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A CASE OF IN SITU CARCINOMA OF THE CONJUNCTIVA TREATED BY 5 FLUORO-URACILE EYE DROP1%

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ABSTRACT

In situ carcinoma of the conjuctiva is a malignant tumoral pathology of the conjuctiva mucus of the eye that the epidemiology is variable in the world. The major risk factor is the excessive exposal to sunlight. The treatment is surgery completed by medical adjuvant such as steroidal anti-inflammatory eye drops, anti-mitotic eye drops, and sugery like cryotherapy and amniotic membrane

KEYWORDS: Amniotic membrane, Carcinoma in Situ, exceresis, 5 Fluoro-Uracile 1%.

INTRODUCTION

We repport a case of 58 years old female patient presenting an in situ carcinoma of the bulbar conjuctiva of the left eye. We have discontinuously performed a serial of treatment including a surgical exeresis, a cryotherapy, an amniotic membrane grafting and instillation of 5FU drops during 6 weeks period. After 24 months of follow up, a recurrence occured at 2nd months of the first serial treatment has been identified, after that, there was a complete recovery. So, a regular follow up of the patients

suffering from an in situ carcinoma is indispensable in order to detect the possible complication and to prevent its change into an invasive carcinoma.

The ocular conjunctiva is a mucus that covers the anterior part of the sclera area. It plays an importante role in maintaining corneal homeostasia by assuring the good quality of lacrymal film. This complex and fragile tissue may be the site of numerous ocular or systemic diseases that can lead to different alterations, a serial of dysplasia, responsible for in situ, then invasive malignant degeneration.[1]

The corneal in situ carcinoma constitutes one particular clinical feature of epidermoid neoplasia of the ocular surface.[2] The main risk factors of these epidermoid neoplasia are solar exposition, the increase in HIV infections and the allergic conjunctivitis. In equatorial Africa, a high prevalence of the aforementioned pathology is noticed. About 1.3 to 2 cases per 100 000 inhabitants have been found each year. In other countries, this prevalence is lower than 0.1 case per 100.000 inhabitants per year. In situ carcinoma of the conjunctiva catches most often the old patients more than 50 years- old. Nevertheless, the increase of papilloma virus infection and HIV has lately changed the epidemiology of this tumoral affection.[3]

OBSERVATION

We report a case of 58 years-old female patient who came, at her first time, into consultation due to the corneal tumefaction of her left eye disturbing her vision. This patient come from a small island of northern part of Madagascar. Four ophtalmologists have already taken car of her 3 months prior to her arrival to the capital. During the anamnese, she said that the corneal tumefaction had started 4 months before her admission to our service. She complained of having a sensation of dryness associated with intermittent redness of the eyes. She had no past history of diabetes, nor immune system deficiency, nor ocular allergy. She neither drinks alcohool nor smokes. She is both a farmer and a street seller that constitute a job which exposes her to the sunlight. Since 4 months, she has received steroid and non steroid eye drops combined with artificial tears but ther was no improvement. During the eye check, the visual acuity of the right eye was 6/6 – Parinaud 2 with the correction of presbyopia. The visual acuity of the left eye was 6/12- Parinaud 6 which is not improvable inspite of the correction. With the aplanation tonometer, the intraocular pression of both eyes was normal. The right eye presented a beginning cortical cataract with biomocroscop, the fundus was normal. On the left eye, we observed a round conjunctival tumor about 8mm of diameter that

invades the nasal side of cornea in 150°. The tumor was multilobular, more or less plane shape, irregular and vascularised (PHOTO 1 and 2).

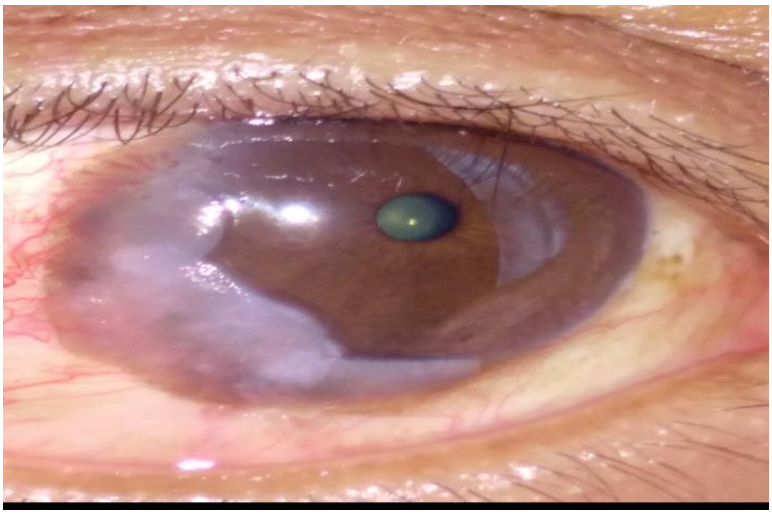

Photo 1: Corneo conjunctival tumor of the left eye.

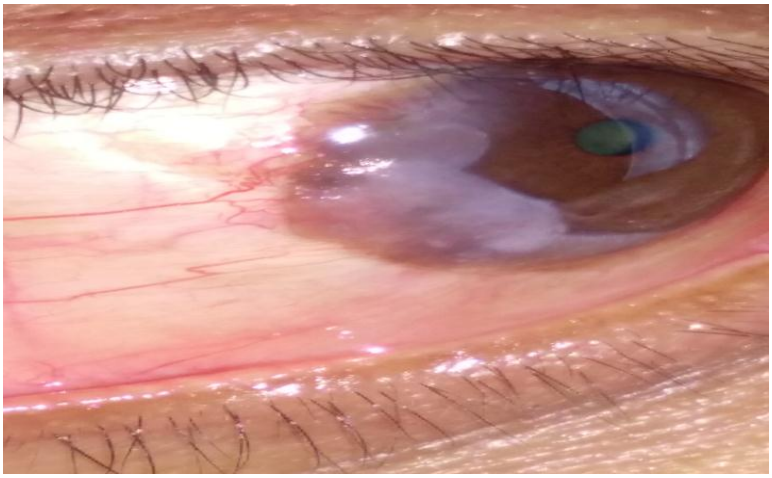

Photo 2: Corneo conjunctival tumor of the left eye.

The examination of the rest of bulbar and palpebral conjunctiva as well as the anterior segment found no abnormality. The fundus of the left eye was normal. We decided to carry out a complete surgical exeresis of the conjunctival and corneal tumor by leaving 4 mm excision margin following by cryotherapy. The operative piece was sent for anatomopathological analysis that made the diagnosis of in situ carcinoma of the conjunctiva with a complete limit of exeresis. The patient was supervised but a tumoral reccurence developed again on the initial site only 2 months after the first surgical intervention.

The cornea healing anomaly resulted to a repeated ocular ache with a recurrent ulceration of the cornea. Consequentely, we reoperated the patient by uprooting the tumoral recurrence

with desepithelialisation of the cornea following by an amniotic membrane grafting. The operative piece was sent back for anatomopathological analysis and the result was the same as those of the preceding result. So, We added the preceding treatment by an antimitotic drop made of our own composition: 5Fluoro-Uracile (5FU) diluted at 1%. This eye drop was discontinuously instillated three times a day during 6 weeks with a five-days interval after each one week cycle.

First, the patient was seen again every week until the end of treatment with 5FU, then every month during 6 months, and finally every 3 months during 18 months. During the last follow up at 24 months, the ocular surface has been entirely restored.

The visual acuity raised up at 6/6 –Parinaud 2 with the correction of the presbyopia. The intraocular pressure of both eyes was normal at 12 mmHg (PHOTO 3). The rest of the ophtalmological examination was normal. We didn't find any complication neither in the anterior segment nor in the posterior segment.

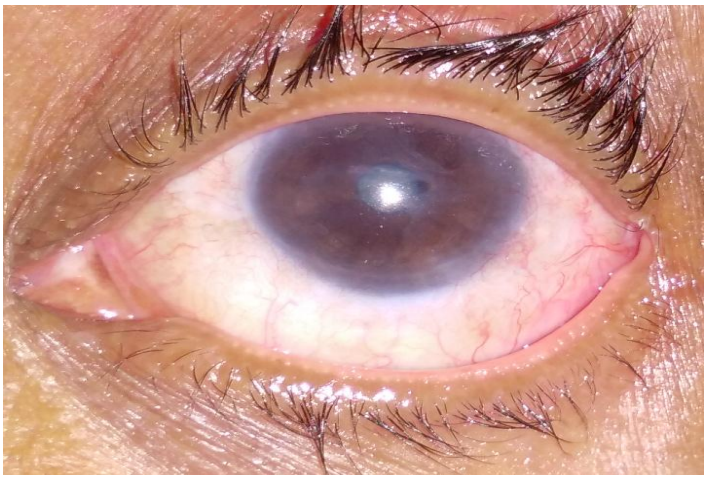

Photo 3: Left eye at last follow up of 24th month.

DISCUSSION

Ocular tumors are classified according to WHO into two categories: The precancerous tumors and the malignant tumors. In situ carcinoma is classified among the second category. Its etiology is still imperfectly known. However, the appearence of dysplasic lesion within the histological transition of cunjunctival area may initiate a malignant degeneration of the tissu where cell renewal is very important and permanent.

The most seen risk factors of the patients having an in situ carcinoma of the conjunctiva are : an important solar exposure that expose the patients to ray ultraviolet B, papillomavirus infection, an iterative physical and chemical agression, dry eye syndrome, active or passive smoking, infection by HIV.[4,5,6] R Newton, F Asadi-Amoli and their associates confirmed that the farmers and the peoople who are exposed to sunlight more than 180 days per year are prone to develop a carcinoma of the conjunctiva comparing to the office workers and the stay-at-home people.[7,8]

In our case, the risk factor that our patient has was the exagerated exposure to the sunlight. For our patient is both a farmer and a street seller. She had no particular medical past history that can help develop the eye tumors. The initial clinical feature of the disease was typical of conjunctival carcinoma. These tumors are mostly sessiles, slightly heightened shape, well limited and vascularised. The capillaries constitute the central axis of one lobule. The tumor has multiple lobules and has an aspect of a raspberry. It begins at the limb within palpebral area and spread horizontally into medial and lateral angle of the eye ball and into the cornea.[5] The visual discomfort triggered by the tumor varies according to its location and extension. The vision may be preserved when the tumor has not invaded yet the cornea. The vision loss is especially due to the corneal invasion degree. The management depends on the cases but always healing by respecting the maximal vision quality. The first treatment is surgery via a complete excision of the lesion with an exeresis margin of 4mm without touching the tumor by dissecting untill the sclera.[3] The surgery is completed by adjuvant treatments that vary according to its availability.[5] The cryotherapy is an additional treatment of conjunctival carcinoma and its advantage is to reduce the risk of recurrences.[9]

Nevertheless, in our case, inspite of the complete excision associated with a cryotherapy of the limit of the exeresis, a recurrence has been observed after 2 months of treatment.

The recurrence is very frequent but variable in this malignant pathalogy of the conjunctiva. S Gichuhi and M S Sagoo followed up many patients over 32 months period, and the recurrences were very variables in 3.2 to 67% of cases. The recurrence was systematic within 6 months when surgical treatment only was performed.[3,10]

Apart from cryotherapy, the instillation of 5 FU diluted at 1% gives good results and less local as well as loco regional complications. The choice of this molecule depends on its

availability, its low cost, its efficiency, and its storage facility.[11] Many protocols have been proposed in the littérature for the cunjunctival cancers:

- Instillation of 5FU 1% drops : one instillation 4 times a day durind 1 week[3]
- Instillation of 5FU 1% drops : one instillation twice a day in 4 cycles in which each cycle last for 4 days and folloying by one week break.[12]
- Instillation of 5FU 1% drops : one instillation 4 times a day in 6 cycles in which each cycle last for 4 days and folloying by 30 days break.[13]

The results of the instillation of 5FU in the eyes of the patients suffering from carcinoma of epithelium conjunctival was evaluated to be effective with the absence of recurrence in more than 2 years after the end of the treatment.

The complications appeared at the moment of treatment and some weeks after the end of the treatment are especially occured by a sensation of dryness and ocular irritation sensation. At long-terme, there is no detectable complication anymore. As a result, 5FU is better tolerated anticancerous molecule to take care of carcinoma of the epithelium conjunctival.

The 5 FU is an anti metabolite that is used to treat different types of epithelial cancers. It efficiency has been proved for its rapid actions to destroy the cancerous cells.[11]

In our case, we adopted a longer treatment with an interval of shorter pauses and less often instillation. We ended to the same conclusions. In fact, the rythm of instillation and the duration of the treatment by 5FU 1% is adjusted according to each case. For smaller and non invasive lesions, a complete excision followed by cryotherapy may be enough to eradicate the cancerous cells.[14]

But if the lesion is wider with corneal invasions, these treatments must be completed by other treatments. When conjunctival substance loss is very important, the reconstitution of the ocular surface is slow. An amniotic membrane graft can accelerate this recontruction and improve the postoperative suite of the patients after the exeresis of in situ carcinoma of the conjunctiva.

Moreover, amniotic membrane has an aticancerous property that diminishes the risk of tumoral recurrence. To illustrate this statement, a follow up of 53 yers old patient made by U Agarval and Al in Glasgow UK showed that a complete exceris of the lesion associated with

amniotic membrane grafting provide better results at 30 months of the follow up, without tumoral reccurence.[15]

The absence of tumoral recurrence has been noted at our patient after the second stage of treatment including a complete and large resection of the tumor, an amniotic membrane graft, and anti mitotic eye drop instillation.

CONCLUSION

Overall, our patient received the totality of all possibilities of the management of epithelial conjunctival carcinoma, at different times and within 24 months of follow up. There was no tumoral reccurence. The major issue during the recurrence is the degeneration into invasive carcinoma. The case we described is the first identified at non invasive stage in our service and the regular follow up of the patient led to anatomy and visual function restoration.[8] Early diagnosis , radical management completed with medical and surgical treatments as well as a regular clinical follow up permit to treat more or less definitely in situ carcinoma of the conjunctiva. However, we are not sheltered of the eventual recurrence. So the long term supervision of the patients is crucial.[14]

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