

Chapter 1

Introduction

Somesh Gupta and Nanja van Geel

A young Indian man with an apparently normal-looking face came to the outpatient department and insisted that he had vitiligo on his face, but which was not visible to the naked eye. When he was examined under a Wood's lamp, a quite extensive vitiliginous area of the face was present which was not visible to the naked eye (Fig. 1.1). This presentation is not often observed in pigmented Indian skin, and is more common in a caucasian population. On careful examination, the patient had a pale skin which resulted in a loss of contrast between depigmented and normally pigmented skin, which is known to occur in skin prototypes 1 and 2, but not in Indian skin. Vitiligo can surprise even after decades of experience of examining and treating the disease. Not surprisingly, the disease has been described by many as enigmatic.

Vitiligo is Clinically Visible as Cutaneous Depigmentations

Vitiligo is characterized by depigmentations of the skin, mucosa, and hair. Vitiligo can occur/present with different clinical characteristics, prognosis, response to treatment, and course. Broadly, the disease is classified into a localized and a generalized form, or segmental and the non-segmental type. Though in general skin depigmentation occurs much earlier during the course of the disease as compared to hair depigmentation, an

exceptional presentation has been described recently, including purely follicular vitiligo, in which only hair follicles are involved and inter-follicular epidermis is spared [1].

Vitiligo is a Disease with an Important Psychosocial Impact

The impact of vitiligo on the quality of life is quite comparable to that of psoriasis, and can be worsened by the social stigma of disease in many cultures [2,3]. Young women in many Asian countries can even suffer more due to gender inequality. Similarly, the disease is more of a concern in people with skin of color due to the increased contrast between depigmented and normally pigmented skin. When evaluating vitiligo treatment, psychological aspects such as quality of life should also be taken into consideration.

Figure 1.2 shows the numbers of articles on psoriasis and vitiligo published since 1980. In contrast to psoriasis, however, vitiligo is not covered by medical insurance in most countries, and currently there is no US-Food and Drug Administration (FDA)-approved repigmentation treatment for vitiligo. This has a negative implication on the interest of the pharmaceutical industry in therapeutic research and drug discoveries in vitiligo.

The present book was aimed at filling this gap, and is intended to place vitiligo in the picture/public eye

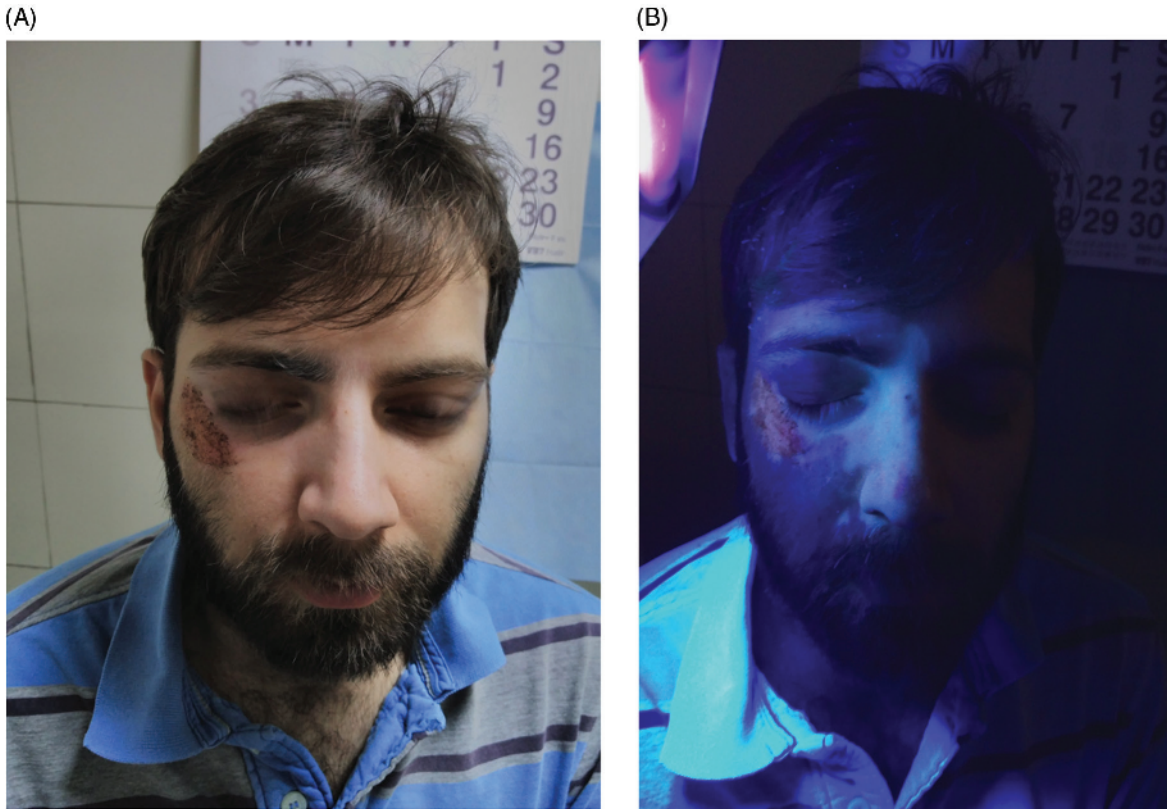


Fig. 1.1 (A) An Indian patient insisted that he had vitiligo on the face, though nothing was visible to the naked eye. (B) On Wood's lamp examination, a segmental vitiligo involving the right upper half of the face became apparent.

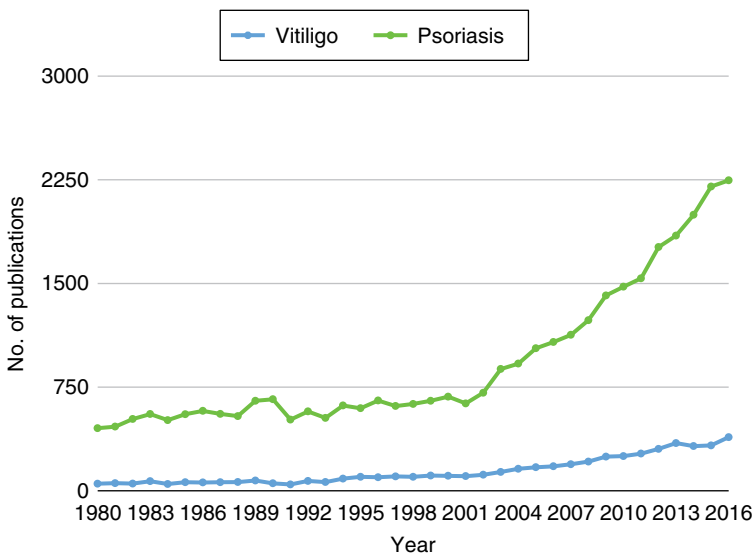


Fig. 1.2 Comparison of the number of publications annually in PubMed since 1980, using the keywords 'Vitiligo' and 'Psoriasis,' respectively.

as a recognized and important disorder. The book is also intended to be a reference for physicians treating patients with vitiligo, and will also demonstrate that vitiligo remains an attractive model to study autoimmunity and understand other diseases, including melanoma.

The Search for New Vitiligo Therapies is on

As skin depigmentations are considered to be asymptomatic, except for sun sensitivity, the prolonged and aggressive use of systemic immunomodulators or systemic steroids is not generally recommended (Fig. 1.3). By using these systemic treatments, lasers and light sources in the spectrum of narrow-band ultraviolet-B, and topical immunomodulators such as calcineurin inhibitors, both an arrest of the disease and a stimulation of melanogenesis can be achieved.

A better understanding of the immunopathogenesis of vitiligo has allowed the identification of many



Fig. 1.3 This patient was treated with prolonged intermittent steroid pulse therapy for vitiligo. He developed multiple striae and depigmentation in all striae, possibly due to the Koebner phenomenon.

possible targets for biological therapies. Although some biological agents have shown promise, in the absence of large, randomized trials such agents are still not included in the mainstream management strategy for vitiligo. Certain experimental treatments that stimulate melanogenesis, such as afamelanotide and prostaglandin analogs, have appeared promising in early trials. The present book will also include an in-depth discussion on newer approaches for the management of vitiligo.

Because of its sociocultural significance, vitiligo has been a disease of interest for alternative medicine since ancient times. In this book, Chapter 19 is devoted to this topic, while depigmentation therapies (bleaching techniques) are explained in Chapter 51. Such treatment can only be considered in cases of highly extensive therapy-resistant vitiligo.

Surgical Management of Vitiligo

Today, surgical treatment is a recognized component in the management of vitiligo, mainly following the introduction of simplified, cell-based therapies.

When medical therapies stabilize the disease but fail to repigment the skin in areas where melanocyte reservoir in the hair follicles is either lost or absent (such as in glabrous skin), the transplantation of melanocytes can be considered. Non-cultured, cell-based transplantation techniques using melanocyte-enriched cell suspensions are rapidly becoming popular. By using only a small piece of donor skin, larger surface areas can be treated without the need for culture techniques. The same donor area can be used again for cell harvesting after its healing [4], though the main limiting factor for surgical repigmentation in vitiligo is disease activity. Furthermore, even when the major part of the transplanted vitiligo patch becomes repigmented, some depigmented areas may still be left behind (Fig. 1.4). One common disturbing outcome is a *peripheral achromic halo*, which has been linked to a possible continued autoimmune activity at the interface between pigmented and depigmented skin.

T helper 17 (Th17) and dendritic cells are known to occur in higher numbers on marginal, actively spreading vitiligo lesions as compared to normally pigmented skin or central depigmented skin [5].



Fig. 1.4 This patient developed an achromic halo after epidermal cellular grafting. Image courtesy of Dr Munish Paul, New Delhi, India.

(A)



(B)



Fig. 1.5 (A) Even in rapidly spreading early vitiligo with extensive body surface involvement, hair follicle melanocytes can be spared and hairs do not become depigmented until the late stages of the disease. (B) In contrast, in alopecia areata the depigmented hairs can be spared, while only pigmented hair are lost.

The Hair Follicle is Considered an Immunologically Privileged Site

Following identification of the melanocyte stem cell reservoir in the outer-root sheath of the lower part of permanent portion of the hair follicle, some excitement has arisen regarding the use of these cells as a potential therapeutic tool for repigmenting resistant areas of depigmentation [6]. The hair follicle has three distinct populations of melanocytes and their precursor cells: (i) the melanocyte stem cells in the bulge region of the hair follicle; (ii) dopa-negative melanoblasts; and (iii) differentiated dopa-positive melanocytes [7]. Notably, the melanocyte stem cells in the bulge region and intermediate tyrosinase-negative melanoblasts lack all three primary targets of autoimmunity of vitiligo (tyrosinase, gp100, and MART-1) [8], possibly preventing an early depigmentation of the hair during the course of the disease (Fig. 1.5). It remains to be determined whether depigmentation of the hairs is due to

exhaustion of the stem cell pool, or to continuous immunological destruction of the melanocytes.

Stability of the Disease and Repigmentation Achieved by Treatment

While different clinical phenotypes are clinically recognized, research groups are currently seeking-biomarkers for disease activity. This may be relevant in predicting the prognosis and selecting medical therapeutic modalities as, for instance, in transplantation. However, the question of whether both lesional and global stability are absolute prerequisites for a successful transplantation remains unsolved [9].

In the present book, an attempt has been made to summarize current knowledge on this very important disease. It is hoped that this will be helpful in your practice.

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