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Basal cell carcinoma - the most common form of skin cancer. Methods of treatment

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Abstract:

Introduction: Basal cell carcinoma is the most common form of skin cancer. The lifetime risk is estimated as 33% to 39% in white men and 23% to 28% in white women. Because of that it is a very crucial disease for public health. In this article will be described main pathways of treatment which are especially recommended and are the most wide used for different types of basal cell carcinoma. Main division of interventions type used in treatment of basal cell carcinoma are surgical (physical) and non-surgical (medical). Surgical (physical) includes surgical standard excision, Mohs micrographic surgery, curettage and cautery, cryosurgery and laser therapy (ablative lasers, pulsed dye lasers). Non-surgical (medical) includes radiotherapy, topical imiquimod, topical 5- fluorouracil, photodynamic therapy, intralesional interferon.

Aim of study: Literature review of the most recommended treatment of basal cell carcinoma.

State of knowledge: In this publication will be desribed a current state of knowledge about basic and the most crucial basal cell carcinoma treatment.

Conclusion: Because of incidence rate of basal cell carcinoma which is very high- there are many reports about treatment of this disease. Treatment of this disease, especially among low risk patients, is very effective.

Keywords: cancer, oncology, dermatology, basal cell carcinoma

Main topic of this publication will be literature review of current methods of treatment of basal-cell carcinoma, but before this fundamental part- for better understanding- will be described different aspects of this type of cancer- epidemiology, etiology, pathophysiology, symptoms and how we formule a diagnosis.

Basal cell carcinoma- epidemiology

Basal cell carcinoma is the most common form of skin cancer. The lifetime risk is estimated as 33% to 39% in white men and 23% to 28% in white women. Some publications reports that nowadays we have the global burden of skin cancers. but the rate of change in skin cancers between 1990 to 2017 was increased the most for squamous cell cancer- it was 310%. Over the last 30 years, estimated incidence rates for basal cell carcinoma have risen between 20% to 80%. Although the frequency and incidence rate- basal cell carcinoma rarely causes metastatic disease or death (1,3).

Basal cell carcinoma- etiology

The majority of basal cell carcinoma are associated with sun exposure. The link between basal cell carcinoma and distance from equator has been reported. There are also several cutaneous conditions

associated with increased risk of basal cell carcinoma. The examples are: xeroderma pigmentosum, Bazex syndrome, seborrheic keratosis or oculocutaneous albinism. Other risk factors for the development of BCC include sun bed use, family history of skin cancers, skin type 1 and 2, immunosuppression, previous radiotherapy, and chronic exposure to toxic substances (2,5,6,7).

Basal cell carcinoma- pathophysiology

Ultraviolet (UV) radiation plays two key roles in the development of BCC: it causes DNA damage and immunosuppression. UVB radiation damages DNA and its repair system and alters the immune system resulting in a progressive genetic alterations and formation of neoplasm. UV-induced mutations in the TP53 tumor-suppressor gene have been found in about 50% of BCC cases. The mutations that activated the Hedgehog intercellular signaling pathway genes, including PTCH, Sonic hedgehog (Shh) and Smoothened (Smo) play a significant role in cutaneous carcinogenesis (8,9).

Basal cell carcinoma – symptoms and clinical variants

The most common clinical variant of basal cell carcinoma is nodular basal cell carcinoma. It is also called classic basal cell carcinoma. It comprises about 60-80% of the cases. The most often location for this type of basal cell carcinoma is head. Cystic basal cell carcinoma is rare variant of this skin cancer- cystic nodes located peripherally to the centrally placed tumor. Infiltrated basal cell carcinoma is presented as a whitish, compact, not-well defined plaque The most common localization is in the upper part of the trunk or the face. This version occurs as erythematous plaque with different sizes (from several millimeters to more than 10 cm). It is about 10-30% of basal cell carcinoma and occurs on the body skin. There are also characterized such types of basal cell carcinoma as micronodular basal cell carcinoma, morpheaform basal cell carcinoma, pigmented basal cell carcinoma or polypoid basal cell carcinoma.
Histopathologically, BCCs are composed of islands or nests of basaloid cells with palisading of the cells at the periphery and a haphazard arrangement of those in the centers of the island (10,11)

Methods of treatment. Literature review.

Main division of interventions type used in treatment of basal cell carcinoma are surgical (physical) and non-surgical (medical). Surgical (physical) includes surgical standard excision, Mohs

micrographic surgery, curettage and cautery, cryosurgery and laser therapy (ablative lasers, pulsed dye lasers). Non-surgical (medical) includes radiotherapy, topical imiquimod, topical 5- fluorouracil, photodynamic therapy, intralesional interferon. Charlotte Clark and co-authors described an evidence-based treatment update (15). They were searching Pub Med, Ovid MEDLINE, the Cochrane Central Register of Controlled Trials and the Cochrane Database of Systematic Reviews. The available data pointed that surgical methods remained the gold standard in basal cell carcinoma treatment. Mohs micrography was appropriately selected option for primary high-risk lesions and appropriately, suitable, alternate options for primary low-risk lesions may include photodynamic therapy, cryotherapy, topical imiquimod and topical 5-fluorouracil. They underline that hedgehog pathway inhibitors can be an option which can especially develop in the future.

Standard surgical excision

Surgery to remove the basal cell carcinoma affected area is still thought as the most effective treatment. Yusuf Gulleth and co-authors presented a systematic analysis which purpose was to answer the crucial question- what is the best surgical margin for a basal cell carcinoma. The conclusion based 16066 number of lesion analysed that 3-mm surgical margin can be safely used for nonmorpheaform basal cell carcinoma to attain 95 percent cute rates for lesion 2 cm and smaller (17,18).

Mohs surgery

Mohs surgery is a surgical technique developed by a surgeon Frederic Mohs in 1938. The main aim of this type of surgical removal is to do it with microscopically control. During the surgery, after each removal of tissue, the tissue is examinated for cancer cells. Main stages of Mohs surgery can be performed as a four steps: surgical removal of tissue, mapping the piece of tissue, freezing and cutting between 5 or 10 micrometers using a cryostat, interpretation of microscope slides, possible reconstruction of the surgical defect.

Mohs surgery is especially recommended for basal cell carcinoma of high risk regions the centrofacial sites (area H). Eim Dika and co-authors presented study aimed to evaluate the recurrence rate of head and neck high-risk basal cell carcinoma comparing Mohs micrographic surgery and conventional surgical excision. Clinical data of patients diagnosed from September 2014 to March 2017, referring to the Dermatology Unit of the Policlinico Sant'Orsola-Malpighi, University of Bologna, were retrospectively evaluated (285 treated with Mohs micrographic surgery

and 378 treated with traditional surgery). Of the 285 patients treated with Mohs micrographic surgery, 9 experienced a recurrence (3.1%). Of the 378 patients treated with traditional surgery, 53 relapsed (14%). The conclusion is that Mohs micrographic surgery should be preferred and is more effective and suitable for patients with basal cell carcinoma located on high risk regions (12,13,14, 19,20,21).

Immunotherapy

Imiquimod is an immune response modifier that is a Toll-like receptor 7 agonist that induces interferon and other cytokines through the innate immune system and stimulates cell-mediated immunity through T cells. Imiquimod has been shown to be efficacious as a topical treatment for basal cell carcinoma (BCC). Imiquimod has received FDA approval, and topical IMQ is approved by the European Medicines Agency for treatment of small superficial basal-cell carcinoma. Eric Marcet Santiago de Macedo presented a prospective, non randomized and uncontrolled longitudinal case series study about imiquimod efficacy in the treatment of nodular basal cell carcinoma. The histological clearence rate was 89.5% and 84.2% at 3 and 39.5 months. This result indicates that imiquimod is a useful treatment for nodular basal cell carcinoma (22,23,24,25).

Photodynamic therapy

Photodynamic therapy (PDT) is an established treatment option for low-risk basal cell carcinoma (BCC). Hongfei Wang and co- authors presented a systematic review and meta-analysis to compare photodynamic therapy with other procedures for the treatment of primary basal cell carcinoma. There was no statistically significant difference in complete clearance rate, 1-year recurrence rate or 5-year recurrence rate, when PDT was compared with cryotherapy. PDT had higher complete clearance rate compared with placebo but no statistically significant difference in complete clearance rate and 1-year recurrence rate when compared with pharmacologic treatment (topical imiquimod and 5-fluorouracil). PDT had a significantly better cosmetic outcome than surgery and cryotherapy (26,27).

Hedgehog pathway inhibitors

For patients with advanced basal cell carcinoma (BCC), including locally advanced or metastatic

BCC not amenable to curative surgery or radiotherapy, hedgehog pathway inhibitors (HHI) vismodegib and sonidegib are approved as first-line systemic treatment. Results from clinical trials highlight that the overall discontinuation rate of HHI treatment varies from 88% to 92% with vismodegib and is approximately 92% with sonidegib (28).

Summary

Basal cell carcinoma as the most common skin cancer is treated effectively. Different types of basal cell carcinoma requires different treatment techniques and methods. Recent years brought us a progress in knowledge about pathophysiology of basal cell carcinoma and it resulted and still can result in new therapies like hedgehog pathway inhibitors. Although we have many possibilities in treatment- we should look forward next reports.

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Conceptualization- Paweł Iwańczuk
Formal analysis- Paweł Iwańczuk
Investigation- Paweł Iwańczuk
Writing- rough preparation- Paweł Iwańczuk
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