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Remote effect of interferons in basal cell carcinoma

Abstract

Basal cell carcinoma is a slow-growing, locally invasive tumor. Locally it can be aggressive, destroy neighboring tissues, cause ulceration and invade deep into cartilage and bone. It is considered a chronic disease because many cases that develop their first basal cell carcinoma will subsequently develop at least one additional tumor, and a group of cases have more than one basal cell carcinoma at the time of diagnosis. HeberFERON is the combination of alpha2b and gamma IFNs with antiproliferative, antiangiogenic and immunomodulatory activity. It is a therapeutic modality used in the treatment of basal cell carcinoma and could have a remote effect on the rest of the tumors.

Keywords: skin cancer, basal cell carcinoma, interferon, remote effect, HeberFERON

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Introduction

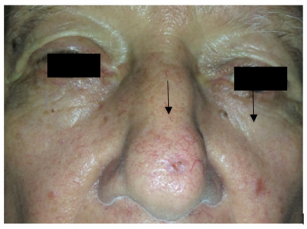
Basal cell carcinoma (BCC) is a slow-growing, locally invasive tumor with limited malignancy and low mortality. Locally it can be aggressive, destroy neighboring tissues, cause ulceration and invade deep into cartilage and bone. It originates in epidermal cells of hair follicles or in pluripotent basal cells of the immature epidermis that have lost their capacity for differentiation and normal keratinization.[1]

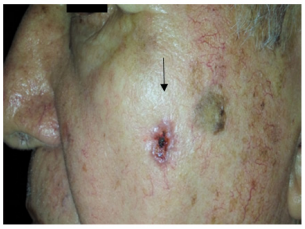
BCC is the most common tumor in humans. It is located on any area of the skin surface, but appears mostly in areas exposed to ultraviolet radiation, mainly the face and neck (up to 80% of all BCCs). Patients with BCC are at high risk for second and subsequent BCCs. In 40% of cases that develop their first BCC, at least one additional tumor will appear within two to three years, so it is considered a chronic disease. A group of patients present more than one BCC at the time of diagnosis, and this could be related to genetic changes and other factors.[2]

Although the treatment of choice for BCC is surgery, it is necessary to take into account that many of these neoplasms are located in the facial region, and the different surgical procedures required cause esthetic and functional complications. Although there is no protocolized treatment for patients with multiple BCCs, the high recurrence rate of the tumors makes it preferable to resort to less aggressive therapies, such as interferons.[2,3]

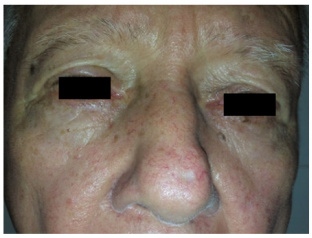
Interferons (INFs) are cell growth regulatory glycoproteins. They are types of cytokines, biological response modifiers and are classified into: Type I (IFN alpha and IFN beta), Type II (IFN-gamma) and Type III (IFN-lambda). Type I has the strongest antiproliferative and antiviral effect. Gamma exerts superior immunoregulatory activity. INFs possess immunoregulatory, antiproliferative and antiviral activity. The immunomodulatory effect includes stimulation of lytic activity of natural killer (NK) cells, specific cytotoxic T cells and macrophages on tumor cells, in addition to modifying antibody (Ab) production by B lymphocytes, regulating histocompatibility antigens (HLA) on cell membranes and stimulating INF-alpha production. Direct antitumor action includes antiproliferative and toxic effects, and binding of surface antigens on the tumor cell. Indirect action results in activation of macrophages, T cells and NK cells, and modulation of antibody production. They may also act at the cell cycle level and in the control of apoptosis.[4,5]

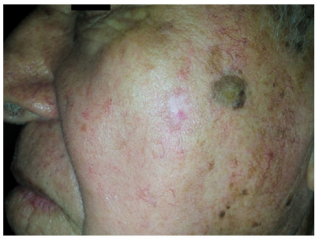
Before treatment, Nasal BCC treated with HeberFERON and two more lesions of BCC on the left cheek.





After treatment, Disappearance of nasal BCC and both tumors on left cheek.





HeberFERON is the combination of IFNs alpha2b and gamma with antiproliferative, antiangiogenic and immunomodulatory activity. The antitumor action is mediated by inhibition of tumor cell growth and induction of apoptosis (programmed cell death). Both IFNs possess antiangiogenic properties, which contribute to decrease tumor vascularity. The clinical response will be more rapid and prolonged than if each IFN were used separately, with a favorable cosmetic and functional aspect. It is indicated in basal cell carcinoma (BCC) of any size, location and clinical and histological subtype.[5]

The remote effect of some treatments in cutaneous cancer has been described, for example, in advanced melanoma. It is supposed that this effect is due to the interaction between radiotherapy and systemic treatments, mediated by a cytokine-dependent immune mechanism and direct damage to leukocytes as a side effect of radiation, which causes an increase in antigenic expression that would give immune cells a greater capacity for recognition and destruction of tumor tissue.[6]

Imiquimod is a toll-like 7 receptors agonist immune response modulator that stimulates innate and cellular immunity, induces apoptosis of neoplastic cells, promotes cytokine secretion at the site of application, mobilization of plasmacytoid dendritic cells, mobilization and activation of Langerhans cells in lymph nodes, activation of specific cytotoxic T lymphocytes, and accumulation of tumor cells. In the field of cancerization, it inhibits the development of new BCCs in the treated area or outside it. This is defined as tumor regression in locations other than where a local treatment has been applied, although reference is also made to the fact that, because of physical proximity to the area under treatment, there may be a direct effect of the therapeutics. In addition to BCC, the effect of imiquimod on the cancerization field in actinic keratoses has been described.[7]

Treatment with HeberFERON of one of the BCCs in patients with several tumors has generated an antitumor effect in other nearby or distant untreated tumors, showing complete responses by disappearance of the tumors, or partial responses by reduction in tumor diameter. This has occurred during the use of the combination of IFNs alpha2b and gamma in routine medical practice. In addition, a 5-year follow-up of a group of patients with complete response to HeberFERON showed that 100% of patients whose tumor disappeared maintained their response, and only 5% of patients developed a second BCC. The characteristics of these IFNs make them pleiotropic proteins with several functions that can exert their antitumor action by stimulating different functions of the organism necessary to control and/or inhibit cell growth, with activation of the Hedgehog system by IFN alpha.[8,9]

The remote effect of intradermal and perilesional administration of HeberFERON in a BCC in patients with multiple tumors may be clinically beneficial, with disappearance or reduction in the size of treated and untreated lesions and decrease in the occurrence of new lesions or both, as well as the presence of tolerable adverse events.[10]

At the Polyclinic Center, some patients with multiple BCC have been treated with the scheme of 10.5 million IU of perilesional and intradermal HeberFERON for three weeks until completing 9 doses, infiltrating only one tumor. The results obtained have been encouraging, showing disappearance or reduction of the treated tumor with effect on the other tumors, inside or outside the cancerization field, reducing its diameter, so this product could be used as a therapy in this type of cases.

Conclusion

HeberFERON is a combination of interferons used in the treatment of basal cell carcinoma with possible remote effect when used in patients with multiple BCCs, so it would probably be a useful therapeutic to avoid frequent surgeries or reduce their size, with the consequent improvement of the patient's quality of life and a good aesthetic response.

Acknowledgments

None.

Conflicts of interest

Authors declare that there is no conflict of interest.

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