

A Case of Skin Necrosis after Extravasation of Intravenous Immunoglobulin

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Abstract

Extravasation of certain drugs can make an injury on the injection site. It occurs more often in the fragile skin of children and old people. Immunoglobulin treats immune-mediated diseases effectively, such as a primary deficiency of antibodies or autoimmune diseases. A 9 months old boy came to hospital complaining of a fever for 5 days. He had bilateral non-purulent conjunctival injection, erythema of the lips and rashes on the hands and feet. On the echocardiography, the left coronary artery was dilated. He was diagnosed with Kawasaki disease. We started an intravenous immunoglobulin injection. After 7 hours, edema and a change in skin color appeared at the intravenous injection site on his right hand. We removed the catheter and applied a cold pack. Under impression of phlebitis, we applied Mupirocin ointment and Prednicarbate ointment with a dressing, twice a day. Within an outpatient follow up period, a skin necrosis with pus emerged. Coagulase negative *Staphylococcus* was detected from the pus by microbial culture study. We referred the patient to the Department of Plastic Surgery, and operated a debridement of the skin necrosis and a full thickness skin graft. He was discharged from hospital without a certain problem. The lesion was cured and left a scar. There was no recurrence or exacerbation on the skin graft lesion within a follow up period of 6 months since the surgery. We report a rare case of skin necrosis after extravasation of intravenous immunoglobulin, which had not been reported in Korea before.

Keywords: Extravasation; Intravenous immunoglobulin; Skin necrosis; Skin graft

Introduction

Intravenous drugs can cause extravasation injuries around the route of vessel [1]. Not only commonly used fluid such as normal saline and dextrose water, but also electrolytes, calcium, anticancer drugs are causes of these injuries [2,3]. The extravasation happens more in children whose blood vessels are small and cannot express their pain and in the elderly whose blood vessels and skin are fragile [4].

Immunoglobulin is used for treatment for many diseases such as primary immunodeficiency disease or autoimmune diseases [5]. However, it has transient side effects, such as fever, headache, myalgia, back pain, chill, nausea, flush, rash and et cetera. More severe side effects rarely happen, such as hemolysis, neutropenia, aseptic meningitis, anaphylactic reaction, thromboembolism and et cetera [5-7]. Skin side effects reported after using IVIG are reported such as eczema, alopecia, erythema multiforme, lichenoid dermatitis, pompholyx [8,9]. There have been two case reports of the skin necrosis after the intravenous immunoglobulin extravasation in worldwide, one is from Australia and the other is from New Zealand [10,11].

We report a case of the skin necrosis after the intravenous immunoglobulin extravasation.

Case

A 9 month old boy came to hospital complaining of a fever for 5 days. He had bilateral conjunctival injection, erythema of the lips and rashes on his hands and feet. On the echocardiography, the left coronary artery was dilated to 2.9 mm. He was diagnosed with Kawasaki disease. We started an intravenous immunoglobulin injection 2 g/kg for 12 hours. After 7 hours, edema and a change in skin color appeared at the intravenous injection site on his right hand. We removed the catheter and applied a cold pack, and resumed the intravenous injection at another site. The other site did not show any changes of the skin condition.

The patient did not have any history of skin disease or allergy. The lesion on the right hand still remained, so we had examined by a

dermatologist. Under the impression that he had developed phlebitis on his right hand, we applied Mupirocin ointment and Prednicarbate ointment with a dressing, twice a day. During the outpatient follow up period, a skin necrosis with pus emerged (Figure 1). The culture study of the pus proved coagulase negative *Staphylococcus*. We referred the patient to the Department of Plastic Surgery, and operated a debridement of the skin necrosis and a full thickness skin graft. In first step surgery, surgeons removed the necrotic tissue and applied Alloderm on the lesion (Figures 2 and 3). Eight days after, they gained a skin graft from the patient's left inguinal area and attached it to the lesion on his right hand (Figure 4). He was discharged from hospital without any problem. The lesion was cured and left a scar (Figure 5). One month after the onset of Kawasaki disease, the diameter of the



Figure 1: The lesion after intravenous immunoglobulin extravasation was covered by the eschar. It had pus and skin necrosis.

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Figure 2: The eschar was removed.



Figure 3: Debridement of the lesion was completed. We measured the extent of the lesion, the diameter was 18 mm.



Figure 4: We operated a full-thickness skin graft on the lesion. This picture shows the condition of the lesion just after the skin graft.



Figure 5: The lesion was healed 15 days after the skin graft.

patient's left coronary artery was normalized to 2.5 mm in the follow-up echocardiography. There was no recurrence or exacerbation of the skin graft lesion within a follow up period of 6 months since the surgery [12-22].

Discussion

Tissue injuries due to the extravasation of intravenous drugs

show a variety of features, from edema and redness to infection and necrosis [1,4,12]. When fluids such as normal saline or dextrose water extravasate and cause edema or redness, almost all lesions improve to normal conditions after conservative management [1,12]. However, when anticancer drugs or electrolyte extravasate and delay in treatment, it can make the tissue injury worse. In that situation, debridement of necrotic tissue and skin graft surgery may be needed [4,13,14].

The extravasation happens more in children and the elderly. The skin and vessels are fragile in the elderly and children have small vessels and they cannot express their pain, so these conditions bring more risk to them. They also make skin and vessels weak and extravasate frequently happens if the patient is taking anticoagulants or steroids. Patients who have cardiovascular disease, diabetes mellitus, or cancer are also at risk because their vessels are also weak and fragile to injury [4].

Prevention is important to keep off extravasation of tissue injuries. The intravenous injection site should be checked every day. Clean dressing around the intravenous injection site is needed when it is contaminated [4,14]. It is better to pierce the vein once when making an intravenous route. Piercing several times making holes and injuries in the vein increases the possibility of extravasation, because drugs can extravasate via the hole in the vessel [10]. Compression between the intravenous injection site and the proximal part should be avoided. Compression causes the reflux of blood stream and extravasation [4,10].

The ideal injection site is the forearm [15]. Small vessels cannot endure the velocity of intravenous drugs, so large and straight vessels are preferred. Injecting near the joint area should be avoided because the catheter can be displaced to the wrong place by the patient's activity, or it can hurt nerves and tendons [4].

If edema or redness is noticed near the catheter insertion site or the patient expresses pain enough that extravasation is doubted, conservative management should be started. Apply a cold pack or warm pack and raise the lesion. Most lesions improve appropriately by these methods [4,14]. It is recommended that subcutaneous injections of hyalurodinase and normal saline to wash out the lesion when anticancer drugs or electrolyte extravasate [4,13,14]. In most cases, conservative management was applied first, and then if the infection or skin necrosis was getting worse, treatment was broadened to dressing, pus drainage, debridement of necrotic tissue and skin graft [1,10,12]. No scar was left when the lesion recovered only by conservative treatment. In contrast, surgical treatment left scars and a few resulted loss of tendon or nerve [1,10].

If the patient has residual pain two weeks after extravasation or if there is minimal healing two to three weeks after injury, despite local therapies already done, surgical intervention is recommended in the preceding study [16]. If anticancer drugs extravasates, the lesion should be treated and watched to see whether it causes skin necrosis or infections for 24 hours [17]. If the patient expresses pain on the extravasation site of vesicant anticancer drug, it is an indication for immediate surgery [15,18].

Intravenous Immunoglobulin is composed of 95% of Immunoglobulin G and a small amount of IgA, IgM and albumin [19]. Intravenous Immunoglobulin has immunomodulating activities from diverse mechanism. It modulates complement activation, saturates Fc receptors on macrophages, suppresses idiotypic antibodies and various inflammatory mediators, including cytokines, chemokines, and metalloproteinases [20].

Immunoglobulin is prescribed in diverse diseases such as autoimmune diseases like idiopathic thrombocytopenic purpura, primary immunodeficiency disease, and Kawasaki disease [5,21,22]. Common side effects of immunoglobulin treatment are transient light inflammatory responses, including headaches, chills, flushness, back pain, nausea [6,7]. However, severe systematic responses including hemolysis, neutropenia, aseptic meningitis, anaphylactic reaction, thromboembolic diseases can also happen in 2~6% [5,6]. Hyperosmolar immunoglobulin containing sucrose as a base rarely causes renal failure and aseptic meningitis has a relationship with a past history of migraines [22]. Skin side effects after using IVIG are reported such as eczema, alopecia, erythema multiforme, lichenoid dermatitis, pompholyx [8,9].

This rare case was skin necrosis after extravasation of intravenous immunoglobulin to treat Kawasaki disease. Intravenous injection is the basic procedure to inpatient treatment and most common approach to vessel. Most extravasations recover fully without a major problem, so they are passed over and less concerned. Delayed or inappropriate treatments after extravasation can bring infections or skin necrosis, even surgical treatment such as skin grafting may be performed. Impaired functioning due to loss of the tendons or nerves rarely happens. Therefore, continuous observation and caution is obligatory whether extravasation has occurred or not during intravenous drug injections and immediate catheter removal and conservative treatment performed if extravasation occurs. It is recommended to establish the treatment guidelines for extravasation to prevent scar and dysfunction on the affected site.

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