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Vitiligo and Associated Diseases: Moroccan Study of 21 Cases

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Abstract **Case Report**

Vitiligo is an acquired pigmentary dermatosis where the destruction of epidermal melanocytes causes leukoderma. This dermatosis can be associated with many autoimmune or other pathologies. Purpose of the series was to study the epidemiological and clinical characteristics of vitiligo and the frequency of associated pathologies, especially autoimmune ones, among thirty patients followed up for vitiligo in dermatology consultations in Marrakech during 4 years (2019-2022). In the present series out of 30 cases 22 (73.3%) were females and 8 (26.7%) were males. The mean age of our patients was 41.20 years. 21 patients (70%) had one or more associated pathologies such as atopic dermatitis, psoriasis, diabetes type I, diabetes type II, dysthyroidism, Sjögren's syndrome, alopecia areata, depression and anxiety. Vitiligo appeared after the associated disease in 40% (12 cases) and had preceded it in 43.3% (13 cases) and concomitantly in only one case (3.3%). Vitiligo is a chronic acquired autoimmune dermatosis, often associated with/or discovered by other autoimmune or other pathologies.

Keywords: Vitiligo, Associated pathologies, Autoimmune pathologies, Prognosis, Quality of life.

BACKGROUND

Vitiligo is an acquired pigmentary dermatosis where the destruction of epidermal melanocytes causes leukoderma, which can occur at any age. The incidence varies between 0.5 and 2% in the general population (Krüger C & Schallreuter KU, 2012). Many causes, including autoimmunity, have been implicated in the etiology of vitiligo (Alikhan A *et al*., 2011). This dermatosis can be associated with many autoimmune or other pathologies. In this work we study the epidemiological and clinical characteristics of vitiligo and the frequency of associated pathologies, especially autoimmune ones, among patients followed up in dermatology consultations for vitiligo.

Material and Methods:This was a case series, collating 30 cases of vitiligo followed up in dermatology consultations in Marrakech during 4 years (2019-2022). For all the selected cases, we recorded the epidemiological and clinical data, in particular age, sex, phototype and the presence of associated pathologies, especially autoimmune pathologies, based on the clinical and immunological findings. The results were recorded on a paper form and then entered on a computerized form and analyzed using SPSS 20.

RESULTS

We collected 30 cases of vitiligo. The mean age of our patients was 41.20 years with extremes of 2 and 75 years. There was a female predominance (73.3%) with a sex ratio = 0.36 (M/F= 8/22). Phototype III was found in 16 patients (53.3%) followed by phototype IV (36.7%) and phototype II (10%). The median age of onset of vitiligo in our series was 27 years, ranging from 3 months to 66 years. The initial location of achromic macules was frequently the lower limb (20%) followed by the trunk (16.7%) and the neck (16.7%). Among these 30 cases, 4 cases had a personal history of atopic dermatitis (13.3%), only 1 case had a history of alopecia areata (3.3%), 5 cases (16.7%) had type II diabetes and 3 cases had type I diabetes (10%), 8 cases (26.7%) had a history of thyroid pathologies, a history of Sjögren's syndrome was present in 2 cases (6.7%), a history of psoriasis was noted in 5 cases (16.7%) (Figures 1A & 1B), depression and anxiety were present in 8 cases (26.7%) and 6 cases (20%) respectively. Two patients were followed for vogt koyanagi harada syndrome (6.7%), a history of rheumatoid arthritis was found in one case (Figure 2), and one case of multiple autoimmune syndrome (association of alopecia areata, autoimmune thyroiditis, type I diabetes and vitiligo) (Figure 3). Twenty-one

patients (70%) had one or more associated pathologies such as atopic dermatitis, psoriasis, diabetes type I, diabetes type II, dysthyroidism, Sjögren's syndrome, alopecia areata, depression and anxiety. Vitiligo appeared after the associated disease in 40% and had preceded it in 43.3% and concomitantly in only 16.7%. A history of familial vitiligo was noted in 9 cases, 2 cases of atopic dermatitis, type I diabetes, anxiety and familial psoriasis, 4 cases of familial dysthyroidism, 3 cases of familial depression, 15 cases of type II diabetes (50%), no cases of familial alopecia areata, lupus or familial lichen. Vitiligo was mainly represented by the generalized vulgar type without mucosal involvement (73.3% of the cases), followed by the acrofacial type (13.3% of the cases), poliosis was noted in 2 cases. Koebner's phenomenon was present on examination in 33.3% of cases. Biologically, blood glucose was disturbed in 63.3% (19 cases), TSH was abnormal in 20%. T4 abnormal in 16.7%. Thyroglobulin antibody and thyroperoxidase antibody were positive in 2 cases each. Antinuclear antibodies (ANA), Anti-Sjogren's syndrome A (Anti-SSA) and rheumatoid factor were positive in one case. The evolution of the vitiligo under topical and/or systemic treatment was marked by a partial remission in 46.7% with no response in 53.3%. The evolution of the associated pathology was marked mainly by stability (63.3%, 19 cases).

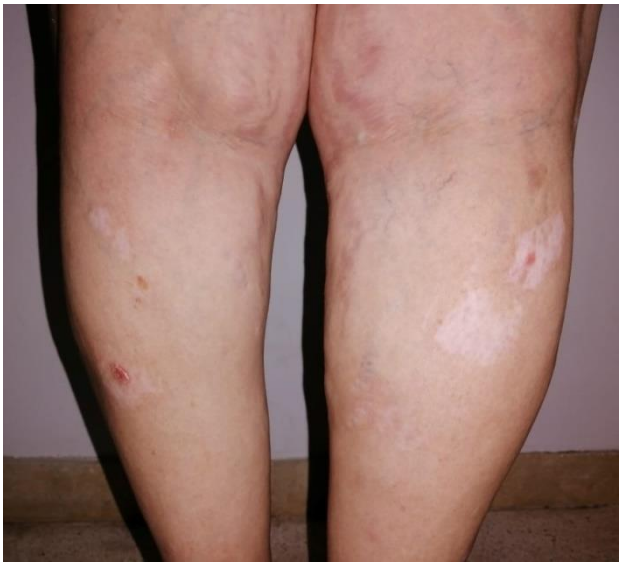

Figure 1A: The clinical aspect of a patient followed for vitiligo with subsequent onset of psoriasis; two erythematosquamous plaques surrounded by achromic halos

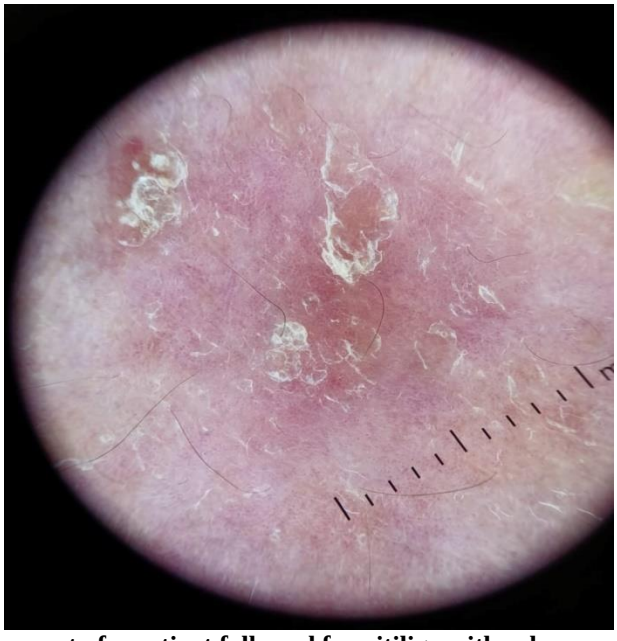

Figure 1B: The dermoscopic aspect of a patient followed for vitiligo with subsequent onset of psoriasis: red dots arranged in a diffuse and regular pattern with scales in the lesion

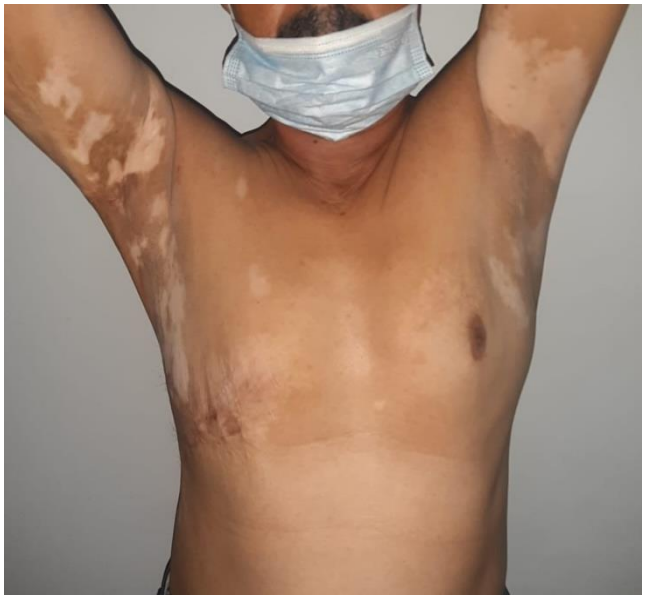

Figure 2: Clinical aspect of vitiligo vulgaris with Koebner's phenomenon following subaxillary burn scars in a patient treated for rheumatoid arthritis

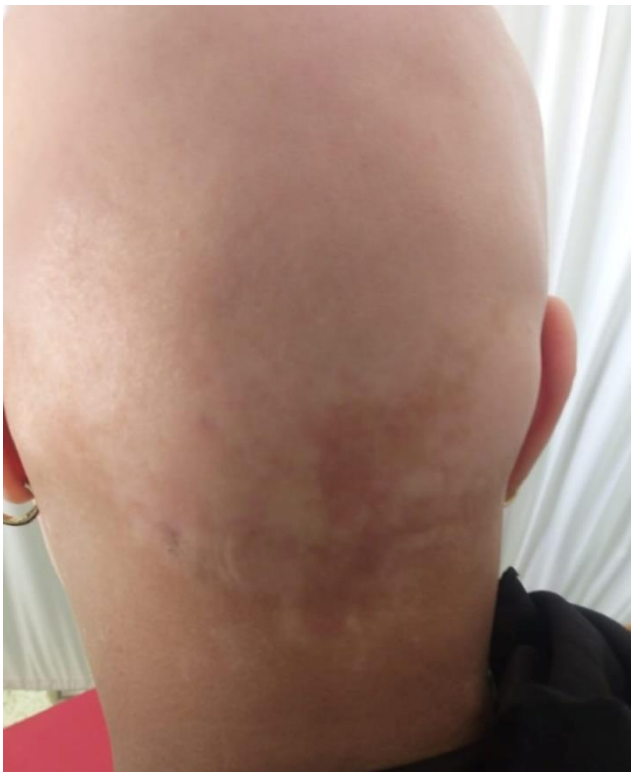

Figure 3: Clinical aspect of alopecia areata universalis associated with acral vitiligo in a young patient followed in endocrinology department for multiple autoimmune syndrome

DISCUSSION

Vitiligo is a chronic acquired autoimmune dermatosis, often associated with or discovered by other autoimmune or other pathologies. The disease usually begins before the age of 20 years and the median age of onset of vitiligo in our series was 27 years. In the literature, vitiligo affects both sexes in a similar way and in our series, we noted a female predominance (73.3%). It is now known that vitiligo is based on a largely autoimmune mechanism and that it has a multifactorial origin, both genetic and non-genetic. About fifteen susceptibility genes have been associated with vitiligo, some of which are involved in skin pigmentation and others are linked to the development of autoimmune diseases. The autoimmune origin of vitiligo, which has long been controversial, has been accepted since the discovery of anti-tyrosinase antibodies in the serum of vitiligo patients.

The literature estimates that 15 to 20% of people with generalized vitiligo suffer from autoimmune hypothyroidism or hyperthyroidism at the same time, and less frequently, other autoimmune diseases may be associated with it, such as rheumatoid arthritis, type I diabetes, alopecia areata, lupus erythematosus, psoriasis, and Sjogren's syndrome. N. van Geel *et al*., found in their study that the presence of associated autoimmune or autoinflammatory diseases seems to influence the clinical profile of patients with generalized vitiligo. Their results support the hypothesis that in the presence of a thyroid disorder, the disease activity of vitiligo is more extensive, especially on the friction areas (N. van Geel *et al*., 2014). A study done by Askour *et al*., on vitiligo and thyroid autoimmune pathologies in 2016, including 253 patients with vitiligo, found that 145 patients (57.3%) had one or more associated diseases, autoimmune diseases were common (43.9%), leading the thyroid pathologies (32%), these pathologies were statistically significantly associated with vitiligo vulgaris (M. Askour *et al*., 2016). Our results agree with those of the literature, in which 70% (21 cases) of our patients had one or more associated autoimmune or inflammatory pathologies, and the generalized type was in the majority (76.7%).

The association of vitiligo and diabetes was studied through some series. Indeed, in recent studies, the frequency of type II diabetes in association with vitiligo is 3%. For type I diabetes, it is in eighth place with a frequency of 1.2%. Thus, our results are consistent with the data in the literature where type II diabetes was present in 16.7% of cases, while type I diabetes in 10% of cases.

In a study of 133 patients with generalized vitiligo, alopecia areata was documented in 5.3% of patients, which the authors found to be consistent with findings in Africa, China, and India (Narita T *et al*., 2011). Another study found that alopecia areata was the disease most significantly associated with vitiligo (Chen YJ *et al*., 2015), while Gill *et al*., found it to be the second most common autoimmune disease in their study group, highlighting a possible shared pathogenesis of the two diseases (Gill L *et al*., 2016). Other studies also report a significant association between vitiligo and alopecia areata with overall rates ranging from 0.5 to 12.5% (Lee H *et al*., 2015, Poojary SA, 2011). In our series, one patient had a multiple autoimmune syndrome combining alopecia areata, autoimmune thyroiditis, type I diabetes and vitiligo.

The association between vitiligo and psoriasis has been described since the 19th century. Epidemiological studies have shown a significant association between these two pathologies. This is also supported by many common genetic predisposing factors between the two conditions, as well as common pathophysiological and immunological mechanisms, such as the Koebner phenomenon. In a case-control study of 463 Italian patients with vitiligo, Arunachalam *et al*., found concomitant vitiligo and psoriasis in 27 (6%) cases. In another study from Iran, 219 patients with psoriasis and 154 cases of vitiligo were examined to determine the frequency of these two diseases simultaneously. Among the patients with vitiligo, 7.79% had psoriasis, whereas 5.48% of the patients with psoriasis had vitiligo. Another study reported the presence of psoriasis in 2.75% of patients with vitiligo (Chen YJ *et al*., 2015). And our results are consistent with the literature, we found 5 cases (16.7%) of psoriasis associated with vitiligo. Studies show a higher frequency of psoriasis and atopic dermatitis in patients with vitiligo, especially in children.

Some studies find a higher frequency of rheumatoid arthritis (RA) in patients with vitiligo (Sheth VM *et al*., 2013, Laberge G *et al*., 2005). Sheth *et al*., reported that 2.9% of their vitiligo patients had rheumatoid arthritis (Sheth VM *et al*., 2013). This is in agreement with the data reported by Zhang *et al*., in which the frequency of RA was significantly increased in both patients with generalized vitiligo and their first-degree relatives (2.2 and 0.59%, respectively), compared with the general population prevalence of 0.34% (Zhang Z *et al*., 2009).

The overall prevalence of anxiety in patients with vitiligo worldwide was comparable to that of other severe skin diseases. This finding emphasizes the need for anxiety awareness in the management of patients with skin diseases (Assiya. Kussainova *et al*., 2020). In our study, depression and anxiety were present in 8 cases (26.7%) and 6 cases (20%) respectively, this can be explained by the religious profile of the participants.

The prevalence of some of these autoimmune disorders is influenced by age, gender, race, and clinical subtype of vitiligo. Our results are consistent with data in the literature regarding the generalized nature of vitiligo as a predictor of association with other autoimmune diseases.

Vitiligo is socially and professionally disabling, hence the importance of psychological support. In patients with vitiligo associated with an autoimmune or other pathology, such as diabetes or thyroiditis, not only the aesthetic prognosis is affected but also the vital prognosis, hence the importance of long-term follow-up in the search for and early management of the associated pathology.

CONCLUSION

General practitioners and specialists should be aware of the comorbidities of vitiligo, especially autoimmune thyroid disorders, and long-term monitoring is necessary in patients with autoimmune disease associated with vitiligo to look for other autoimmune diseases for appropriate management.

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