-von Simson G. Hereditary sensory and autonomic neuropathies: types II, III, and IV. Orphanet J Rare Dis 2007; 2:39.
- 5. Lafreniere RG, MacDonald ML, Dube MP, et al. Identification of a novel gene (HSN2) causing hereditary sensory and autonomic neuropathy type II through the study of Canadian genetic isolates. *Am J Hum Genet* 2004; 74:1064-73.
- Bar-On E, Floman Y, Sagiv S, et al. Orthopaedic manifestations of familial dysautonomia: A review of one hundred and thirty six patients. *J Bone Joint Surg Am* 2000; 82-A:1563-70.
- 7. Barbacid M. Structural and functional properties of the TRK family of neurotrophin receptors. *Ann NY Acad Sci* 1995; 766:442-58.
- 8. Indo Y, Tsuruta M, Hayashida Y, et al. Mutations in the TRKA/NGF receptor gene in patients with congenital insensitivity to pain with anhidrosis. *Nat Genet* 1998; 13:485-8.
- Rosemberg S, Marie SKN, Kliemann S. Congenital insensitivity to pain with anhidrosis (Hereditary sensory and autonomic neuropathy type IV). *Pediatr Neurol* 1994; 11:50-6.

# The Effect of Sulfur Mustard on Victims' Offspring; What Is the Challengeable Issue?

### Bita Najafian<sup>1</sup>, MD; Majid Shohrati<sup>2</sup>, PhD, and Amin Saburi<sup>2\*</sup>, MD

- Pediatrics Department, Faculty of Medicine, Baqiyatallah University of Medical Sciences, Tehran, Iran
- 2. Chemical Injuries Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran

Received: Feb 01, 2012; Accepted: Feb 15, 2012

#### Dear Editor,

We read with interest the Mirsadraee et al's article entitled "Prevalence of Asthma in Children of Chemical Warfare Victims" in the third issue of 2011 [1].

They skillfully reported an interesting investigation about the effect of Mustard Gas (MG) on the victim's offspring. They demonstrated that the asthma was more common amongst children of MG victims compared to the control group. Also they generalized their findings as "chemical agents may increase the prevalence of asthma in the offspring of chemical warfare victims". But it seems that there are some remarks which should be considered before generalizing the results.

Asthma is one of the most common chronic immune based disorders identified with restrictive pattern in pulmonary function test. There are so many factors which promote asthma in children. Exposure to the cigarette smoke can predispose children for asthma or at least one episode of upper respiratory tract infection<sup>[2]</sup>. In the mentioned study, the prevalence of parental smoking in group with MG exposure was significantly higher than in the control group; therefore it can disturb the findings.

Also, the children with low socioeconomic situation are predisposed for asthma<sup>[3]</sup> and because of low physical ability to work and high medication cost, the chemical warfare veterans (CWVs) likely are in low socioeconomic situation. Therefore, the authors should have matched cases for the socioeconomic situation but there is no precise information about it.

E-mail: aminsaburi@yahoo.com

<sup>\*</sup> Corresponding Author; Address: Chemical Injuries Research Center, Baqiyatallah University of Medical Sciences, Mollasadra St, Tehran, Iran

On the other hand, PTSD and other psychiatric disorders are common in CWVs<sup>[4]</sup> and also previous reports demonstrated the association between parental psychiatry distress and offspring asthma<sup>[5]</sup>. It is needed to consider the CWV's psychological status before assessing their children for stress related disorders.

Although there are evidences about the relationship between chemical warfare contact and genomic mutation of multi-potential cells such as spermatogonia<sup>[6]</sup>, report about the offspring's somatic anomaly in parental SM exposure is so limited<sup>[7]</sup>.

Nevertheless, one conflicting evidence that may question the effects of MG on victims' offspring is the different manifestation in victims and their children which in the mentioned study was considered as asthma. The clinical manifestation of MG lung injury in majority of exposed patients is Bronchiolitis obliterans (BO)<sup>[8]</sup>. The mechanism of BO is related to the chronic inflammation due to deficiency of antioxidants but the well defined mechanism for asthma is immune system imbalance<sup>[9]</sup>.

studies Also, few have pointed cellular/molecular similarities between these two disorders (MG lung injury and asthma)[10]. Recently, the role of glutathione as an antioxidant and therefore its related enzymes such as glutathione S-transferase was discussed in asthma similar to MG lung injury<sup>[9,11]</sup>. On the other hand, the significant role of interleukin-5 and eosinophils (an effective cytokine and immune cell in asthma) in the long term complication of chemical lung injury was identified<sup>[12]</sup>.

The pure impacts of MG regardless concomitant complication must be evaluated in further investigations to confirm its effect on the genome of offspring due to victim's genome mutation in reproductive germ cells. It seems that there are several queries to charge MG as a guilty of victims' offspring sequels. Future investigation should be focused on the genomic evaluation of victim's reproductive germ cells and its relation with offspring disorders regarding the role of gender<sup>[13]</sup> and also duration of exposure<sup>[14]</sup> for adjusting these confounders.

Key words: Sulfur Mustard; Mustard Gas; Asthma

## References

- 1. Mirsadraee M, Mozaffari A, Attaran D. Prevalence of asthma in children of chemical warfare victims. *Iran J Pediatr* 2011;21(3):294-300.
- Shiva F, Nasiri M, Sadeghi B, et al. Effects of passive smoking on common respiratory symptoms in young children. *Acta Paediatr* 2003;92(12):1394-7.
- 3. Chen E, Strunk RC, Trethewey A, et al. Resilience in low-socioeconomic-status children with asthma: adaptations to stress. *J Allergy Clin Immunol* 2011;128(5):970-6.
- 4. Ebadi A, Ahmadi F, Ghanei M, et al. Spirituality: a key factor in coping among Iranians chronically affected by mustard gas in the disaster of war. *Nurs Health Sci* 2009;11(4): 344-50.
- 5. Fang F, Hoglund CO, Arck P, et al. Maternal bereavement and childhood asthma-analyses in two large samples of Swedish children. *PLoS One* 2011; 6(11):e27202.
- Amirzargar MA, Yavangi M, Rahnavardi M, et al. Chronic mustard toxicity on the testis: a historical cohort study two decades after exposure. *Int J Androl* 2009;32(4):411-6.
- Abolghasemi H, Radfar MH, Rambod M, et al. Childhood physical abnormalities following paternal exposure to sulfur mustard gas in Iran: a case-control study. Confl Health 2010; 4:13.
- 8. Ghanei M, Harandi AA. Long term consequences from exposure to sulfur mustard: a review. *Inhal Toxicol* 2007;19(5):451-6.
- 9. Shohrati M, Ghanei M, Shamspour N, et al. Glutathione and malondialdehyde levels in late pulmonary complications of sulfur mustard intoxication. *Lung* 2010;188(1):77-83.
- 10. Mirsadraee M, Attaran D, Boskabady MH, et al. Airway hyperresponsiveness to methacholine in chemical warfare victims. *Respiration* 2005; 72(5):523-8.
- 11. Schroer KT, Gibson AM, Sivaprasad U, et al. Downregulation of glutathione S-transferase pi in asthma contributes to enhanced oxidative stress. *J Allergy Clin Immunol* 2011;128(3): 539-48.
- 12. Emad A, Emad Y. Relationship between eosinophilia and levels of chemokines (CCL5 and CCL11) and IL-5 in bronchoalveolar lavage fluid of patients with mustard gas-induced pulmonary fibrosis. *J Clin Immunol* 2008;28(4): 298-305.
- 13. Sasser LB, Cushing JA, Dacre JC. Dominant lethal study of sulfur mustard in male and female rats. *J Appl Toxicol* 1993;13(5):359-68.
- 14. Jafari M. Dose- and time-dependent effects of sulfur mustard on antioxidant system in liver and brain of rat. *Toxicology* 2007; 231(1):30-9.