The Vitiligo Clinic at the Department of Dermatology, Akademiska Sjukhuset in Uppsala, Sweden

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A special interest in vitiligo research and treatment has since many years been established at the clinic of Dermatology and Venereology, Uppsala University Hospital. A reshape of the reception for vitiligo out-patients was conducted at our clinic in 2004. The main purpose since then is to offer professional advice regarding diagnostical issues and specialised treatment, such as melanocyte transplantations. In order to enrich our knowledge about this group of patients we also do clinical immunological research and aim to further develop the surgical techniques.

Vitiligo is a frequently occurring disease affecting approximately 1% of the population world wide. The most common form, *vitiligo vulgaris*, is symmetrical and the aetiology is believed to be autoimmune. Most often vitiligo is seen as the only disorder in an otherwise healthy individual but sometime it is clearly associated with other autoimmune disorders in the patients themselves and also among other family members. The most frequently seen association is hypothyroidism. More than half of the patients will get their first vitiligo manifestation before 20 years of age and it may lead to life-long suffering as very few of these patients will experience any spontaneous repigmentation. The disease fluctuates with occasional, sudden deteriorations but in general the disease is slowly progressive. In a few severe cases extensive areas will be affected leaving only a few spots still pigmented. Extensive vitiligo is more frequently associated with other autoimmune manifestations and may also be part of an autoimmune polyendocrine syndrome which also may include Addison's disease, diabetes type I, hypoparathyroidism, gonadal insuffiency and a mucocutaneous candidiasis.

The less commonly occurring *segmental vitiligo* engages one or more, non-symmetrical area of the skin representing the extension of a sensory nerve. Some of these patients may experience stress or neurological trauma prior to the first appearance. In contrast to vitiligo vulgaris, this form usually also engages the underlying hair follicles leading to white hairs within the lesions. A common location affected is the extension of one or more of the branches of the trigeminal nerve in the face. Although an inflammatory mechanism may be involved in the aetiology, possibly mediated through pro-inflammatory neuropeptides such as neuropeptide-Y and calcitonin gene-related peptide (CGRP) released at the nerve-endings locally in the skin, segmental vitiligo usually responds poorly to traditional UV-light and anti-inflammatory treatment. Once manifested segmental vitiligo is stable and rarely progrediate or spontaneously regresses.

A not as frequently seen group of patients, which is, however, the most important to identify, consist of people with congenital hypopigmentations. *Piebaldism*, affecting about 1:14.000, equally distributed among men and women and seen in all races, is perhaps the most obvious manifestation of these. Melanocytes are initially derived from the early embryonic nerve system. Dominantly mutated genes may, however, prematurely arrest migration of some melanocytes during fetal development. These patients are then born with white areas usually located on the ventral surfaces of mid parts of the trunk, extremities and head. A white forelock of hair over the mid-frontal scalp is a hallmark of this disease. Successful treatment of this group of patients is only possible by means of autologous melanocyte transplantation which results in life-long and complete repigmentation of all treated areas.

Non-surgical treatment of vitiligo

A great number of different approaches for treating vitiligo have been tried over the years. Still none of these has showed to be curative and few have been proved effective when evaluated in larger studies. So far UV-light treatment and local application of potent glucocorticoids are regarded as the most attractive non-surgical alternatives. The introduction of

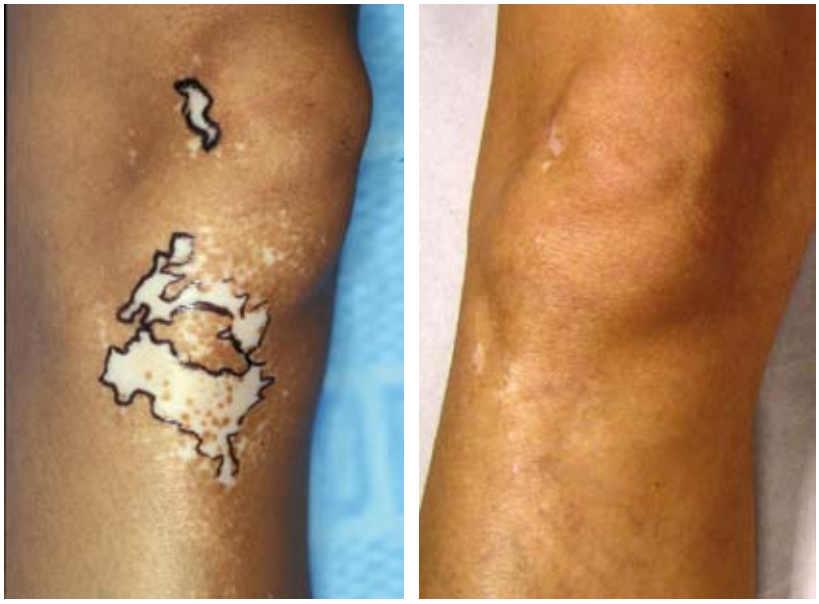

Fig.1. a) Vitiligo lesion on a knee before treatment with autologous melanocyte transplantation. b) The same lesion a few years after the transplantation.

narrow-band UVB (311 nm) and new topical immunomodulators such as tacrolimus (Protopic®) are promising contributions to the treatment procedures. The usage of folic acid and vitamin-B12 has shown to be of no significant benefit to the vast majority of vitiligo patients in recent studies.

Several recent studies have shown advantages in using 311 nm UVB light (TL01) compared to traditional topical PUVA in regard of both side-effects and treatment efficacy and is also considered as effective as tablet-PUVA treatment. The combination of potent topical steroids with UVB is believed to augment the repigmentation, and this combination is frequently used in treatment of generalised symmetrical vitiligo today. Promising results have been reported with topical use of tacrolimus (Protopic®) and pimekrolimus (Elidel®). At our clinic a recent study of 0.1% Protopic® in local immunomodulating management of vitiligo showed good repigmentation of vitiligo lesions in the face in about 80% of the study patients, but poor effect on the body lesions. The treatment is simple and there are no documented severe side-effects in contrast to those seen with local steroid usage. Therefore this treatment is especially suitable for children with vitiligo in the face. Due to documented carcinogenic effects in sun-related skin cancer forms seen with long-term systemic immunomodulating treatments, these drugs, even if administered locally only, should never be combined with UV-light treatment.

Autologous melanocyte transplantation

Transplantations with the patients' own melanocytes have been performed for several years. We have at our clinic, which is one of the pioneer centres for surgical managements in vitiligo, experience of several techniques since about 15 years (1). Melanocytes may be transplanted by use of biopsies, suction blisters, skin transplants or cultured melanocyte suspensions. Since the start some 400 patients have been transplanted at our clinic. Studies have shown the positive value of these methods being an effective, convenient and outpatient-based alternative to conventional treatments on the important condition that suitable patients are selected. Congenital leukodermas such as piebaldism are all successfully treated and the repigmentation is then permanent. Segmental vitiligo also most often results in 100% repigmentation following transplantation. Our experience shows that patients with symmetrical vitiligo showing no sign of activity, i.e. no lesions have grown and no new lesion have appeared during the past two years, also have a good prognosis for repigmentation of the transplanted area (Fig.1). For this group of patients the results, however, are not as good at lesions on knuckles, fingers and feet. We nowadays usually do not transplant these areas.

We have previously published a long-term follow-up study evaluating and comparing three different methods performed in various anatomical locations and different types of leukoderma (2).

Our standard transplantation procedure is performed during a one

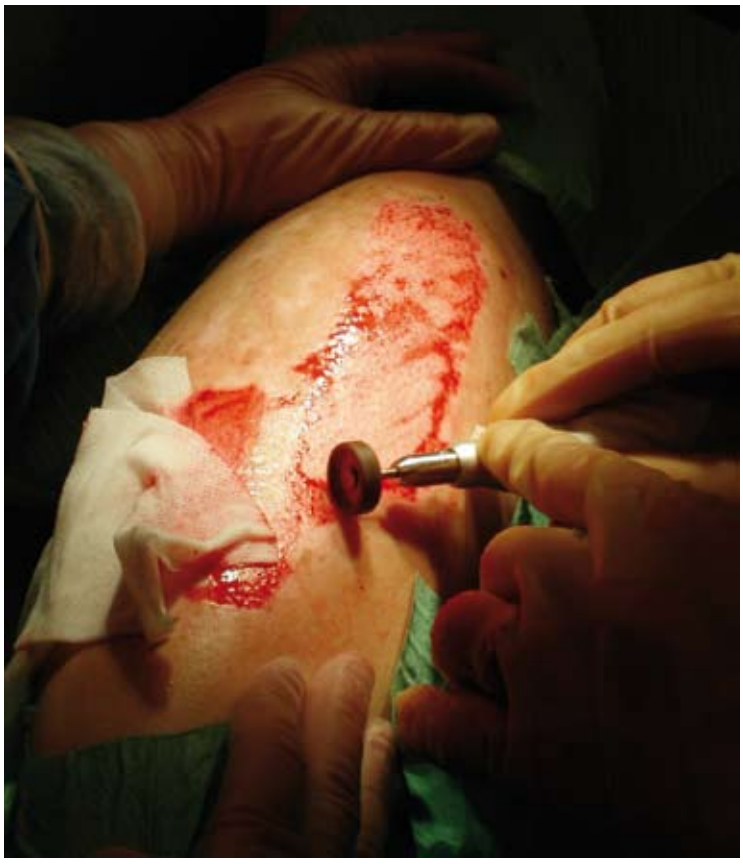

Fig.2. The outermost epidermis down to papillary dermis is removed through dermabrasio.

day visit at the clinic and we usually cover about 150 cm^2 during one session. For this we take a superficial 3x5 cm shave biopsy of normal buttock skin containing the upper epidermis down to the basal membrane level, where the melanocytes are located. The outermost epidermis, down to the basal membrane, is then grinded off at the vitiligo lesion through a dermabrasio procedure (Fig. 2). This is performed under local anaesthesia. The free-prepared melanocytes and basal keratinocytes are then spread over the surface (Fig. 3). The transplantation is completed within a few hours and the patient then rests in the clinic ward during the following first critical hours to make sure the transplanted melanocytes will settle properly. The patient can then leave the hospital, but depending on the location and size of the treated lesions has to restrict movement and be off work for up to eight days. The dressing is removed after 8–9 days and after that no more precautions are usually necessary. Both the donor site and the transplanted area will heal without scar formation and usually with perfect colour match. Extensive vitiligo areas may also be transplanted if the melanocyte fraction is first cultured and expanded for a couple of weeks.

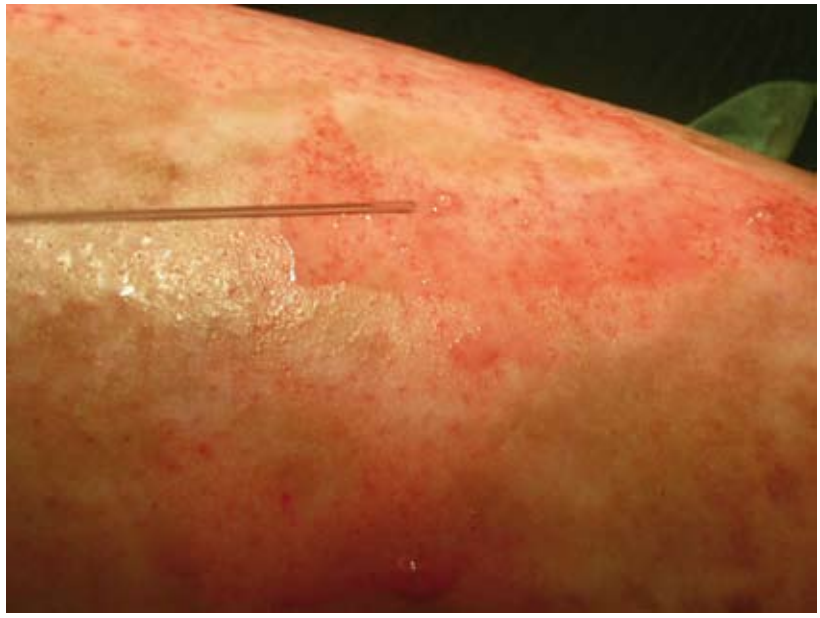

Fig.3. The free-prepared melanocytes are stored in a solution and spread over the prepared vitiligo surface with a Pasteur-pipette.

Research projects

Studies on immunological mechanisms regarding T lymphocytes and autoantibodies are ongoing in our lab since some years back (3). There are possibly further autoantigens related

to vitiligo of potentially prognostic value to be identified. T-cell reactivity against individual autoantigens in patients with vitiligo related to malignant melanoma is furthermore of great importance for future immunological treatment of the malignant disease. New serological activity markers for both malignant melanoma and vitiligo are needed. Animal cohort studies are now starting up at our research department that will come up with possible candidate genes associated to vitiligo. These genes will then be used in screening of the genetic pool built up at our vitiligo reception in order to be able to identify human genes related to the disease. A comparative study of using laser technique versus traditional dermabrasio during vitiligo transplantation has also started.

Information and Patient Support

The demand and pressure from the patients have been quite extensive throughout the years. Many patients have expressed that they get not enough support from the medical care system. Some years ago we therefore founded the Nordic Vitiligo Association (www.vitiligo.nu), to improve this communication, emotionally support the patients and provide a forum.

At an international level the European Vitiligo Task Force (EVTF) was also founded some years ago. This group consists of highly specialised researchers and clinicians in the field of vitiligo. Information about the group and their activities can be accessed through the webpage for the Nordic Vitiligo Association or through our department's vitiligo website (www.medsci.uu.se/dermatology/vitiligo).

References

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