A MAJOR BURN INJURY IN A LIVER TRANSPLANT PATIENT

BRÛLURE GRAVE CHEZ UNE TRANSPLANTÉE HÉPATIQUE

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SUMMARY. Immunosuppressive therapy may aggravate the clinical course of a burned patient, primarily affecting wound healing and thus complicating permanent wound coverage. We hereby present the successful management of a 48-year-old female liver transplant recipient with a major burn injury, aiming to elucidate the effects of the patient's immunosuppression on surgical treatment. After admission to the Burns ITU, the patient underwent serial debridement of the burn and coverage with cryopreserved allografts. Despite immunosuppression, no prolonged survival of the allo-epidermis was documented. Nevertheless, a variable degree of vascularized allo-dermis was clinically identified. She subsequently underwent skin autografting and was discharged home with most of the wounds healed. Although there are isolated reports of survival of skin allografts in immunocompromised patients, in our case the allografted skin did not provide permanent wound coverage. However, it permitted a staged surgical management, allowing the immunosuppressive regime to change, the skin donor sites to heal and it also provided a dermal scaffold for successful skin autografting.

Keywords: immunosuppressive therapy, burn injury, liver transplant, allografts

RÉSUMÉ. *Un traitement immunosuppresseur peut obérer l'évolution d'un brûlé, en raison de ses interactions avec la cicatrisation. Nous présentons la prise en charge couronnée de succès d'une patiente de 48 ans transplantée hépatique victime d'une brûlure grave, dans le but de faire le point sur la relation traitement chirurgical/chirurgie du brûlé au stade aigu. Après son admission en réanimation pour brûlés, la patiente a bénéficié de plusieurs séances d'excision/allogreffe. Malgré le traitement immunosuppresseur, les allogreffes ne sont pas restées en place plus longtemps. Cependant, une vascularisation, à un degré variable, de l'alloderme a été cliniquement observée. Elle a pu retourner à son domicile après autogreffes, les brûlures quasiment entièrement cicatrisées. Au contraire de quelques rapports d'intégration d'allogreffes chez des patients immunodéprimés, celles de notre patiente ont été rejetées. Elles ont toutefois tenu suffisamment longtemps pour permettre un changement de l'état immunitaire, la guérison des sites donneurs et le développement d'un sous-sol apte à recevoir les autogreffes.*

Mots-clés: *traitement immunosuppresseur, brûlure, transplantée hépatique, allogreffes*

Introduction

Immunosuppressant drugs adversely influence the wound-healing process by interacting with some of the inflammatory mediators.[1]

Thus, immunosuppressive therapy may seriously aggravate the clinical course of a burned patient. Most importantly, it predisposes them to infection and by impairing wound healing complicates permanent wound coverage.[1]

We hereby present the successful treatment of a liver transplanted patient with a major burn injury, aiming to elucidate the effects of immunosuppression on its therapeutic management.

Case report

A 48-year-old female was acutely admitted to the St Andrew's Burns ITU after she sustained a flame burn at her home. She had had a liver transplant in 2009 for alcoholic cirrhosis and she was under immunosuppressive treatment with Sirolimus. She was also suffering from paroxysmal atrial fibrillation, dilated cardiomyopathy, alcoholism (8-10 units/day), depression and anxiety.

The mechanism of injury was that her dress caught fire while she was cooking. Although her husband was present when the incident happened, the patient refused any first aid.

The primary survey revealed a 26% TBSA, mixed-depth burn to her left arm and hand, chest, abdomen, thighs and legs *(Fig. 1)*. Resuscitation started on admission, using the Parkland's formula. Additionally, the burn wounds were cleaned and appropriately dressed.

The following day, under advice from the Liver Transplant Unit, Sirolimus was discontinued because it severely impairs wound healing.[1,2] Furthermore, her immunosuppressive regime was changed to Azathioprine and Prednisolone.

She also had tangential excision of the burns and coverage of the wounds with meshed cryopreserved allografts. On the 10th day post-admission, she underwent further debridement and replacement of the allografts.

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Table I - Clinical events during the patient's stay in the Burns ITU and Burns Rehabilitation Ward

DATE	CLINICAL EVENT	IMMUNOSUPPRESSIVE THERAPY	LOCATION
DAY 1	Admission	Sirolimus 1mg	Burns ITU
DAY 2	Debridement & allografting	Azathioprine 75mg & Prednisolone 20mg	Burns ITU
DAY 10	Debridement & allografting	Azathioprine 75mg & Prednisolone 20mg	Burns ITU
DAY 14	Skin biopsies	Azathioprine 75mg & Prednisolone 20mg	Burns ITU
DAY 16	Admission to burns rehabilitation ward	Azathioprine 75mg & Prednisolone 20mg	Burns rehabilitation ward
DAY 28	Skin biopsies	Azathioprine 75mg & Prednisolone 20mg	Burns rehabilitation ward
DAY 31	Autografting: lower extremities & re-allografting: trunk, left arm	Azathioprine 75mg & Prednisolone 20mg	Burns rehabilitation ward
DAY 60	Pulmonary sepsis & re-admission to burns ITU	Azathioprine 75mg & Prednisolone 10mg	Burns ITU
DAY 62	Debridement & autografting: trunk, left arm	Azathioprine 75mg & Prednisolone 10mg	Burns ITU
DAY 68	Re-admission to burns rehabilitation ward	Azathioprine 75mg & Prednisolone 10mg	Burns rehabilitation ward
DAY 88	Discharged home	Azathioprine 75mg & Prednisolone 10mg	Burns rehabilitation ward

Fig. 1 - The patient at the time of presentation. Note the thickness of the burn injury.

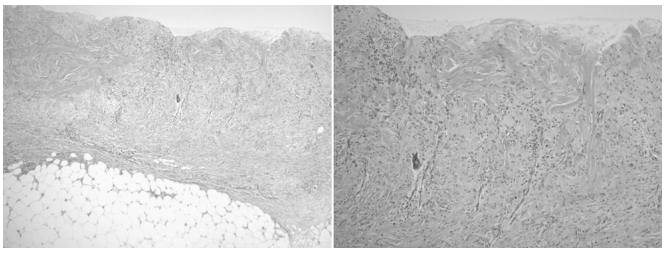

Fig. 2 - Histological appearance: loss of epidermis but there is evidence of dermis neovascularisation.

Fig. 3 - The patient at the second follow up appointment, 4 months post-discharge.

There are a few reports in literature of human skin allografts surviving and providing definitive coverage in immunocompromised patients.[3,4,5] Our team was hoping for a similar result. Despite the severe immunosuppression, no prolonged survival of the allo-epidermis was documented. However, a variable degree of vascularized allo-dermis was clinically identified.

The skin-allografts covered the patient's wounds for nearly 3 weeks (from day 10 to day 31 post-admission), while skin biopsies were taken four and eighteen days after the second application of allografts (day 14 and day 28 post-admission) (*Table I*). The histological examination confirmed the clinical picture with allograft rejection but with a variable degree of neovascularisation of the allodermis *(Fig. 2)*.

One month post-admission, on day 31, she underwent skin autografting of the lower extremities and re-allografting of the trunk and left arm.

Unfortunately her course was complicated by a sepsis episode that was attributed to pulmonary infection and not to wound sepsis. After one month, (on day 62 post-admission), and with sepsis successfully resolved, she underwent excision of the allografts and autografting of the remaining areas.

During the last two operations, allogeneic keratinocyte solutions were employed to both grafted and skin donor sites in order to accelerate re-epithelialization.[6]

The autografts on her lower extremities were completely healed after one month while the healing of her donor sites from the first autografting operation was further delayed.

Both autografts and donor sites from the second operation healed faster.

The patient was discharged home with most of her wounds healed. She remains under follow-up as an outpatient and no further reconstructive issues have been addressed so far *(Fig. 3)*. Her clinical course is summarised in *Table I*.

Discussion

To the best of our knowledge, this is the first reported case of successful management of a significant burn injury in a liver transplanted patient.

The patient suffered a flame injury at her home and surprisingly did not seek medical aid promptly after the accident. This can be explained either by her being intoxicated at the time of the injury or by reduced sensation in her abdominal wall. This is a known complication of liver transplantation surgery where T8 and T9 intercostal branches are divided during the subcostal incision.[7]

The immunosuppressive therapy was promptly changed after the patient was admitted and she remained stable during the first two months (*Table I*). Prednisolone was gradually reduced after the septic episode.

After debridement of all her burns, the patient's wounds were covered with cryopreserved skin allografts. The allografts were initially replaced 8 days after the first application while new allografts were applied on her trunk and left arm 3 weeks after the second application.

The use of skin allografts is an established way to provide temporary wound coverage. It minimises electrolyte and fluid loss, decreases wound pain and promotes reepithelialisation by providing dermal elements into the burn wound.[8]

The patient could certainly have been similarly managed by using skin autografts alone. However, a staged approach was decided with application of cryopreserved allografts.

The bibliography is inconclusive regarding immunosuppression and survival of skin allografts[9] and there are a few reports where the skin allografts survived in cases of immunocompromised burned patients.[3,4,5]

We were undeniably hoping for allograft survival when we opted for a staged management. This approach was justified, as the patient had received a liver transplant and had severe immunosuppression. Nevertheless, in our case, allografts did not provide permanent wound coverage. However, they permitted a staged surgical management, allowing the immunosuppressive regime to change, the skin donor sites to heal and they also provided a dermal scaffold for skin autografting.

Moreover, the median time between donation of the cryopreserved allografts and surgical application was 14.4 months. There are reports that suggest that the viability of cryopreserved skin allografts decreases over time.[10,11] This could explain the failure of our allografting as the median age of the allograft sheets which were applied was more than 12 months.

Overall, definitive skin cover was delayed to allow the unfavourable effects of Sirolimus on wound healing[2] to be gradually minimized. It has been suggested that Sirolimus prevents fibroblast proliferation and inhibits angiogenesis.[12] Furthermore, this delay permitted us to medically optimize the patient prior to every single surgical treatment.

During the last two autografting operations, allogeneic keratinocytes were applied to both grafted and donor areas aimed at enhancing healing. Although recent studies support this method as a useful adjunct in the surgical treatment of burns,[6] in our case it was not documented or proved that the usage of allogeneic keratinocytes accelerated wound healing.

Conclusion

Concluding, we would like to underline that immunosuppression transmits to the already frail burned patient an additional morbidity factor by increasing susceptibility to infections, wound sepsis and delayed healing. Prompt treatment, both surgical and medical, as well as a multidisciplinary approach to such complex cases, will positively influence the final prognosis.

We favour the use of allografts in burned patients with significant comorbidities because they allow for staged procedures, providing us with the time required to augment the patient's general conditions.

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