Case Report

Adenoid Cystic Basal Cell Carcinoma Arising in Rhinophyma

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ABSTRACT: Adenoid cystic is a rare histological subtype of basal cell carcinoma. Basal cell carcinoma (BCC), the most common form of skin cancer is a slow-spreading tumor with local malignancy, with a high cure rate and favorable prognosis when is diagnosed in the early stages. Rhinophyma is one of the four subtypes of rosacea and it is histopathologically characterized by sebaceous glands hypertrophy. Disseminated annular granuloma (GAD) is a rare inflammatory dermatosis with uncertain etiopathogenesis, clinically represented by papules with annular or arciform aspect. UV radiations aggravates rosacea and are involved in the etiopathogenesis of BCC and can have a triggering or an aggravating effect on GAD. The association of adenoid cystic BCC with rhinophyma it is rare and more than that, the presence of both in association with GAD is not described in medical literature. We present the case of a 78-year old male patient, with personal history of prolonged exposure to UV radiations, that was admitted to the Dermatology for 4 nodular tumors, located on the face. The skin of the nose and menton with thickened, hypertrophied, irregular, red appearance and dilated pores. Also, on the upper limbs and trunk, the patient had, erythematous papules with arciform and ring shape with hypopigmented centers. We performed surgical excision of the tumors and biopsied an annular lesion. Microscopic examination showed nodular basal cell carcinoma with areas of adenoid cystic carcinoma and actinic degeneration of collagen and gigantocellular granulomatous inflammation. The skin biopsied from the upper limb showed annular granuloma appearance.

KEYWORDS: *Basal cell carcinoma, adenoid cystic, rhinophyma, histopathology.*

Introduction

Basal cell carcinoma (BCC), the most common form of skin cancer, represents approximately 80% of the non-melanomatous skin neoplasm at the human white race.

It is a slow-spreading tumor with local malignancy, with a high cure rate and favorable prognosis when is diagnosed in the early stages [1].

Histopathologically, BCC has variable aspects and often the different subtypes coexist.

The most recent classification of histological subtypes, regarding the risk of recurrence, divide the BCC as: BCC with low risk (nodular, superficial, pigmented, infundibulocystic, fibroepithelial) and BCC with high risk (squamous, sclerosing/morpheaform, infiltrative, micronodular, with sarcomatoid differentiation) [2].

Rhinophyma is one of the four subtypes of rosacea. Rosacea is a centrofacial dermatosis, which associates in varying proportions vasomotor hot flashes, telangiectatic erythema, papules-pustules and hyperplasia of the sebaceous glands [3].

Disseminated annular granuloma (GAD) is a benign, rare inflammatory dermatosis, with uncertain etiopathogenesis, clinically represented by papules with annular or arciform aspect. Ultraviolet (UV) radiations can have a triggering or an aggravating effect.

Histopathologically, the development of the GAD lesion is characterized by collagen degeneration associated with palisadic granulomatous inflammation [4].

UV radiations aggravates rosacea and are involved in the etiopathogenesis of BCC. Prolonged exposure to UV radiations of rosacea cases is considered to increase the risk of BCC development [5].

Case Report

We present the case of a 78-year old male patient, from rural area with a personal history of prolonged exposure to UV radiations, that was admitted to the Dermatology Department of the Craiova Emergency County Hospital for 4 nodular tumors, sized between 1-1.5cm, located on the face: 1 on the nasal pyramid, 2 on the right zygomatic region and 1 on the skin part of the upper lip (Figure 1, Figure 2).

They seemed to have appeared two years ago like papules and had a slow growth evolution.

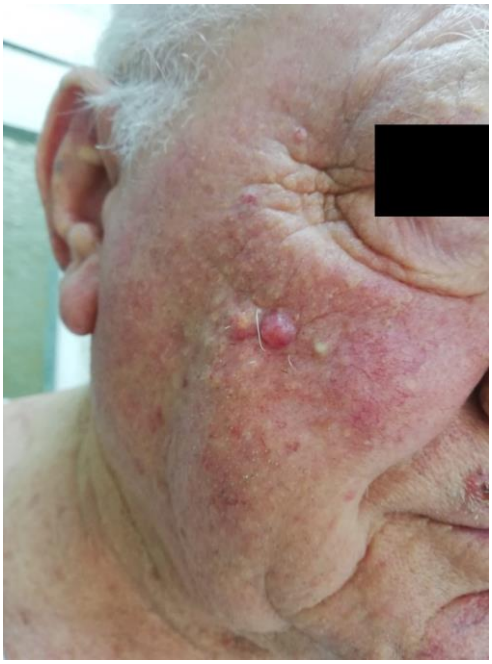

Figure 1. Nodular tumors on the zygomatic area.

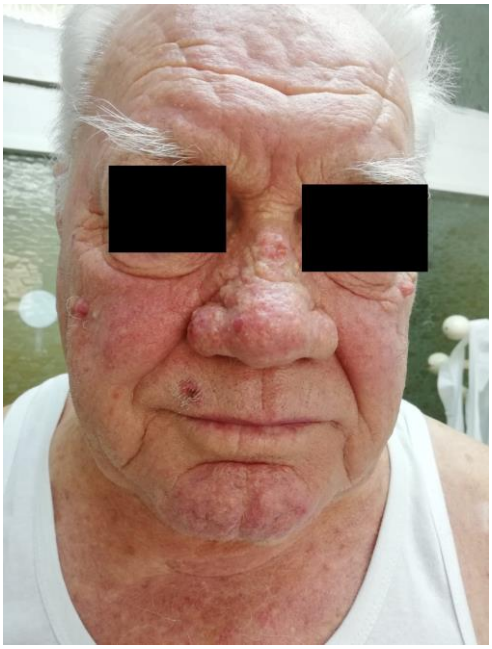

Figure 2. Nodular tumors on the nasal pyramid and on the skin part of the upper lip.

On physical examination we found an obese patient with a body mass index (BMI) of 31,54kg/m^2, phototype II (according to the Fitzpatrick classification), with the skin on the face with erythematous appearance, telangiectasia and the skin of the nose and chin with thickened, hypertrophied, irregular, red appearance and dilated pores.

Also, on the upper limbs and trunk, the patient had, from three years, erythematous papules with arciform shape and ring shape with hypopigmented centre (Figure 3).

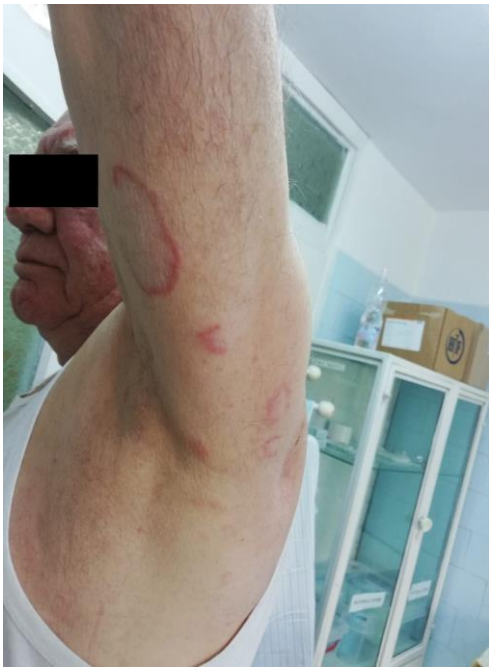

Figure 3. Erythematous papules with arciform shape and ring shape with hypopigmented center on the upper limbs.

We performed a surgical excision of the tumors and biopsied an annular lesion.

The excised specimens were fixed in 10% neutral buffered formalin and processed by routine protocols for paraffin embedding, sectioning and hematoxylin-eosin staining in the department of pathology from the same hospital.

The written informed consent of the patient regarding the publication of these data has been obtained.

Microscopic examination showed that the tumor on the nose was a nodular basal cell carcinoma with areas of adenoid cystic carcinoma (Figures 4-6), invasive in the hypodermis, but with clear surgical margins.

The nodular variant of basal cell carcinoma showed basaloid cells with scant cytoplasm and hyperchromatic nuclei, very low mitotic activity, peripheral palisading of the cells delineating the islands, some peritumoral stromal clefting and the presence of scanty myxoid stroma.

The adenoid cystic subtype of BCC presented cells with basaloid appearance that formed structures with microglandular arrangement, sometimes with mucine in the ductal spaces and abundant peritumoral inflammatory infiltrate. In other areas we observed large cyst with debris and hyperplasia of sebaceous glands.

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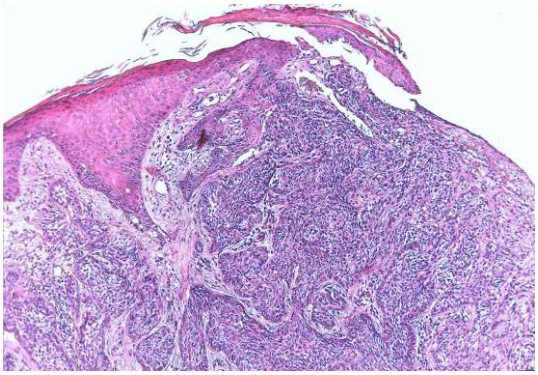

Figure 4. Basal cell carcinoma, nodular type, proliferating cells that forms islands of basaloid cells arising from epidermis and extending into superficial and deep dermis. H-E staining, x10.

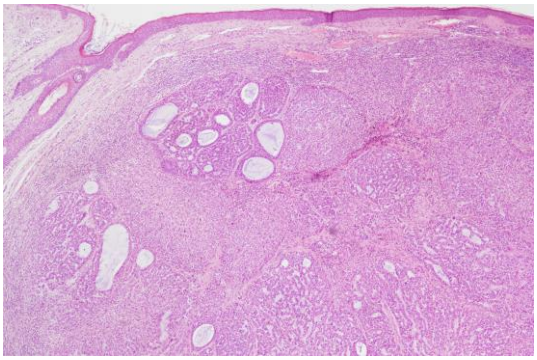

Figure 5. Adenoid cystic subtype of basal cell carcinoma. Cyst-like structures with intracystic mucin accumulation, surrounded by basaloid cells' arrangement and abundant peritumoral inflammatory infiltrate. H-E staining, x5.

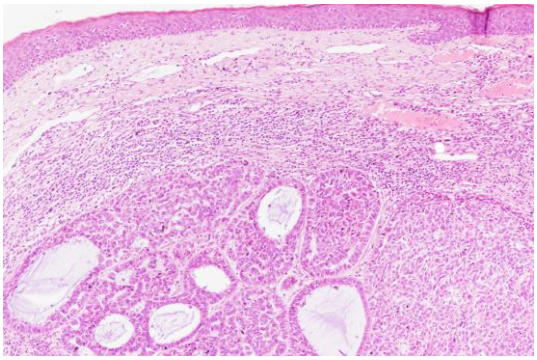

Figure 6. Adenoid cystic subtype of basal cell carcinoma (continuation). Adenoid elements with mucin accumulation, abundant peritumoral inflammatory infiltrate. H-E staining, x10.

The tumors excised from the right zygomatic area were also deemed adenoid cystic basal cell carcinoma and the lateral surgical margins presented actinic degeneration of collagen fibers and chronic inflammation (Figure 7).

The skin biopsied on the upper limb showed annular granuloma appearance (Figure 8).

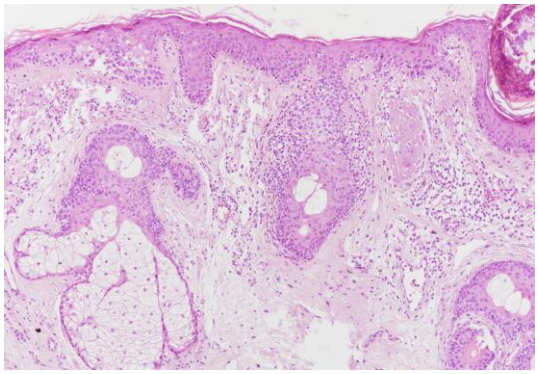

Figure 7. Area with actinic degeneration with diffuse chronic inflammatory reaction, hyperplasia of the sebaceus glands. H-E staining, x10.

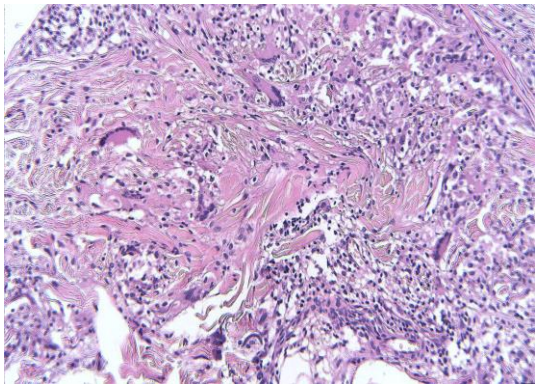

Figure 8. Dermis with epithelioid and gigantocellular cells around slightly degenerated collagen fibers. H-E staining, x20.

Discussion

Cancer is a condition caused by an imbalance between the inflammatory mechanism and the body immune response [6].

The research regarding the link between cancer and rosacea are rare, but among the skin cancers, BCC is the only one that is strongly associated with rosacea [7].

Exposure to UV radiations plays an important role in both the etiopathogenesis of rosacea and BCC [8].

The main mechanism of UV radiations in the pathogenesis of rosacea is that of inducing reactive oxygen species and degradation of the extracellular matrix, favoring the development of the inflammatory process.

Under the action of UVB the synthesis of endothelial growth factor from keratinocytes increases and UVA stimulates the degradation of dermal collagen.

It also increases the amount of proinflammatory mediators in the skin (IL1β, IL6, IL10, TNFα, CXCL8). CXCL8 has a role in maintaining the recruitment of neutrophils at the site of inflammation [9].

Regarding the role of UV radiations in the mechanism of BCC carcinogenesis, these cause UV-specific changes in the nucleotides located at the level of the p53 protein and PTCH (ligand protein involved in the Hedgehog signaling pathway) [10].

BCC, the most common malign non-melanomatous skin tumor, represents the consequence of the interaction between UV radiations, phenotype (UV sensibility) and genotype (somatic mutations and germ line mutation) that play a role in etiopathogenesis [11].

BCC is usually located on the head and neck, mostly affecting the nasal and malar region. Fair skin (phototype) and UV radiations exposure represent an important risk factors for this tumour type as well as for rosacea [12,13].

The new classification of rosacea includes 4 subtypes: erythemato-telangiectatic; papulopustulosis; rhinophyma; ocular rosacea.

Rhinophyma is characterized by modifications of nasal pyramid which include intense and persistent rash, dense telangiectasia, pustules, nodules and hyperplasia of sebaceous glands.

The particular rosacea types are known as: granulomatous rosacea, fulminans rosacea, steroid rosacea and drug-induced rosacea.

The coexistence of BCC with rhinophyma was first described by Wende and Bentz in 1904 [14].

Arguments regarding the coexistence of the two lesions were brought by Brubaker and Hellstom as well, suggesting that the papillary buds from the basal layer of the dilated follicular represent susceptible areas for the malign transformation.

More than that, those authors consider that this area presents a series of proliferative cellular changes, from hyperplasia to BCC, and they also affirmed that the BCC incidence is 5% at the rhinophyma patients.

A few hypotheses were issued to explain this association, and this were: tissue fibrosis caused by an inflammatory chronic process due to UV radiations exposure; skin trauma; hypertrophic and hyperplasic changes can represent precursor and favorable lesions for malignant transformation on the sun exposed areas [15,16].

Both BCC and rosacea are lesions that develop on the sun exposed areas with various clinically and histopathologically features.

The clinical diagnosis may be difficult in case of carcinomatous lesions masked or co-existing with tissue hypertrophy and skin deformation as in rhinophyma.

Rhinophyma is histopathologically characterized by sebaceous glands hypertrophy, connective and vascular tissue hypertrophy.

For granulomatous rosacea the microscopic aspect is represented by granulomatous and gigantocellular inflammation.

Regarding our patient, at the microscopic examination we found actinic degeneration of collagen with granulomatous and gigantocellular inflammation areas, highlighting histopathologically granulomatosis rosacea lesions alongside with adenoid cystic basal cell carcinoma area.

If the BCC lesions are neglected, especially the aggressive types which are associated with extensive invasion in dermis with destruction of the collagen at this level, the identification of tumoral edges becomes difficult from a histopathological point of view, especially in case of association with rhinophyma [17].

From a histopathological point of view regarding the aspect of BCC, this represent a malignant proliferation derived from the basal cells from the epidermis and the basal cells from the external sheath of the hair follicle, these cells being considered pluripotent epithelial cells [2].

Both clinically and histopathologically, there are BCC types with subtypes with distinctive appearance.

The histopathologically types, according to the World Health Organization (WHO) 2018 classification, are: the nodular type with adenoid, cystic and keratosis subtype; the superficial type; micronodular; fibroepithelial (Pinkus tumor); morpheaform (sclerosing, desmoplastic); infiltrative; basosquamous; pigmented; BCC with sarcomatoid differentiation; with adnexal differentiation (infundibulocystic).

According to the last medical revision regarding the recurrence risk, BCC was divided as: low risk (nodular, superficial, pigmented, infundibulocystic, fibroepithelial) and high risk (basosquamous, sclerosing/morpheaform, infiltrative, micronodular, with sarcomatoid differentiation) [2,18,19].

Clinically, the nodular type is the most common type and it is initially presented like a pearly papula, subsequently taking the shape of translucent nodule with a smooth surface, round edges and telangiectasis on the surface; these lesions mostly occur on the head and neck.

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Both, the clinical appearance and common enteropathogenic factors of BCC and rosacea were presented at our patient.

Prior to the most recent WHO classification (2018), basal cell carcinoma adenoid cystic subtype was considered a distinct type, but in the present case it is considered a subtype of the nodular type of BCC [18,19].

Histopathologically, the tumoral cells with a basaloid appearance create structures with a glandular or cribriform arrangement with mucine in the ductal space and palisadic arrangement in the periphery, the cells are structured in a lacy shape, combined with connective tumoral tissue.

This histological appearance was observed at our patient as well [2,19].

For this histological subtype, the frequency is not entirely known, different studies have reported values between 1,3% to 20,91% [20,21].

The subtypes adenoid cystic, morpheaform, infundibulocystic and pigmented are rare morphological variants and represent altogether approximately 10% of the total of BCC [18,20].

As a synthesis of these studies, it is suggested that in contrast to other histological variants of BCCs, the adenoid cystic BCC subtype has a tendency to develop on other skin regions as well [21,22].

It seems it is a histological type with a low malignity grade, in comparison to other histological subtypes, like the morpheaform type which has a higher malignity grade when considering its evolution.

Because the clinical aspect of BCC adenoid cystic subtype is not always suggestive and the evolution is slow, this tumoral form of BCC can be wrongly diagnosed as a benign process of adnexal structures [2,19].

The management of the adenoid cystic subtype of BCC remains similar to the other BCC types and the manner of therapeutic approach depends on the anatomical localization, the size of the tumor, the aspect of edges, the recurrence risk, and patient's immunosuppression, but the first approach remains the surgical excision [23,24].

In the studied medical literature, we could not find the association of GAD with rhinophyma complicated with BCC.

Characteristically, the GAD lesions are presented as a papular shape cutaneous lesions, with 1-3mm diameter, varying color from intense red to pale erythematous aspect, and they can be located on any region of the body.

The lesions can become coalescent, with annular and arciform appearance, with centrifugal extension.

Even though any region of the skin can be involved, the lesions tend to be located symmetrically on the acral and trunk regions. GAD is usually presented with asymptomatic cutaneous lesions which can improve during winter but worsen during sunny seasons and this fact can explain the involvement of UV radiations in the pathogenesis of this disease [4,25].

Conclusions

Adenoid cystic BCC is a rare histological type, and few cases of its association with rosacea were reported in medical literature. More than that, the presence of both in association with GAD is not described in medical literature.

The exposure to UV radiations plays a very important role in etiopathogenesis of rosacea, BCC and GAD.

In present, histologically the adenoid cystic form is considered a nodular BCC subtype with a low risk of recurrence, the therapeutic approach being similar to the other types of BCC, with the surgical excision remaining the gold standard.

Starting from this presentation and the revision of the medical literature information, regarding the association of the three types of affections, future research is necessary.

Conflict of interests

None to declare.

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