



## A Five-Day-Old Victim of Chemical Terrorism was Exposed to Sulfur Mustard

### Sülfür Mustarda Maruz Kalan Beş Günlük Kimyasal Terörizm Kurbanı

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#### ABSTRACT

Sulfur mustard (SM) is a blistering chemical warfare agent and it has cytotoxic effects on ocular, respiratory, cutaneous, and hematological systems. We presented acute hematological effects of high-dose SM exposure on a five-day-old victim who was exposed to SM in Syria in 2015, during a chemical attack. Following onset of typical ocular, respiratory, and cutaneous symptoms of SM, the patient was evacuated to Türkiye on 18th hour after the exposure with an initial diagnosis of second-degree chemical burn. The patient died on 14th day after the exposure. Severe thrombocytopenia, reactive leucocytosis followed by mild leukopenia, isolated lymphopenia, and anaemia were observed after SM exposure. Besides symptomatic treatment, granulocyte-colony stimulating factor (G-CSF), packed red blood cells transfusions, and platelet transfusions were administered for the treatment of hematological complications. Monitoring hematological indices daily, advanced medical interventions including G-GSF treatment for SM-induced neutropenia, and aggressive resuscitation with multiple blood transfusions could reduce the impact of myelosuppression in victims of SM.

#### Key Words

Sulfur mustard, myelosuppression, chemical terrorism.

#### Öz

Hardal gazı (SM), kabarcıklı bir kimyasal savaş ajanıdır ve oküler, solunum, kutanöz ve hematolojik sistemler üzerinde sitotoksik etkilere sahiptir. 2015 yılında Suriye'de bir kimyasal saldırı sırasında SM'ye maruz kalan beş günlük bir kurbanda; yüksek dozda SM'ye maruz kalmanın akut hematolojik etkilerini sunduk. SM'nin tipik göz, solunum ve deri semptomlarının başlamasının ardından hasta, maruziyetin ardından 18. saatte ikinci derece kimyasal yanık ön tanısıyla ülkemize tahliye edildi. Hasta maruziyetin ardından 14. günde öldü. SM maruziyetinden sonra şiddetli trombositopeni, reaktif lökositoz ve ardından hafif lökopeni, izole lenfopeni ve anemi gözlemlendi. Semptomatik tedavinin yanı sıra hematolojik komplikasyonların tedavisi için granülosit-koloni uyarıcı faktör (G-CSF), paketlenmiş kırmızı kan hücresi transfüzyonları ve trombosit transfüzyonları uygulandı. Hematolojik indekslerin günlük olarak izlenmesi, SM kaynaklı nötropeni için G-GSF tedavisi dahil ileri tıbbi müdahaleler ve çoklu kan transfüzyonu ile agresif resüsitasyon, SM kurbanlarında miyelosupresyonun etkisini azaltabilir.

#### Anahtar Kelimeler

Hardal gazı, miyelosupresyon, kimyasal terörizm.

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## INTRODUCTION

Sulfur mustard (SM) is a blistering chemical warfare agent which was first used during World War I. In more recent history, SM was also used against thousands of Iranians during the Iran-Iraq War in the 1980s [1]. There were at least two reported chemical terrorist attacks which SM was used against civilians in North Syria in 2015 and 2016 [2, 3]. SM is an alkylating agent, and its cytotoxic effects are responsible for acute ocular, respiratory, cutaneous symptoms and hematological signs of SM exposure [1, 4].

In our previous study, we reported a family who was exposed to SM in Syria. One of them, a five-day-old girl died on 14th d after SM exposure [2]. The aim of this study is focused on describing acute toxic effects of SM on hematological parameters in a severely exposed infant. The study was approved by Gulhane Ethics Committee of University of Health Sciences, Ankara, Türkiye (19/50).

## MATERIALS and METHODS

A family of four was exposed to SM in Syria in 2015 during a chemical attack initiated by non-state actors. The family was evacuated to Türkiye 18 h after the exposure with a preliminary diagnosis of second-degree chemical burn. The case, a five-day-old infant, had bilateral conjunctivitis, photophobia, oropharyngeal edema, rhinorrhea, and productive cough during admission. She also exhibited erythema, extensive edema, and blisters (Figure 1), which affected 46% of her total body surface area (TBSA). She was transferred to a neonatal intensive care unit (NICU) in Gaziantep on 3rd d following the exposure [2]. She was hospitalized in NICU with leucopenia, and moderate lymphocytopenia.

During the NICU stay, antibiotic eye drops (gentamicin) were applied for eye lesions. Rifamycin S.V., mupirocin 2%, and fucidic acid 2% were used topically for the treatment of cutaneous lesions. She received ventilatory support due to respiration failure. Intravenous amino acids and lipids, minimal enteral nutrition with supplemented formulas were used for supporting the nutrition. Fluid and electrolyte replacement were monitored and assessed daily. Histamine-2 receptor antagonist (ranitidine) was used for stress ulcer prophylaxis.

The effects of SM on main hematological parameters

of the patient including white blood cell (WBC) counts, neutrophil counts, lymphocyte counts, hemoglobin (Hb) levels, and platelet counts are shown respectively (Figure 2).

The patient was admitted to the hospital on 18th h following SM exposure with leukocytosis ( $18.5 \times 10^3 \mu\text{L}$ ), neutrophilia ( $15.8 \times 10^3 \mu\text{L}$ ), and isolated lymphopenia ( $0.428 \times 10^3 \mu\text{L}$ ). However, reactive leukocytosis was followed by significant leucopenia and the lowest WBC count was noted as  $1.23 \times 10^3 \mu\text{L}$  on 7th d.

Although an initial neutrophilia was observed at 18th h, neutrophil count dramatically decreased at the end of 24th h. Neutrophil count reduced 98% in the first week and it was noted as  $0.30 \times 10^3 \mu\text{L}$  on 8th day. Following granulocyte-colony stimulating factor (G-CSF); filgrastim treatment on 7th, 8th, and 9th d following the exposure, neutrophil count was  $10.73 \times 10^3 \mu\text{L}$  on 12th d but it again decreased to  $8.25 \times 10^3 \mu\text{L}$  on 14th d.

Anemia is another main acute hematological effect of SM exposure. After SM exposure, Hb levels decreased approximately 50%. The lowest Hb level was reported as 8.5 g/dL on 7th d. Several packed red blood cells (RBC) transfusions were administered on 7th, 10th, and 14th d for the resolution of symptomatic anemia. We observed the initial effect of RBC transfusion on 8th d. Hb level was still below the normal range until the end of 14th d despite additional RBC transfusions.

Severe thrombocytopenia was defined as a platelet count of  $50 \times 10^3 \mu\text{L}$  for neonates and a platelet count less than  $30 \times 10^3 \mu\text{L}$  was reported as a major criterion for platelet transfusion [5]. A 96% reduction ( $452 \times 10^3 \mu\text{L} > 22.5 \times 10^3 \mu\text{L}$ ) in platelet count was noted on 7th d and multiple platelet transfusions were given on 8th, 9th, 10th, 12th, and 14th d after the exposure. However, platelet count depression occurred in the next seven days despite multiple platelet transfusions and severe thrombocytopenia was observed until patient death on day 14 after SM exposure.

## DISCUSSION and CONCLUSION

Although bone marrow suppression is the most serious effect of SM poisoning, it is rarely seen but it causes higher mortality rates due to aplastic or ineffective hematopoiesis and severe immunosuppression [1, 4, 6]. SM has dose-dependent acute toxic effects on rapidly

proliferating cells in the bone marrow and the existence of the myelosuppression, which is a significant indicator of poor prognosis is an early complication of high-dose SM exposure ( $>1000 \text{ mg} \cdot \text{min}/\text{m}^3$ ) [7].

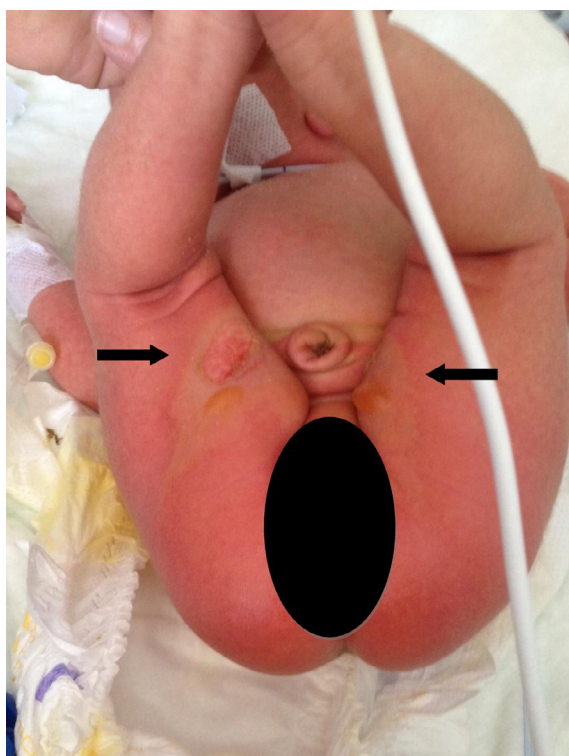
After SM exposure in humans, bone marrow function is suppressed by alkylation of DNA strands and this pathological mechanism leads to impaired cell repair mechanism which causes several hematological complications including leukopenia, thrombocytopenia, and anemia following initial leukocytosis [4].

In our previous study, we observed initial neutrophilic leukocytosis and notable isolated lymphopenia (100%) which were followed by thrombocytopenia (75%), anemia (62.5%), and leukopenia/neutropenia (37.5%) respectively in SM-exposed patients ( $n=17$ ) [6, 8]. However, in our case, all hematologic complications including thrombocytopenia, anemia, and leukopenia/neutropenia were developed simultaneously around 7th d and the chronology of hematological complications was not incompatible with previous reports on victims who were exposed to SM in First World War and in Iran-Iraq War. High dose exposure of SM which caused early onset of severe pancytopenia, could be the reason for this phenomenon. For this reason, we concluded that cases

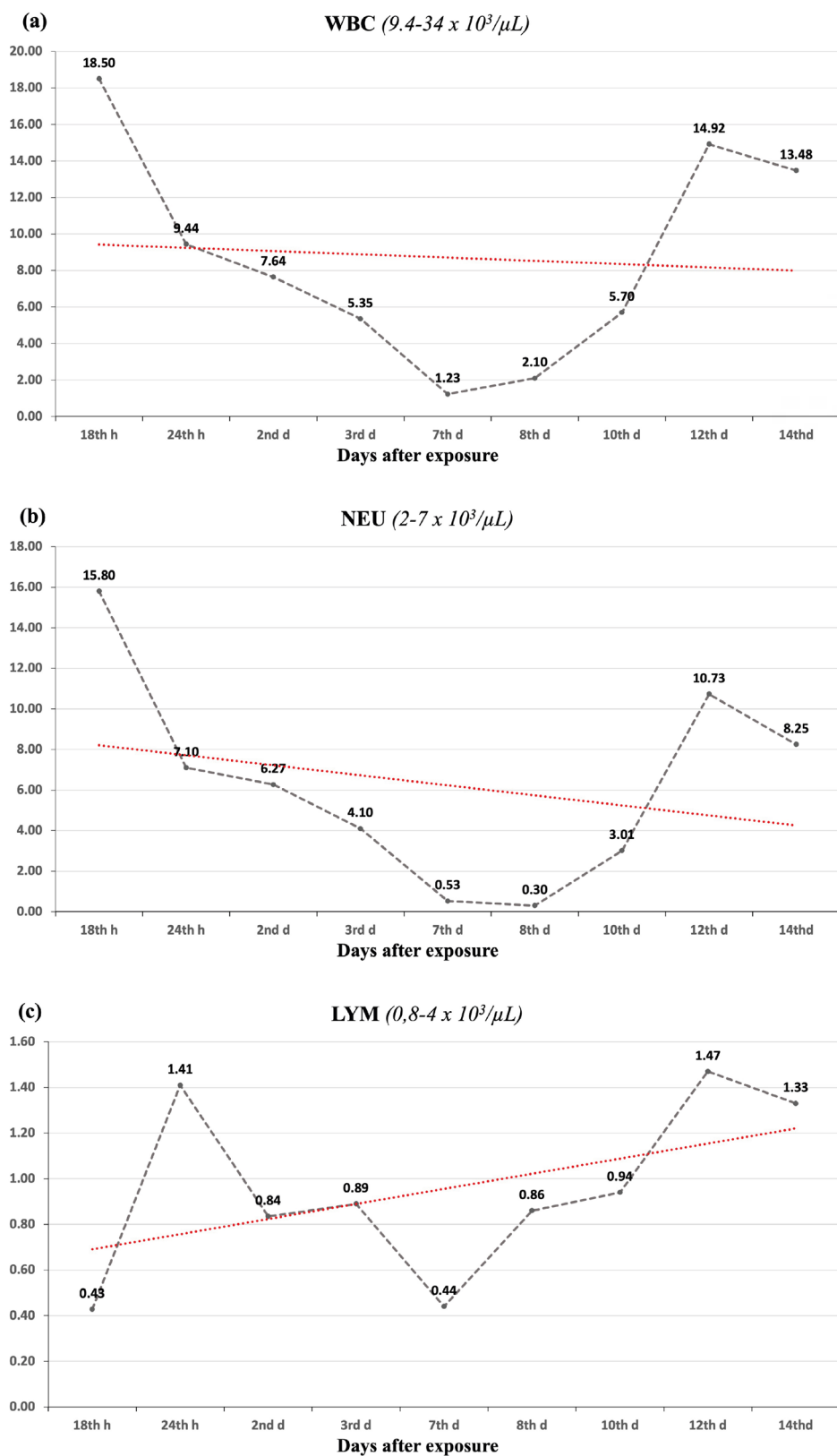
who were assumed to be exposed to more than  $1000 \text{ mg} \cdot \text{min}/\text{m}^3$  SM dose, should be followed daily with whole blood counts for the early diagnosis of pancytopenia which causes immunosuppression.

It was stated that clinical application of G-CSF in chemotherapy-induced myelosuppression reduced the duration of both severe neutropenia and antibiotic therapy, and the total hospital stay length of hospitalization [9]. We also concluded that G-CSF should be administered as soon as possible when neutrophil counts started to decline because early administration could increase survival rates by reducing the duration of neutropenia and possibility of septic shock.

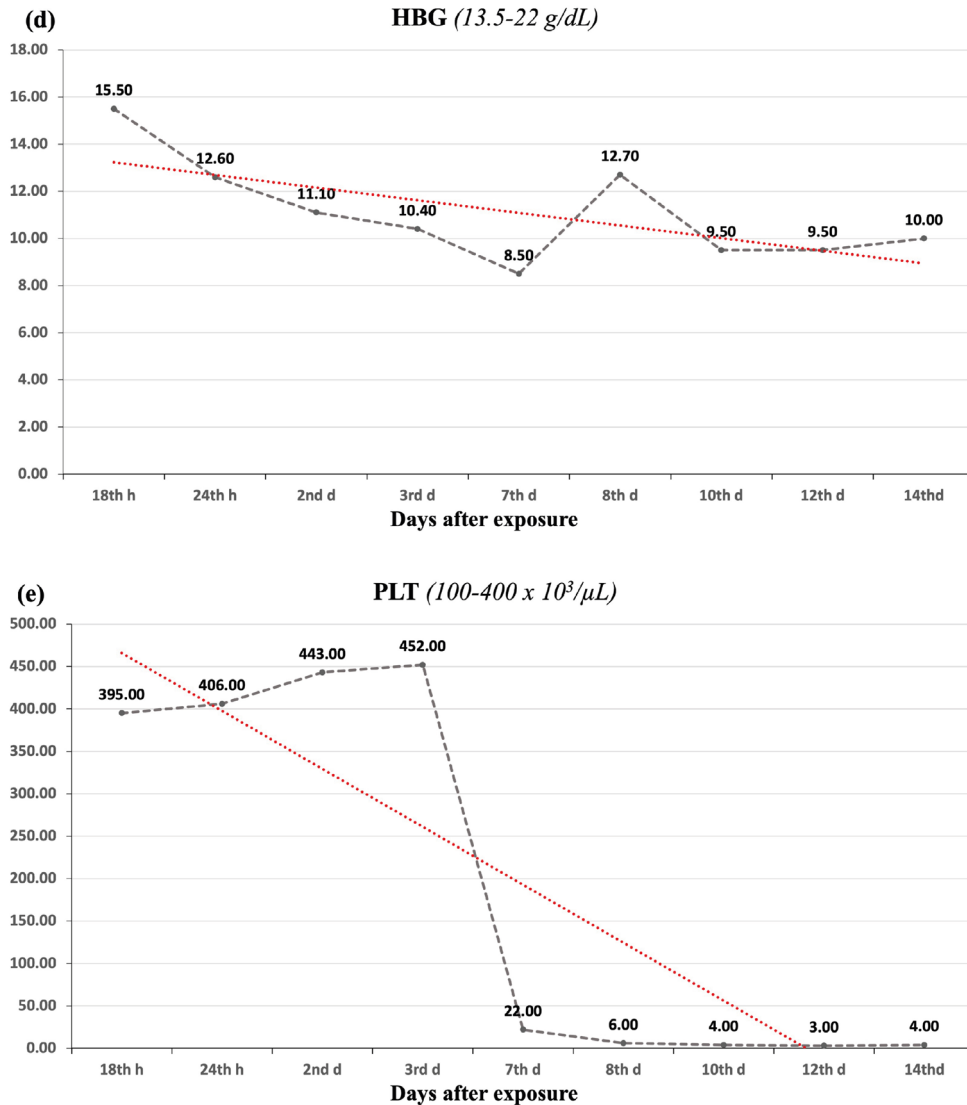
The case survived only two weeks after SM exposure. It was concluded that severe myelosuppression and fluid/electrolyte imbalance due to extensive burn predisposed cardiorespiratory arrest. Treatment of fatal hematological complications of SM exposure is still a big challenge for health professionals and recent studies showed that daily monitoring of hematological indices, advanced medical interventions including G-CSF treatment for SM-induced neutropenia, and aggressive fluid resuscitation with multiple blood transfusions could reduce the impact of myelosuppression in victims of SM.



**Figure 1.** Typical cutaneous symptoms (erythema and blisters) 18 h after SM exposure.



**Figure 2.** The time-course of hematological findings of SM exposure including (a) WBC counts (b) neutrophil counts (c) lymphocyte counts (d) Hb levels, (e) platelet counts during the intensive care stay. Continue



**Figure 2.** The time-course of hematological findings of SM exposure including (a) WBC counts (b) neutrophil counts (c) lymphocyte counts (d) Hb levels, (e) platelet counts during the intensive care stay.

### Conflict of Interest

The authors report no conflict of interest.

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