Case Report

Seven Cases of Cultured Epidermal Autograft (JACE®) for Giant Congenital Melanocytic Nevus after Removal by Electric Dermatome and CO₂ Laser

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ABSTRACT

Giant congenital melanocytic nevus (GCMN) must be treated from the point of view of either cosmetics or the risk of malignancy. Since 2016, cultured epidermal autograft (JACE®) for GCMN has been covered by insurance in Japan, but there are few reports on its usefulness and postoperative course.

We performed excision of the nevus with electric dermatome and CO₂ laser excision, followed by cultured epidermal autograft in seven cases and 11 sites of GCMN in the extremities and trunks. In all cases, 90% of the grafts engrafted and became epithelialized in about one week. All cases showed a reduction in the brown color of the nevus. Recurrence occurred in one site, and hypertrophic scar formation was found in the wound after transplantation in six cases. While cultured epidermal transplantation for GCMN can more safely reduce color tone with a small donor size compared to the conventional procedure, it remains necessary to determine how to reduce the risk of complications such as recurrent nevi and hypertrophic scar formation.

Key words: cultured epidermal autograft, giant congenital melanocytic nevus, skin transplantation

Introduction

Giant congenital melanocytic nevus (GCMN) is generally defined as a nevus with a diameter of ≥ 20 cm in adults and ≥ 6 cm on the trunk or ≥ 9 cm on the head in neonates.

The morbidity rate is between 1/20,000 and 1/500,000. The risk of transformation from GCMN to malignant melanoma is between 0 and 3.8%, half of which will occur by the age of three years, and the prognosis after onset is poor. Therefore, it is critical to begin treatment as early as possible. In addition to the possibility of malignant transformation, GCMN patients must consider the cosmetic risks.

GCMN is often difficult to excise simply because of its size. Abrasion by CO₂ laser and disruption of melanin or Q-switched yttrium aluminum garnet (YAG) laser, which is commonly used for the treatment of pigmented nevus, requires at least one week for re-epithelialization after treatment, and post-inflammatory pigmentation can also occur. In addition, melanocytes in the skin remain, and it is considered difficult to completely remove the color. Alternatively, skin grafts may be selected, but new scars can be created at the donor site. Dermatome and curettage may be performed especially on newborns, but, as with lasers, re-epithelialization takes time and carries the risk of infection.

In Japan, the cultured epidermal autograft (JACE®; Japan Tissue Engineering Co. Ltd., Gamagori, Japan) was approved for coverage by public health insurance in 2007 for burns exceeding 30% of the body surface area. Beginning in 2016, its application expanded to GCMN.

We have previously transplanted an enzymatically separated epidermal skin sheet graft, after the excision of GCMN with an electric dermatome. Based on this experience, in the cases presented herein, GCMN was removed by dermatome until the color tone was completely improved, at which point a cultured epidermal autograft was performed. Only a few cases of the transplantation of cultured epidermal autograft for GCMN have been reported, and there have been no reports on the effects or postoperative courses in multiple cases. Herein, we report seven cases of GCMN on the extremity and...
trunk treated with transplanted cultured epidermis autografts.

Patients and methods

Patients

From June to December 2017, we examined cases in which cultured epidermal autograft was performed for GCMN at our own facility. Eleven sites of cultured epidermal transplantation were performed on seven patients, with three males and four females. Patient age ranged from 1 year 8 months to 9 years 1 month, with an average age of 6 year 4 months. None of the patients had other complications involving intraparenchymal or intrathecal melanin deposits in the central nervous system. Informed consent was later obtained from the patients’ parents.

Methods

Skin removal for the purpose of creating a cultured epidermis and removal of the GCMN and transplantation were performed independently.

To create a cultured epidermis, the normal skin of the abdomen was cut under general anesthesia, using a template, for a total size of 2 cm × 2 cm, and the donor part was simply sutured. The collected skin was immersed in 70% ethanol and stored, and a cultured epidermis was created at Japan Tissue Engineering Co., Ltd. (Gamagori, Japan).

Approximately one month after skin removal, GCMN removal and cultured epidermal autograft were performed. Under general anesthesia, the nevus lesion was removed as much as possible with an electric dermatome and a CO₂ laser. Nevus excision using an electric dermatome was performed at 350–450 µm until the color of the nevus was completely reduced, and the CO₂ laser was used to evaporate the nevus tissue until the color tone was completely reduced. One case had small nevi scattered elsewhere on the body that were simultaneously removed, and the CO₂ laser was used to remove the GCMN.

With the infant patients, care was taken to minimize blood loss and gauze soaked in epinephrine solution was placed immediately after the pigmented lesions were removed.

The cultured epidermis was 8 cm on the short side × 10 cm on the long side (effective area 80 cm²), placed so as to partially overlap the wound after removal of the nevus and then covered and fixed with a silicone-faced wound dressing (SI-Mesh®, ALCARE Co. Ltd., Tokyo, Japan). The extent of hypertrophic scarring at the treatment site was evaluated in the range of 0–2 points. 0: None, 1: Mild, 2: Severe.

Results

In all cases, more than 90% of the cultured epidermis was engrafted and the color tone was reduced. The grafts healed without infection, and re-epithelialization was observed in about one week. Only one site showed recurrence though the color tone was improved at one month after surgery. Nine sites in six cases had postoperative hypertrophic scars, and two sites had operations of scar contractures that required contracture release. The length of follow-up after the operation ranged from 15–21 months, and the mean length was 18.9 months. All donor wounds healed in one week with no adverse events. A summary of the results is shown in Table 1.

Presentation of representative cases

Case 1 (Pt. number 2 in Table 1)

A three-year-old girl had a GCMN on her back. A partial resection had been performed twice in childhood, but most of
the lesions remained and the scar was enlarged. Under general anesthesia, the entire area was excised with a 300-mm-deep electric dermatome until the brown color disappeared. After excision, the cultured epidermis was transplanted and the engraftment was good. One year after the operation, there was no recurrence of color tone, but hair growth was observed in part of the thigh. There was no hypertrophic scar formation.

Case 2 (Pt. number 5 in Table 1)

A seven-year-old boy had GCMN on his buttock, abdomen, and bilateral thighs. Under general anesthesia, the entire area was resected with an electric dermatome at a depth of 300–450 mm until the brown color disappeared. The operation was performed in two parts, first on the front surface and then on the rear surface. After excision, the cultured epidermis was transplanted and the engraftment was good. There was no recurrence of color tone in the second half of the operation, but the wound formed a hypertrophic scar.

Case 3 (Pt. number 7 in Table 1)

A one-year-old girl had GCMN on her abdomen, back, and bilateral thighs. Under general anesthesia, the entire area was excised with a 300-mm-deep electric dermatome until the brown color disappeared. The operation was performed in two parts, first on the front surface and then on the rear surface. After excision, the cultured epidermis was transplanted and the engraftment was good. There is no recurrence of the nevus, but there is marked hypertrophic scar formation on her back.

Fig. 1. A 3-year-old girl with a GCMN on her back, treated with cultured epidermal autograft. Before treatment (A), after dermabrasion (B), after cultured epidermal transplantation (C), and 1 year after the operation (D). There is no recurrence of the nevus, but there is marked hypertrophic scar formation on her back.

Fig. 2. A 7-year-old boy with a GCMN on his back, buttock, and thigh, treated with cultured epidermal autograft. Before treatment (A) (B), after dermabrasion (C) (D), and half a year after the operation (E) (F). There is no recurrence of nevus, but there is marked hypertrophic scar formation on the groin and buttock.
Discussion

GCMN treatment requires complete color reduction and cosmetic considerations. Since September 2016, JACE has been approved for the treatment of GCMN, which is difficult to address using standard treatments.

All our cases could have been treated by conventional skin grafting, curettage, laser, or reconstructive surgery using a tissue expander. However, previous reports indicate that even if the nevus cells are mechanically removed or reduced by laser treatment, the incidence of cancer at the treatment site does not increase. In addition, reconstruction surgery leaves large scars on normal skin beyond the treatment site, resulting in cosmetic problems. For the above reasons, we opt to remove nevus tissue using an electric dermatome and CO\textsubscript{2} laser with transplantation of cultured epidermal autograft for cases of GCMN.

In the cases with improvement, the engraftment rate was good and there were no adverse events before engraftment. In all cases, the color tone of the nevi was improved, but in one case, recurrence was observed in the transplanted part. Some limitations of this technique include the incomplete improvement of color tone and the risk of recurrence. In GCMN patients, even if all of the skin is removed, the removal procedure may not be complete because nevus cells may be present in adipose tissue or muscle. In almost all cases, the nevus was mainly removed by the dermatome and the color was improved; however, in the case with recurrence, it may have occurred due to remnant nevus cells in the subcutaneous adipose tissue. To determine the removal depth of nevus tissue, the tissue must be analyzed histologically. In addition, the recurrence rates of other devices, including CO\textsubscript{2} lasers, should be investigated.

Another limitation of this procedure is the risk of hypertrophic scar formation. In six cases, postoperative hypertrophic scar formation was observed. Thus far, it has been reported that hypertrophic scar formation is frequently observed in sites where mechanical stress is applied, such as the back and groin. In the case of cultured epidermal autograft, the process of re-epithelialization and wound healing may apply repeated tension to these parts. However, with the combined therapy of curettage and cultured epidermal transplantation, cultured epidermal transplantation has been reported to have a significantly shortened healing time and to prevent hypertrophic scars. It is necessary to further analyze the tendencies of scar formation.

This series of cases suggests that the appropriate indication for cultured epidermal autograft is in cases of shallow nevus, where the nevus tissue has been removed using an appropriate method, avoiding the back, groin, and moving parts that are likely to form scars.

Cases and sites excluded from this indication should be treated with existing GCMN treatments such as simple resection, skin grafting, and expanders.
Conclusion

Cultured epidermal autograft in the treatment of GCMN can be expected to safely improve color tone with fewer donors, but improvements to suppress postoperative hypertrophic scar formation should be made.

Acknowledgments

None.

Conflicts of interest

The authors declare no conflicts of interest associated with this manuscript.

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