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Xeroderma Pigmentosum: The children of the moon

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Abstract: Xeroderma pigmentosum is a rare photodermatosis of genetic origin, with an autosomal recessive inheritance characterized by increased sensitivity to ultraviolet light. We conducted a retrospective study within the department of plastic, reconstructive, aesthetic surgery and burned of the Mohammed VI University Hospital of Marrakech, over 11 years, which allowed to collect 21 cases of children with xeroderma pigmentosum who have all benefited from at least one surgical intervention in our department. The average age of our patients at the first consultation was 10 years old, with extremes between 3 and 26 years old. A male predominance was noted with 12 boys for 9 girls. The concept of solar exposure was constant in all our patients. Inbreeding of parents was found in 87% of cases (18 patients) and a similar case in fraters was found in 6 patients. On the cutaneous level, all patients had pigmented macules in the photoexposed areas associated with cutaneous xerosis. The preferred site of tumors was the photoexposed areas and more particularly the cephalic extremity in 100% of cases. This was squamous cell carcinoma in 43% of cases, basal cell carcinoma in 29% of cases, melanoma in 15% of cases, and precancerous lesion in 13% of other cases. The number of tumors operated in a single time and in the same patient ranged from 2 to 8. Secondary locations, particularly in the lung, were found in 42% of cases. Surgical treatment consisted in the majority of cases of tumor resection followed by closure by direct sutures, or directed healing of the loss of substance then cover by thin skin graft after verification of the margins. In other cases, we opted for semi-thick excision-grafting in aesthetic units (frontal, jugal, nasal). Two of our patients initially benefited from the introduction of an expansion prosthesis at the level of the trunk, and secondarily from excision-grafting of total skin in aesthetic units. Two more of our patients were exentered by the infiltrating nature of the globe and orbital fat. In addition, local recurrence was noted in 4 patients. And finally recurrences were frequent with an average of 4 hospitalizations per patient, in front of the repetitive appearance of new tumor lesions. The primary prevention measures undertaken were solar eviction with internal and external photoprotection (application of a high-index sunscreen on the photoexposed zones to be renewed every two hours, wearing a hat and sunglasses).Thus, xeroderma pigmentosum is a rare disease for which there is no curative treatment at present, and only photoprotection reduces the risk of cutaneous cancer. The severity of clinical expression and the early onset of cutaneous tumors during XP depend on the level of genetic alteration but also on the degree of respect for the means of photoprotection. Surgery is the main treatment of malignant skin tumors and must be as early as possible to limit the aesthetic damage. The gene in question has been identified and opens the way for gene therapy.
Keywords: xeroderma pigmentosum, malignant tumors, DNA, surgery, gene therapy.

INTRODUCTION

Hereditary photodermatoses are a group of rare diseases that are often caused by a genetic deficiency or dysfunction of various components of the DNA repair pathway. The result is clinically extreme photosensitivity, with many syndromes presenting an increased risk of malignant skin tumors. Among these malignant potential syndromes, xeroderma pigmentosum is described [1].

Xeroderma pigmentosum (XP) is an autosomal recessive genophotodermatosis that is rare and disabling and characterized by increased sensitivity to ultraviolet light. It is divided into seven complementarity groups XPA up to XPG and a variant XPV group. It associates cutaneous, ocular and sometimes neurological involvement [2]. The association of XP and thyroid abnormalities has been reported by several studies with a higher frequency in group XPC patients [3].

The skin in patients with XP is characterized by severe solar damage with a poikiloderma-like appearance making difficult the clinical diagnosis of malignant tumors. Dermoscopy on these types of skin

finds its place to increase the sensitivity of the clinical diagnosis of melanocytic tumors and pigmented basal cell carcinomas. Indeed, the latter are more frequent in dark phototypes and can be confused with melanoma at the only clinical examination [4].

To date, the pillar of therapy remains strict photoprotection [1]; Indeed, prevention is based on screening and early treatment of children being followed for XP, as well as photo-protection and genetic counseling [5], with genetic therapies under development [6].

MATERIALS AND METHODS

We conducted a retrospective study within the department of plastic, restorative, aesthetic surgery and burned of the Mohammed VI University Hospital of Marrakech, over a period spanning 11 years, from January 2007 to December 2017, which allowed to collect 21 cases of children with xeroderma pigmentosum who have all benefited from at least one surgical intervention in our department.

The establishment of a record of exploitation made it possible to count the information relating to the age and the sex of the patients, their personal antecedents and in particular the solar exposure, the family antecedents including the notion of consanguinity of the parents thus the presence of similar cases in the family, the number and size and the location of the tumors, their histological nature, the surgical treatment undertaken, the postoperative and long-term evolution as well as the recurrences and the notion or no recidivism.

RESULTS

The average age of our patients at the first consultation was 10 years old, with extremes between 3 and 26 years old. A male predominance was noted with 12 boys for 9 girls. The concept of solar exposure was constant in all our patients. Inbreeding of parents was found in 87% of cases (18 patients) and a similar case in fraters was found in 6 patients. On the cutaneous level, all patients had pigmented macules in the photoexposed areas associated with cutaneous xerosis. The preferred site of tumors was the photoexposed areas and more particularly the cephalic extremity in 100% of cases. This was squamous cell carcinoma in 43% of cases, basal cell carcinoma in 29% of cases, melanoma in 15% of cases, and precancerous lesion in 13% of other cases. The number of tumors operated in a single time and in the same patient ranged from 2 to 8. Secondary locations, particularly in the lung, were found in 42% of cases.

Surgical treatment consisted in the majority of cases of tumor resection followed by closure by direct sutures, or directed healing of the loss of substance then cover by thin skin graft after verification of the margins. In other cases, we opted for semi-thick excision-grafting in aesthetic units (frontal, jugal, nasal, ...). Two of our patients initially benefited from the introduction of an expansion prosthesis at the level of the trunk, and secondarily from excision-grafting of total skin in aesthetic units. Two more of our patients were exentered by the infiltrating nature of the globe and orbital fat. In addition, local recurrence was noted in 4 patients. And finally recurrences were frequent with an average of 4 hospitalizations per patient, in front of the repetitive appearance of new tumor lesions. The primary prevention measures undertaken were solar eviction with internal and external photoprotection (application of a high-index sunscreen on the photoexposed zones to be renewed every two hours, wearing a hat and sunglasses).

DISCUSSION

The xeroderma pigmentosum is a rare disease, it is a photodermatosis of genetic origin, with an autosomal recessive inheritance, which reaches both women and men. The condition was first described by Karposi and Hebra in 1874 and then in the literature, describing the course of this disease [7]. The genetic disorder is linked to an enzyme deficiency causing a defect in the process of repairing lesions induced on DNA by the ultraviolet radiation of sunlight, thus leading to the early appearance of malignant skin tumors [4]. This is a defect in the genes of the excision-nucleotide resynthesis repair system in the first seven genetic groups (XP A-G) and an abnormality of the transcription genes for the eighth group (XPV) [8].

It is characterized by the appearance in the first months of life and after the first solar exposure, of ephelides and brown macules on the photoexposed zones. The skin becomes atrophic with areas of hyper and hypopigmentation, a great dryness of the mucous membranes and photophobia. Without sun protection, early actinic keratoses, papules, plaques, nodules, macules, horns [4] and then carcinomas (basocellular and squamous cell) develop, often with death in the second decade.

There is often an eye damage with keratitis, to be systematically searched for by a good ophthalmological examination. It is then understood that it is impossible to dissociate the eye from the skin, the cutaneous, mucosal and ophthalmological symptoms being closely intertwined [9]. Neurological impairment such as mental retardation may also be found [2, 5]. Also, some cases of internal cancers have been reported during this pathology, including gynecological cancers during the XPC [10] and thyroid cancers [3].

The seven types of classic XP differ slightly in their symptoms and severity:

-XPA: Very severe form with significant neurological abnormalities.

-XPB: Very rare (less than 10 cases in the world), recovery with Cockayne syndrome.

-XPC: The most common form, absence of neurological problems. It is the most severe form, with the development of a large number of cutaneous but also internal tumors (acute leukemia, ovarian carcinoma and cerebral glioma [2] at an early age [8].

-XPD: Very heterogeneous, always accompanied by more or less important neurological abnormalities. Would also be associated with the development of colorectal cancer [11].

-XPE: Rare. Relatively mild symptoms without neurological disorders.

-XPF: Rare form probably underdiagnosed due to a discreet dermatological picture where the immediate photosensitivity predominates, with few skin lesions. It concerns almost exclusively the Japanese population. The DNA repair is complete but extremely slow, and therefore the risk of skin cancer seems low, allowing even clear phototype patients to lead an almost normal life [12].

-XPG: Very rare, it only affects a few people, recovery with Cokayne syndrome [6].

Epidemiologically, this is a rare condition. For example, its prevalence in Tunisia is estimated at 1 in 10,000 [2]. It is even more rare among black populations [5]. The average age of appearance of the first cutaneous tumor varies from 10 years old in our series, to 13 years old [4], and up to 21 years old [13], with an almost exclusive localization at the cephalic extremity [4, 5, 13]. In some studies, boys and girls are equally affected [4, 13], in contrast to our series where a male predominance was noted with 12 boys for 9 girls, or other studies that noted a female predominance [2, 8].

Diagnosis is first clinically assisted by dermoscopy which finds its place in the early diagnosis of malignant tumors in XP and therefore helps guide the choice of the most conservative treatment possible [4]. Histologically, the most common tumor is basal cell carcinoma in some studies [4, 8], while squamous cell carcinoma was found in others, as well as in our study [5, 13], and finally melanoma.

The management of cutaneous tumors is a vast field of action which concerns both the general practitioner, who is most often the first to mention the diagnosis, but also the dermatologist for the confirmation of this one (cutaneous biopsies and histopathological examination) and referral to therapeutic management. Some situations are simple and can be managed by an isolated practitioner. Others, especially malignant tumors, require a multidisciplinary approach. The treatment is provided by the dermatologist or the plastic surgeon [14]. The presence of a suspicious skin lesion should motivate a consultation in pediatric plastic surgery, any delay may change the overall prognosis and management. The decision of excision makes use of various criteria which certainly include the diagnosis but also the possibilities of reconstruction. The time chosen for the surgical management depends on the medical emergency to excision (benign tumor, spontaneously regressive, at risk or not of pejorative evolution, malignant tumor), the cosmetic repercussion and the psychological experience but also phases learning and growth dynamics of the child [15].

The main treatment remains the iterative surgical excision, followed by direct closure when the size of the loss of substance allows, coverage by a local flap, a skin graft or even artificial dermis. In patients with XP, reconstruction often poses a big challenge due to the presence of contiguous and co-incidental tumors, precluding the use of local flaps as a reconstructive option [7]. Surgery of excision in aesthetic units followed by a skin graft taken in a healthy zone (thin or semi-thick expanded skin) is a good way both therapeutic and preventive. Other therapeutic means may be offered such as imiquimod, dynamic phototherapy or cryotherapy. Clinical surveillance may be warranted for benign tumors [4].

CONCLUSION

Thus, xeroderma pigmentosum is a rare disease for which there is no curative treatment at present, and only photoprotection reduces the risk of cutaneous cancer. The severity of clinical expression and the early onset of cutaneous tumors during XP depend on the level of genetic alteration but also on the degree of respect for the means of photoprotection [8]. Surgery is the main treatment of malignant skin tumors and must be as early as possible to limit the aesthetic damage. The gene in question has been identified and opens the way for gene therapy.

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