CASE REPORT

Chemical leukoderma. A condition not always diagnosed. Presentation of two cases and very brief review of the subject.

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ABSTRACT

In recent times the use of depigmenting products such as hydroquinone, vitamin C, topical retinoids among others, are of indiscriminate and frequent use and, usually there is an almost total ignorance that these products are often not free of side reactions sometimes alarming for the patient, one of these reactions being an unwanted bleaching of varying intensity that is known as chemical leukoderma. If we add to this leukoderma caused by occupational causes or by the use of products that in their composition have incriminated substances such as hydroquinone or paraterbutylphenol, we must accept that sometimes this chemical leukoderma is not diagnosed and it is classified as vitiligo or other diagnoses of hypopigmentation or achromia.

We present two patients with chemical leukoderma, one due to the use of depigmenting agents and the other due to the use of a watch with a rubber strap.

INTRODUCTION

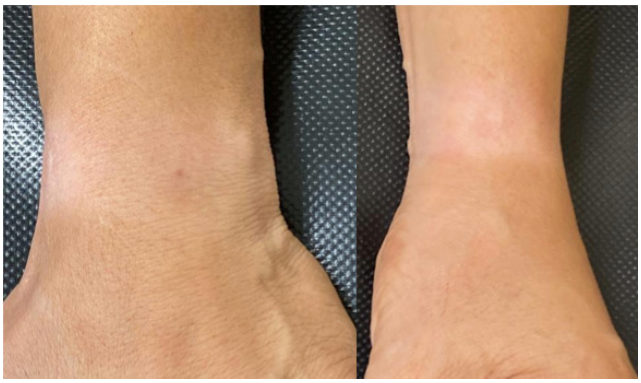
Chemical leukoderma is a condition that is also known by other names such as: contact leukoderma, contact vitiligo, chemical vitiligo or contact depigmentation, and whose etiology is directly related to repeated exposure to specific chemical compounds, especially certain phenol and catechol derivatives that cause the problem through selective melanotoxicity with the consequent destruction of epidermal melanocytes, being important to make clear that these chemicals cause damage only in those people who have a specific susceptibility.[1]

If we remember that skin hyperpigmentation is one of the most common dermatological conditions affecting the skin and that its incidence is rapidly increasing worldwide, having an important impact on the psychological aspect of the patient and having also demonstrated that the quality of life index of this group of patients improves significantly with a successful treatment to lighten their spots, it is understandable the desire of these patients to use products that help them in their problem and sometimes, and this is the serious thing, without any medical supervision because definitely, these lightening treatments are the cause of well-known complications such as: irritation, post-inflammatory hyperpigmentation, exogenous ochronosis and often forgotten, chemical leukoderma.[2]

PRESENTATION OF CASES

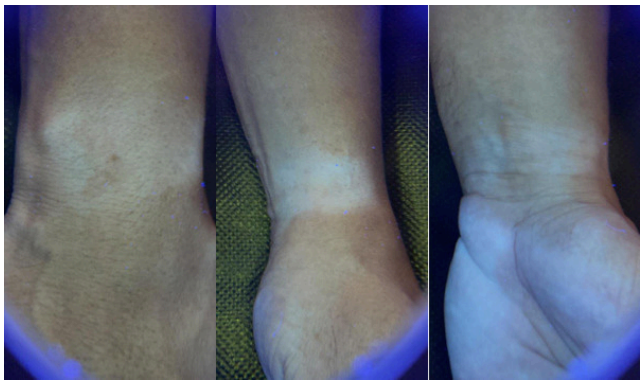
Case No.1

This is a 56-year-old male patient, with no significant personal or family history, who consulted for presenting, with a year of evolution, a plaque that varies between acromic and hypochromic, located specifically on the left wrist (Photo 1 and Photo 2), with the lesion settling on the lateral and lower face of the same and largely respecting the upper and central area.



Photos 1 y 2: Acromic and hypochromic spots located on the wrist, taking the entire circumference, except the central area of the back of the wrist.

Wood's light examination confirms the characteristics of both coloration and location of the aforementioned lesion. (Photos 3, 4 and 5)



Photos 3, 4 and 5: Examination with a black light lamp to highlight the location and characteristics of the compromised areas.

The patient refers us to have consulted with another specialist who, with the clinical diagnosis of vitiligo, performed fifteen sessions of phototherapy and topical treatment with a hydrogel containing superoxide dismutase plus copper and zinc, and also, application of a topical steroid, fluticasone propionate with improvement of the picture, for which the treatment was suspended six months ago. Shortly thereafter, the condition reappeared completely, which led to her consultation with our center.

Upon examination, the anatomical disposition of the lesion is impressive, which totally adjusts to the location of the watch, which we observed has a rubber strap (Photo 6). The patient indicates that this watch is new but that he has been using the same type of rubber strap for many years.

Foto 6: Wristwatch with synthetic strap that imitates the leather used by the patient for years.

With the already reported knowledge of chemical leukoderma caused by rubber straps in the wristwatch,[3] this diagnosis was established and we indicated to the patient the total suspension of its use and as initial treatment the daily application of a cream containing L phenylalanine and on weekends the local application of a preparation with essential oil of bergamot, prior to sun exposure.

In spite of the short time that has elapsed since his consultation, the patient has told us by telephone that his condition has improved.

Case No.2

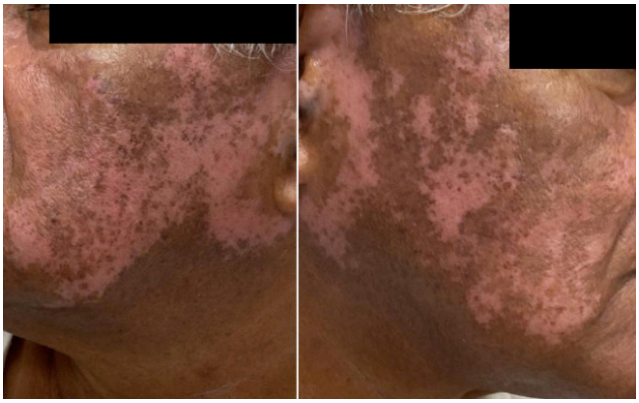
A 70-year-old male patient consulted for presenting confluent hyperpigmented spots on his face with more than four years of evolution. The patient indicates that he self-medicated with a depigmenting cream containing hydroquinone whose percentage he cannot specify, which he initially used only at night but later used morning and night, apparently only for the affected pigmented areas, but later applied it to his entire face. Over the years, without being able to specify exactly when, she presented irritation and depigmentation in areas not affected by dark pigmentation, being able to observe the presence of highly pigmented spots and other areas with erythema and achromia (Photos 1 and 2). No acromic or hypochromic areas were observed in any other part of the body. (Photo 3) Surprisingly, the patient consults for the dark spots without worrying about the irritated areas or the acromic areas. The depigmenting cream had been discontinued two months before the consultation.

With the observation of the lesions and their specific location on the face, the history of years of application of depigmenting cream and the absence of lesions in other parts of the body, we concluded that it was a chemical leukoderma, alternating with areas of facial melasma.

We instruct the patient not to use any similar cream and we administer a low potency steroid cream and a gel containing superoxide dismutase and re-examine the patient after one month, waiting for the irritation to disappear in order to start repigmenting therapy.

DISCUSSION

Chemical leucoderma expresses the presence of an acquired hypopigmented dermatosis caused by repeated exposure to certain chemical compounds, most of them being derived from phenols



Photos 1 y 2: The photos show the presence of hyperpigmented spots alternating with areas of erythema and depigmentation.

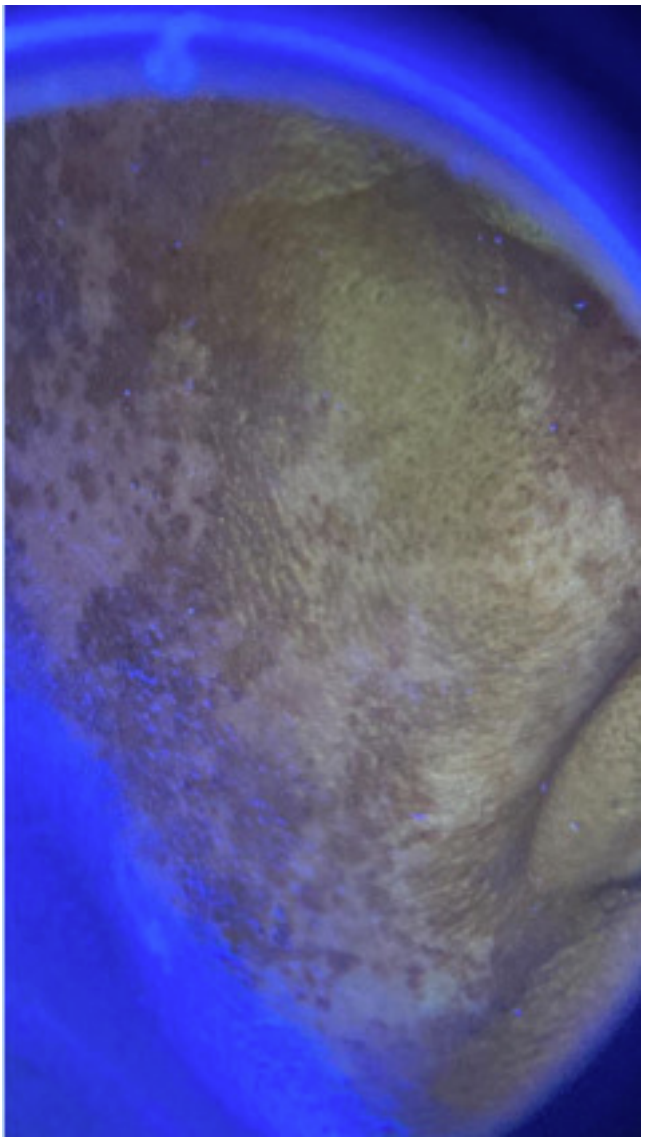


Photo 3: Examination with a wood light that allows better visualization of the acromic and hypochromic zones.

and catechols and other contributing toxins such as sulfhydryls, mercurials, arsenic, etc. It is important to remember that these and many other products are detrimental to melanocytes but only for those patients who have a specific genetic susceptibility. The first or one of the first reports of chemical leucoderma was by Oliver et al in 1939, who reported it in workers wearing acid-treated rubber gloves in a leather processing company, with hydroquinone monobenzyl ether, an antioxidant used in the rubber industry, being identified as the causative agent.[4] In the 1960s and 1970s, cases of occupational leucoderma caused by phenolic compounds were reported in different countries, especially paraterbutylphenol (paratertiary butylphenol), widely used in the manufacture of adhesives[5] such as the "bindi" adhesive commonly used in India. Exposure to paraterbutylphenol is widespread in the synthetic leather industry (watch straps), plastics and germicidal detergents.[6] Leucoderma lesions have also been reported due to the use of colored threads in close contact and rubbing with the skin.[7]

The picture presents with solitary or confetti macules and depigmented patches generally limited to contact sites and less frequently in remote areas. The face was the most frequently involved area. Associated pruritus was relatively frequent. No correlation was found between the time of exposure and the degree and extent of depigmentation.[8] The etiological agents are very varied, from cosmetics to adhesives, to rubber products such as condoms, sandals, watch straps, insecticides, lubricating and motor oils, agents used in chemical laboratories, diverse substances used as depigmenting agents such as creams combining hydroquinone with tretinoin,[9] depigmentation in oral mucosa by Neem (Azadirachta indica),[8] hair dyes[10] and many other agents.

It is of interest the knowledge of the existence of a chemical leukoderma syndrome of which it is not yet clear whether systemic chemical exposure, by inhalation, ingestion or injection, can cause it and it is difficult to prove that the systemic findings are attributed to the chemical process because these findings, both clinical and laboratory, are common in the general population. However, according to these authors, the possibility that systemic organ involvement in chemical leukoderma may be a consequence of lymphatic and/or hematogenous dissemination of the causative chemical substance should be considered.[6] The characteristics of the syndrome are detailed in the table below and taken from Ghosh.[8]

Chemical leukoderma syndrome (modified by Ghosh and Mukhopadhyay,2009)[8]

Stage I	Lesions only at the site of contact
Stage II	Lesions locally disseminated to through the lymphatics Lesions at distant sites through the lymphatics
Stage IIIA	hematogenous dissemination Lesions in distant sites with involvement
Stage IIIB	of systemic organs
Stage IIIC*	Systemic introduction (injection, inhalation or ingestion) other than skin contact causing chemical leukoderma with or without systemic organ involvement
Stage IV	Distant spread of Stage IV vitiligo-like lesions even after 1 year of strict avoidance of exposure to causative chemicals ("chemical vitiligo")

Numerous therapies have been proposed once the causative agent has been discontinued such as: topical steroids, narrow band UV radiation, oral steroid pulses, eximer laser, etc.

CONCLUSION

We present two cases of a condition that may be unintentionally ignored or misdiagnosed if important data are not taken into account, such as the location of the lesions, their clinical characteristics, exposure or contact with the multiple agents involved, absence of personal and family history (although there are reports of presentation of the process in patients with familial vitiligo) and, above all, the innate medical curiosity so necessary to detect and investigate when something does not fit the diagnosis, above all, the innate medical curiosity so

necessary to detect and investigate when something does not fit the diagnosis, as in the case of our patient with leukoderma induced by the rubber strap of his wristwatch with a history of diagnosis and therapy of vitiligo, a very understandable fact given the lesional similarity of both pictures. The knowledge of the problem worldwide has led to restrict the use of these products and therefore the cases have decreased, but not disappeared, this decrease leads many to ignore or forget its existence, so it is important this type of reminder reports.

REFERENCES

1. Bonamonte D, Foti C, Romita P, et al. Colors and contact dermatitis. Dermatitis 2014;25:155-162.
2. Odedra S., Yoo J. The risk of chemical leucoderma with skin-lightening therapies. Clinical and Experimental Dermatology 2021: 46,; 1391–1393
3. BajakAK., Saraswat A., Srivastav PK. Chemical leucoderma: indian scenario, prognosis, and treatment. Indian J Dermatol 2010;55:250-4
4. Oliver EA, Schwartz L, Warren LH. Occupation leukoderma. J Am Med Assoc 1939; 113:927–928.
5. Okmura Y, Shirai T. Vitiliginous lesions occurring among workers in a phenol derivative factory. Jap J Dermatology 1962; 7:617–619.
6. Bonamonte D.,Vestita M., Romita P., Filoni A., Foti A., Angelini G. Chemical Leukoderma. Dermatitis 2016;27: 90-99
7. Kumar S., Bandyopadhyay D. Chemical leukoderma induced by colored strings. J AM ACAD DERMATOL 2009; 61:909-910
8. Gosh S., Mukhopahyay S. Chemical leucoderma: a clinico-aetiological study of 864 cases in the perspective of a developing country. British Journal of Dermatology 2009; 160:40–47.
9. Ramani R., Gopinath H., Prabhakaran., Santosh T. A cautionary tale in skin lightening: chemical leukoderma. Pigment International 2023;181:175-176
10. Jadhav PB. Chemical leucoderma of oral and labial mucosal surfaces from neem [Azadirachta indica]. A case series. Indian Dermatol Online J 2020;11:433-435.
11. Huang W, Goon A, Chong WS (2014) Chemical Leukoderma to Hair Dye in a Singaporean Indian – A Rare, Adverse Cosmetic Outcome in Relation to a Ubiquitous Cosmetic Product. J Clin Exp Dermatol Res 2014;5: 237.