

Mustard Gas Induced Ocular Injuries

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Mustard gas is a lipophilic, highly cytotoxic agent that rapidly penetrates tissue, and the eye is one of the organs mostly affected,^[1] but skin, respiratory, gastrointestinal, and renal systems as well as the bone marrow may also be affected.^[2] Mustard gas related ocular injuries can be divided into immediate, chronic, and delayed-onset phases. Acute manifestations of varying degrees, including eyelid erythema and edema, chemosis, subconjunctival hemorrhage, epithelial edema, punctate erosions, and corneal epithelial defects, develop in 75–90% of exposed individuals and can follow three different courses: complete resolution, persistent smoldering inflammation (chronic form), or reappearance of lesions after a latent period of quiescence (delayed form).^[3,4]

Late complications, developing after 1 to 40 years, can cause progressive and permanent reduction in visual acuity and even blindness, and they occur in approximately 0.5% of those initially severely wounded.^[2,3] A wide range of late ocular involvements have been reported, which include chronic blepharitis, decreased tear meniscus, conjunctival vessel tortuosity, limbal ischemia and stem cell deficiency (LSCD), corneal scarring and neovascularization, thinning, epithelial irregularity, recurrent or persistent epithelial defects, and secondary degenerative changes including lipid/amyloid deposits.^[2,3,5]

The management of the acute phase is relatively straightforward, chiefly consisting of symptomatic therapy to address the patient's discomfort and ocular inflammation. This approach includes topical antibiotics, preservative-free lubricants, and anti-inflammatory agents. Topical steroids and non-steroidal anti-inflammatory drugs are found to be beneficial in ameliorating the initial inflammatory response and in postponing the development of corneal neovascularization, when given during the first week after exposure.

However, to date, no definitive treatment for delayed-onset mustard gas induced keratitis (MGK) is available. Therapy is tailored based on the type and severity of involvements and varies from symptomatic treatment to surgical interventions for dry eye, corneal epithelial instability, limbal stem cell deficiency, and

corneal opacity. According to our experience, we initially performed only penetrating keratoplasty (PKP) and observed relatively acceptable outcomes, especially when corneal opacity is centrally located, and there is no severe limbal involvement. However, in cases demonstrating severe dry eye, limbal ischemia, or peripheral corneal involvements, a high rate of graft failure due to rejection reactions or opacity was noted. Our subsequent study confirmed that limbal stem cell deficiency can develop after exposure to mustard gas.^[6] This observation led us to make efforts to address ocular surface abnormalities using punctal plaque, punctal occlusion, temporary or permanent tarsorrhaphy, and stem cell transplantations. At first, limbal stem cells were harvested from first-degree relatives, including parents, siblings, or children (living-related conjunctival-limbal allograft; lrCLAL). However, we noticed that lrCLAL cannot provide adequate corneal and scleral lamellae, and cadaveric eyes should also be available if tectonic graft is needed. Therefore, the technique of limbal stem cell transplantation was changed to keratolimbal allograft (KLAL), which can provide more stem cells. Another advantage worth mentioning is that KLAL makes it possible to harvest corneal and limbal blocks from the same donor, if both transplantations are to be performed simultaneously, reducing the antigenic load to the recipient's immune system. Additionally, we have learned that the majority of corneal involvements are limited to the anterior stroma, leaving the posterior stroma and endothelium relatively intact.^[7] Therefore, the routine practice in our center is to carry out lamellar keratoplasty (LKP) for corneal involvements and KLAL for LSCD, which can be performed simultaneously or sequentially. When indicated, performing both operations at the same time can reduce the number of operations and anesthesia, which is a significant concern in patients with respiratory problems and inherent anesthesia induced risks. Additionally, during a simultaneous operation, only one donor can be used to provide both corneal and stem cells, hence reducing the load of antigens presented to the recipient's immune system. For this reason, and as LKP eliminates the risk of graft failure secondary to endothelial rejection reactions,

the outcomes of sequential and simultaneous LKP and KLAL may not differ.

Another important issue is the systemic chemotherapy in patients who undergo stem cell transplantation. Different agents, including systemic cyclosporine A (Sandimmune; Novartis Pharma, Tokyo, Japan), tacrolimus, and mycophenolate mofetil (CellCept, Hoffmann La Roche, Nutley, NJ) are started at the time of surgery. The dose is reduced after 6 months and discontinued after 1–1.5 years, according to condition. Cell blood counts, blood pressure, and renal and liver function tests are monitored at appropriate intervals in collaboration with a kidney transplant expert to monitor for possible complications of immunosuppressive therapy.

Our center has been involved in the management of the majority of mustard gas victims with ocular involvements since 1980, and more than 250 patients with chronic and delayed-onset MGK, who were wounded during the Iraq-Iran war, are now registered in our hospital. Our experience in the management of MGK and the lack of international guidelines led us to prepare guidelines for the prevention, diagnosis, and treatment of MGK. In these guidelines, which were written by our team, we try to share our experience with other local and international ophthalmologists who are involved in the management of victims of mustard gas.^[8]

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