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Radical Resection of Giant Congenital Melanocytic Nevus and Reconstruction With Meek-Graft Covered Integra Dermal Template

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Background.
Giant congenital melanocytic nevi represent a surgical challenge, particularly in cases in which the size of the nevus exceeds certain extend and malignant transformations have to be considered.

Objective.
To discuss through case report considerable surgical options when extensive giant congenital melanocytic nevi with malignant transformation are encountered.

Methods.
We present an unusual case of a giant congenital melanocytic nevi of the entire back of a 44-year-old patient. To achieve radical resection with direct appropriate wound closure and acceptable outcome, the integument of the entire back was excised and covered with Integra, followed by split-thickness skin grafting after stable integration of the matrix.

Results.
The approach resulted in a complete excision of the tumor and acceptable cosmetic and excellent biomechanical outcome.

Conclusion.
The introduced practice demonstrates a useful alternative to established methods, particularly if tumor excision in large areas and subsequent wound closure might be achieved in one procedure.

The surgical treatment of giant melanocytic nevi is still challenging, and major reconstructive surgery might be considered in huge tumors. Techniques available include full- and split-thickness skin grafting as one-step procedures, tissue expansion before tumor, excision, and subsequent defect closure in at least two-step procedures. In addition, free tissue transfer can play a role in the reconstruction of delicate areas, and also a combination of these techniques might be a surgical option. In cases in which malignant transformation is evaluated and surgical intervention is urgently required, previously described options cannot be used because of the mandatory long period of prefabrication or extent of defect to be covered. On the other hand, split-thickness skin grafting of these extended areas may result in scar contraction, compromising the patients' quality of life. To circumvent this drawback, a commercially available dermal template was used to graft an excised giant congenital melanocytic nevus area covering the complete back of a patient. Subsequent skin grafting of the integrated template resulted in a good clinical outcome.

The 43-year-old woman was first seen in August 1998. She presented herself with a giant congenital melanocytic nevus of the lumpy-bumpy type, which covered the entire back. The patient complained of a nodule that developed in the nevus. The nodule was excised and revealed a nodular melanoma with an intraepithelial component (Clark level V, infiltration depth 5.0 mm) arising within a congenital melanocytic nevus. Conventional staging procedures, including positron emission tomography, did not demonstrate lymph node involvement or distal metastases at this time. Microsatellite analysis was performed on microdissected tissue as previously described. 1 It demonstrated chromosomal instability in the melanoma, as shown by a loss of heterozygosity at microsatellite marker D9S259. Microsatellite instability (MSI) at marker D14S53 was present in the melanoma as well as in the nevus compartment. In November 1998, we excised a second suspicious area within the congenital nevus, which revealed a superficial spreading melanoma (Clark levels II to III, infiltration depth 0.7 mm). After the last operation, the patient received immunotherapy with interferon-, 3 million IU per week. She was staged on a regular

basis, receiving sonographic examinations of both axillae and inguinal areas. Six months later, two punch biopsies were performed at two different areas of the congenital nevus at the right lumbar region (Figure 1), which again revealed two superficial spreading melanomas that were surgically excised. For further staging, positron emission tomography and nuclear magnetic resonance tomography were performed that demonstrated suspicious findings at the right lateral thorax as well as in the right axilla. The decision was made to excise completely the nevus down to the muscle fascia. The excised nevus measured 30 40 cm, and the resulting defect was completely covered with Integra. Additionally, a radical lymphadenectomy was performed on the right axilla and both inguinal regions. After the operation, the patient had to lie in a prone position to avoid any shearing forces, ensuring the stable integration of the dermal template. Sequentially, punch biopsies were taken to observe the integration and revascularization of the substitute. When the complete maturation of the matrix was observed (Figure 2), split-thickness skin was taken from both thighs 20 days later. After removal of Integra's top silicone layer, grafting of the skin was performed in Meek technique, expansion ratio 1:4 (Figure 3). Multiple small remaining defects had to be covered by repeated Meek grafting 14 days later, resulting in complete healing of the defect. Again, after skin grafting, the patient remained in the prone position until a sufficient confluence of the neoepidermis was observed. Histologic examination of the excised nevus revealed melanoma metastasis in the cranial as well as in the caudal portion. Within the tissue from radical lymphadenectomy, one single lymph node metastasis in the axilla was identified; all other tissue showed no transformation. The grafted area has been carefully followed, but no metastases or local recurrences were observed 2 years after resection and final coverage. When the patient presented the last time, 30 months after grafting, a smooth, highly flexible hypopigmented neo-skin was observed without any signs of wound contraction (Figures 4A,B). The range of motion of both arms was normal, and the patient felt subjectively comfortable. According the Vancouver scar scale, 2 the grafted area was rated 1 (pigmentation 1 point, vascularity 0 points, pliability 0 points, height 0 points).

Melanocytic naevi are believed to develop from epidermal melanocytes that completed their migration from the neural crest to the dermoepidermal junction in fetal life or to arise from dermal melanocytes that became arrested in the dermis during fetal migration and never reached their normal site. Approximately 1% to 6% of all newborns present with congenital melanocytic nevi. In contrast, large or "giant" congenital melanocytic nevi (GCMN) comprising 5% body surface area or greater in infants and more than 20 cm in adolescents and adults are rare birthmarks, as Karvonen et al. 3,4 reported only one case of a GCMN in 4,346 Finnish newborns. Giant congenital melanocytic nevi are associated with a greatly increased risk of malignant transformation, and lifetime risk has been estimated between 4% and 7%. 57 In some cases, the central nervous system can be involved in form of leptomeningeal melanocytosis or neurocutaneous melanosis. 8 Beyond size and the extent of dermal involve-ment, which seem to be correlated to melanoma risk, it has been speculated that GCMNs with irregular surfaces bear a higher risk of malignant transformation and that cellularity, immaturity, and the occurrence of cytologic atypia in GCMN may represent additional risk factors for malignant melanoma. 6

In this case, the giant congenital melanocytic nevus was large and demonstrated an irregular and papillomatous surface. Three malignant melanomas developed within this nevus, which hints to a genetic predisposition for malignant transformation of the nevus cells. A recent study furnished evidence that the occurrence of MSI may distinguish dysplastic from benign acquired melanocytic nevi. 9 Our finding that MSI was present in the nodular melanoma, as well as in the GCMN of the patient, suggests that MSI might be implicated in malignant transformation of genetically unstable GCMN as well.

In cases in which surgical excision is indicated, procedures have to be planned carefully with respect to cosmetic and functional outcome. In the neonatal period, curettage and use of pulsed CO2 laser seem promising with satisfactory results. 10,11

However, this treatment strategy is not applicable in adult patients in which malignant transformation has to be or is already evaluated histologically. Gosain et al. 12 have analyzed their clinical procedures and results in a 20-year retrospective study in order to establish an algorithm of surgical management for giant congenital nevi extending more than 20 cm2. As main surgical "tools," tissue-expanded flaps or grafts, serial excision, and either full-thickness or split-thickness skin grafts can be considered.

When adjacent structures are not distorted, serial excision is the preferred treatment modality for lesions that can be excised in not more than two procedures. 13 Because increased morbidity is often associated with the use of tissue expanders or skin grafts at or just proximal to the knee or elbow joints, serial excision is also preferred for use in these areas. If more than three procedures are required to complete the resection, the former options should be considered. Tissue expansion is recommended for lesions involving the head, neck, or torso, as the reconstructive outcome, particularly in the head and neck, is far superior to that obtained with skin grafting. 14,15 On the other hand, the use of this technique on giant nevi located on arms or legs should be considered carefully because of the restricting circumference of skin envelope, resulting in increased morbidity of the expanded tissue. 12 In these cases, skin grafting is recommended. When extensive regions require more than one set of tissue expanders, a subsequent set of expanders can be inserted at the time of the initial flap advancement. 16 Although a filling delay is necessary, serial expansion is preferable, as it avoids the need for a repeated operation for insertion of tissue expanders. 1719

Full-thickness skin grafts are always preferable to a split-thickness graft for reconstruction of the eyelids or ears. Using expanded flaps or serial excision in these locations often results in distortion of involved structures. Another option is the use of expanded full-thickness grafts when donor skin limitations are problematic. 18,20 Most often, the best outcome can be achieved when using multiple surgical techniques, particularly when the face or biomechanically strained anatomic regions, such as the knee or elbow, are involved. Microsurgical techniques have to be considered to obtain aesthetical and functional reconstruction in various areas. 21

Complete excision with consecutive skin grafting without appropriate substitution of a dermal component can result in severe deformities due to contraction processes. Most of these cases require secondary plastic surgery. 22 To overcome this drawback, a dermal substitute might open new possibilities.

Integra is a dermal substitute that is composed of glycosaminoglycans and chondroitin-6-sulfate, 2325 covered by a silicon layer. The template gained Food and Drug Administration approval in 1996 and was introduced in Germany the same year. Clinical application of the matrix requires at least a two-step procedure: Initially the wound is excised and covered with the dermal equivalent. The upper silicon layer is left in place until complete maturation by ingrowing capillary networks and migrating fibroblasts is achieved. Antiseptic dressing changes have to be performed on a daily basis to ensure clean condition of the wound site. In case of sufficient recapillarization, skin grafting can be performed. Until now, the template has been used mainly in burns and has been proven as a useful tool in stable reconstruction of grafted areas, previously excised down to muscle fascia. 2628 It has been demonstrated that the combined use of Integra and cultured autologous autografts can result in a stable neoskin, circumventing the drawbacks of the cultured epithelium when used without a dermal template. 2931 Besides the use in acute traumatic surgery, Integra is also used in secondary reconstructive surgery. 32

In this case, Integra was the first option in order to allow direct radical excision of the genetically unstable giant congenital melanocytic nevus followed by immediate closure of the wound and resection of the axillary and inguinal lymph nodes. Other options such as tissue expansion would have caused a considerable delay in this situation. Furthermore, the good biomechanical and cosmetic outcome in the presented case makes Integra a conceivable alternative to established approaches in surgical therapy of GCMN. Despite the good outcome, potential users have to keep in mind that the application of Integra requires sophisticated nursing: Until complete biointegration of the template, the patient should be kept in a position that avoids shear forces or pressure that could inhibit rapid revascularization and adhesion of the material. It has to be pointed out that an aseptical technique is mandatory to prevent infection at the wound site. During maturation of the matrix, macroscopic appearance, such as the color of Integra, changes while revascularization is steadily ongoing. The second step of the reconstitution involves skin transplantation. In our case, we decided to use the MEEK grafting technique in order to avoid large donor site defects and related potentially increasing morbidity. The approach presented resulted in a highly satisfactory surgical result with no tumor recurrence since 2 years.

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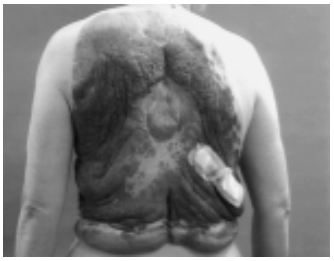


Figure 1. Giant congenital melanocytic nevus covering a patient's back. Situation after performance.....

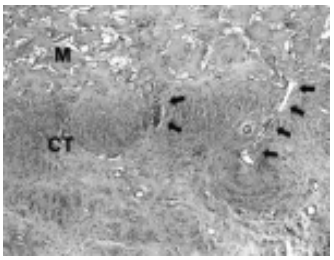


Figure 2. Punch biopsy taken intraoperatively before skin coverage. Integra (M) is stably attached t...

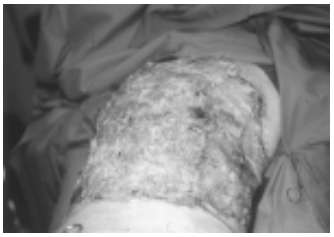
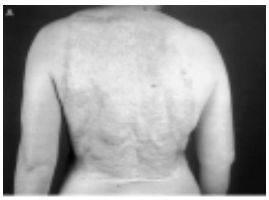


Figure 3. After grafting, the dermal matrix is covered with skin islands attached to silk carriers f...



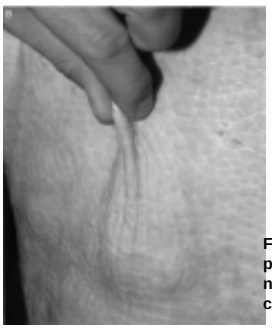


Figure 4. (A) Overall aspect of patient's back 30 months after nevus excision, immediate Integra cov...