Case report

SMO (SMOOTHENED TRANSMEMBRANE PROTEIN) INHIBITORS (VISMODEGIB) IN TREATMENT OF BASAL CELL CARCINOMA (BCC) OF OCULAR ADNEXA.

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SUMMARY

Basal Cell Carcinoma (BCC) is one of the well spread malignant skin cancers. Eighty percent of it occurs in the head-neck area of which 20% in the eyelids. The major genes for BCC are: PTCH1 and PTCH2. PTCH1 suppresses transmembrane Smoothed (SMO) protein, while PTCH2 have his role unclear, but there are evidences for involvement in Hedgehog signalling pathway. From all cases of BCC of adnexa, advanced BCC represents a small percentage of 1-10%. Advanced BCC has his two forms of metastatic mBCC and local advanced laBCC. The surgical approach is a mainstay in the treatment of BCC. Some cases the anatomical and functional results are expected to be poor, due to difficult location of the tumour, such patients with laBCC and mBCC can benefit from medical treatment together with surgery and radiotherapy or alone. Systemic treatment, as of Vismodegib is a good candidate for these patients with mild to moderate side effect's profile.

Keywords: basal cell carcinoma, Eyelid, Oncology, Vismodegib, Ophthalmology, free cutaneous graft

INTRODUCTION

Basal Cell Carcinoma (BCC) is one of the well spread malignant skin cancers (Figure 1). Eighty percent of it occurs in the head-neck area of which 20% in the eyelids. Eyelid BCC are distributed like: 50% - lower lid, 30% - medial canthus, 15% - upper lid and 5% - lateral canthus [1 - 4]. It occurs when skin's basal cells develop a mutation of its DNA [5]. The major genes for BCC are: PTCH1 and PTCH2 [6]. PTCH1 suppresses transmembrane Smoothed (SMO) protein, while PTCH2 have his role unclear, but there are evidences for involvement in Hedgehog signalling pathway [7, 8]. Risk factors are UV radiation in sunlight [9], pigment characteristics (more pigmented people demonstrate less incidence of BCC), family history and previous incidences add more. Epidemiological data show the distribution in between 3-10 % worlds wide [10, 11]. There are 5 well known symptoms requiring our attention in the diagnosis of BCC: 1. Open sore that doesn't heal, 2. Reddish patch or irritated area, 3. Nodule or shiny bumps, 4. Pink growths or warty like lesions, 5. Scar like lesions [12,13].

Aetiology and risk factors are grouped like: 1. Age over 50 years. 2. History of sun or UV exposure, 3. Fair skin, 4. Male Caucasian gender, 5. History of skin cancer, 6. Chronic infections or skin inflammation [14, 9].

Fig. 1.

VARIANTS OF BCC

From all cases of BCC of adnexa, advanced BCC represents a small percentage of 1-10%. That group of advanced BCC is divided into following two sub-subgroups: local advanced BCC (laBCC) and metastatic BCC (mBCC). mBCC represents 0.5% within the subgroup of the advanced BCC [15,16]. According to some authors, mBCC group has a history of system metastasis, poor prognosis and average life expectancy 8-14-month (5 years life expectancy is less than 10%), while local advanced BCC (laBCC) subgroup is consist of lesions which infiltrate underlying tissues and bones and still have surgical options [17]. Treatment of BCC of adnexa is surgical in general, but there are some cases in which BCC progress to mMCC (around 1%) or to laBCC (less than 10%) which need not only surgical treatment but medical and/or radiation as well [11,15,17].

Some studies identified quoted factors as poor prognostic factors: size more than 3 mm, facial location, incomplete resection, longstanding lesions or near vascu-

lar location [18-26]. Small sized tumours are excised easily, but tumour recurrences are common in places where complete resection is not easy due to attempts to cause less anatomical damages. Scar formation makes distinguish between tumour recurrence and healing process extremely difficult in first months [27]. Recurrences of already operated BCC shows aggressive subtype of the primary tumour and usually related to worse prognosis, especially in morpheaform cases [28].

A few histology forms are differentiated. Among them, nodular and superficial are less aggressive, while others like morpheaform, basosquamous (ref. as metatypical or mixed) and infiltrating BCC forms require more clinical aggressive behaviour like radiation or new medical agents [29, 30]. They are associated with far greater rate of occurrences than other forms [31, 32]. Recurrences are not rare, some authors quote more than 12% [33].

CASE REPORT

A 59-year white woman was admitted in our ophthalmology clinic in June 2018 for evaluation and treatment of lesion on the temporal part of the right lower eyelid with at least 6 months history. A 1 cm lesion at the temporal part of the lower lid and involvement of whole lower eyelid margin was found on physical examination (Figure 2).

Fig. 2.

The patient has been treated in two stages. First stage – excision and blepharoplasty (Figure 3), second stage – medical treatment.

Fig. 3.

At the first stage, we performed surgical excision and later on blepharoplasty. After excision –the positive result of BCC confirmed the diagnosis. Clear wound edges and wound bottom confirmed in histology. For blepharoplasty, free cutaneous graft technique has been used (Figure 4). On the fourth postop month, good cosmetic and anatomical results have been achieved (Figure 5).

Fig. 4.

Fig. 5.

Two months later, the patient came back with a new occurrence surrounding the graft. Moreover, BCC lesion on the eyelid margin showed marked progression. (Figure 6, 7)

Fig. 6.

Fig. 7.

Detailed reconsideration of reoperation shows a great possibility for bad anatomical and cosmetic results. As we expected bad anatomical result - the decision to treat the patient with vismodegib was a natural choice.

Treatment, Dosage

The Patient was approved from the commission of Oncology for treatment with vismodegib. Treatment with 150 mg daily was initiated in October 2018 and lasted till April of 2019.

Outcome and Follow-up

Improvements noted from the very first month (figure 8). The patient received vismodegib for 6 months with remarkable outcome (figure 9). During the active treatment, the patient was monitored on a monthly basis, while after the end of the treatment on three months basis.

Fig. 8.

Fig. 9.

DISCUSSION

Surgery approach is the mainstay with a higher success rate. In these cases, we apply wide surgical excision with histological margin control. Surgery approach has to be wisely considered in order to achieve the best possible functional and aesthetic outcome [34].

When the surgery may lead to unpredictable results in terms of anatomy or physiology structural integrity, the other possible options are radiotherapy or medical treatment [35, 18]. US Food and Drug Administration approved in 2012 Vismodegib for the treatment of locally advanced or metastatic basal cell carcinoma (BCC) [36], which provides surgent with another option of treatment of BCC

on bearable level of side effects. We have our excellent first outcomes in this case, even though some authors report vismodegib resistance in cases with deep tumor planes involving bones or cartilages [37].

CONCLUSION

The First choice of treatment is surgical. In the case of inoperable patients or unpredictable functional and structural outcomes, medical treatment with vismodegib provides good results with mild to moderate side effects.

DISCLOSURE

The authors report no conflict of interests.

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