Introduction

Basal Cell Carcinoma (BCC) is one of the most common skin cancer in Caucasian population [1]. BCC, first described by Jacob in 1824 [2], most commonly occurs in adults, especially in the elderly population. Among this population, individuals with fair skin, blond or red hair, light eye colour and sun-damaged skin are easily affected [3]. In fact, exposure to ultraviolet radiation plays a key role in the genesis of this tumour.

Typically BCC is a slow-growing, non-metastasizing tumor, locally aggressive with frequent regional recurrences; according to Pinkus, the stromal dependence of the tumour provides an explanation for the non-metastasizing nature of BCC [4].

Metatypical BCC, also known as Basosquamous Carcinoma (BSC), is a subtype of BCC. It is similar to BCC for the gross aspect and regional recurrences, but it has the capacity to spread and develop metastasis. This terrible characteristic endangers the life of the patient if it is not readily recognized by the physicians. Herein we present a report of two patients affected by BSC originating in the nasal region and external ear that after a series of devastating local recurrences metastasized to the lung and bones in one case. The true incidence of Basosquamous Carcinoma may be higher, with underreporting arising because of rarity of diagnosis and lack of awareness on the part of clinicians. Our experience suggests that a deep biopsy is often necessary to discover a BSC that appears as BCC but with local aggressive features.
Herein we present a report of two patients affected by BSC originating in the nasal region and external ear that after a series of devastating local recurrences metastasized to the lung and bones in one case.

Case report

Patient 1

A fair skin and blue eyes 70-year-old man was referred to our ENT Institute for recurrence of BCC in 2005. The patient presented with a small right medial canthal skin lesion extended to the lateral wall of the nasal pyramid. He had no significant medical history and he smoked 40 cigarettes a day.

The patient presented a seven years history of recurrences of skin tumours in head district managed in other hospitals.

In 1998 he referred a skin lesion to the right ala of the nose that was excised and scheduled for BCC. After one year he showed a local recurrence of BCC in right retro-auricular region that was excised and repaired by a Thiersch graft. In 2001 a new recurrence was present in the right lateral wall of the nasal pyramid. This lesion was excised and the nasal wall was repaired using a dermo-epidermic inguinal graft. However after two years (in 2003) the tumour reappeared in the same region and it was treated with surgical excision and Thiersch graft reconstruction. In 2005 the tumour involved the right inferior eyelid and it was extended to the omolateral internal canthus and the nasal pyramidal wall. When we observed the tumour we programmed a new biopsy of the lesion and a CT of head and neck region. Fourteen multiple biopsies were taken along the peripheral margins of the tumour: from the right maxillary region, from the right inferior margin of the orbit, from the right superior and inferior internal canthus (deep in the canthal lesion) and from the skin of the right nasal bone.

In twelve biopsy fragments histological examination confirmed a BCC infiltrating the bone tissue. One tissue fragment from superior internal canthus showed a massive inflammatory reaction while fragments from deep skin biopsy showed the presence of small dark-staining cells with peripheral palisading. Biopsy fragments taken from the centre of the tumour demonstrated basal cells differentiating into intermediate cells and into keratotic squamous cells which presented singly or grouped into pearls (Fig. 1). The nuclei of these cells varied a little in size and staining intensity. Mitotic figures were rare.

CT examination of head and neck district showed a dyshomogeneous mass of 7 cm to 5 cm that involved the anterior wall of the right maxillary sinus and invaded the sinus cavity. Inferiorly, soft tissue was infiltrated over the right superior lip as superiorly the bone pavement of the orbit, the lower eyelid and the nasal bone. The right nasal and lacrimal bones and the ipsilateral ethmoidal-lamina papyracea appeared eroded and decalcified by the mass. Right eye seemed to be not involved even if there was a strong doubt about the real possibility of a future or possible infiltration. There was not clinical or radiological evidence of cervical and/or distant metastasis. The tumour was classified as T3N0M0.

A surgical approach was decided and the patient was informed of the possibility to sacrifice the right eye in case of neoplastic infiltration. The patient signed the informed consent. A right maxillectomy with right ethmoidectomy was performed. During the surgery the tumor was observed to be in close contact with the right eyeball and medial rectus muscle, so it was decided to opt for an exenteratio orbitae. The intra-operative histological examination of the surgical margins was negative for tumour persistence.

The surgical area was reconstructed with a right-sided latissimus dorsi myocutaneous flap. The definitive histological examination confirmed the previous diagnosis of BSC of the skin with concomitant large invasion of bony structures. The patient was included in a close follow-up program consisting of clinical examinations (monthly during the first year) and CT evaluations (once every eight months for the first two years). Successively the patient was clinically observed every six months with one CT evaluation per year. We decided not to treat the patient with radiation or chemotherapy because the surgical margins were free of disease and because there is no standardized approach for this type of tumor. In September 2010 during the clinical examination the patient reported recurrent episodes of hemoptysis, dyspnoea and lower left rib pain. A chest radiograph and CT scan were performed and they showed multiple bilateral lung lesions and a fracture of the left eighth rib suggesting widespread metastases. Successively a CT-guided needle biopsy of pulmonary nodules was performed. Histopathological examination revealed a BSC with features consistent with the primary lesion (Fig. 2). The patient was included in a chemotherapy protocol with Doxorubicin and Cisplatin for the management of the metastases.

Patient 2

A 68-year-old male patient was admitted to our Department complaining of a chronic disturbance of the left external auditory canal. Visual inspection of the ear revealed an
infiltrating lesion of the external canal involving the tragus, the concha and the initial portion of the helix (Fig. 3). Otoscopy showed medial extension of the lesion reaching the middle part of the ear canal. The tympanic membrane and the annulus seemed free from disease. Head and neck examination was normal and it did not reveal clinically appreciable lymph nodes. A temporal bone CT scan was performed and it showed no involvement of the surrounding bone. The patient underwent a fresh frozen section and subsequent surgical excision of the lesion that included the external 2/3 of the ear canal, tragus, concha and helix with a margin of healthy skin. The bone of the external auditory canal appeared clinically and histologically not infiltrated by the lesion, but a canalplasty was performed in order to remove bone tissue which was in close contact with the tumor and in order to improve wound healing. The surgical field was reconstructed by an advancement flap, a temporalis fascia covered the external canal bone and the pinna was reconstructed with the remaining portion.

The definitive histopathology demonstrated the presence of a BSC in biopsy specimen. Small dark-staining cells with peripheral palisading were present. In the centre of the tumor there were islands of basal cells differentiating into intermediate ones and into keratotic squamous cells grouped into pearls (Fig. 4).

In consideration of the metastatic potential of this kind of tumor, the patient was systemically evaluated by thorax and abdomen CT scan and bone scintigraphy. All examinations performed were negative for metastatic disease.

After 5 years of follow up, the patient is still free from disease without any local recurrence.

Discussion

BSCs of the skin are a rare variant of BCCs with the features of both basal cell and squamous cell carcinomas and higher tendency for recurrences and metastases [8].

This tumor was first described by Beadles in 1894 [9] in a case of rodent ulcer and it was better reported by MacCormac in 1910 [10] in a series of rodent ulcers which showed basal cell and squamous cell tumours present side by side without a transitional zone. However, during the years, the existence of BSC was object of debates between the pathologists. In 1928 these lesions were classified as Metatypical Carcinomas [11] while in the 1950s and 1960s Lennox and Lever excluded the existence of these tumours [12, 13]. Today the existence of these lesions is largely accepted by the physicians.

BSCs were also known in English Literature as Basaloid Squamous Cell Carcinomas, Basaloid Squamous Carcinomas, Metastatic Basal Cell Carcinomas, Keratotic Basal Cell Carcinomas, Aggressive Basal Cell Carcinomas and this aspect complicated and confused the signalization of this neoplasms [6, 14, 15]. However, in order to avoid confusion, Lopes De Faria in a 1985 study advised to call BSC only those lesions
characterized by features of BCC and Squamous Cell Carcinoma (SCC) separated by a transitional zone [16]. Specifically, he postulated that BSC specimens should be characterized by distinct areas of BCC and SCC with an intermediate stage of differentiation. This intermediate tissue was considered to be a transitional tissue and not an area of BCC with atypical cells.

It should be distinguished from the “collision tumor” which has distinct areas of SCC and BCC but lacks in transitional zone [17]. Unfortunately, as reported by Leibovicht et al. in 2005, uncorrected histopathologic diagnosis is frequent, especially if only one superficial biopsy is obtained [18]. This aspect is in accordance with our experience. In the first reported case only one deep biopsy fragment out of fourteen showed the feature of BSC while in our second patient only the definitive histopathological evaluation clarified the diagnosis of BSC.

Approximately two-thirds of reported cases of BSC arise from a primary one located in the facial region [19], above all in the central face area and more specifically in the perinasal zone [17]; unfortunately BCCs arise from the same location and this can to confuse the diagnosis.

Snow in 1994 and successively Motegi in 2006 demonstrated that primary lesions greater than 3 cm in diameter has a rate of metastatic disease of 1.9% and that the risk of spread increases to 50% for tumours over 10 cm; on the contrary, rarely smaller lesions cause metastatic disease [20, 21].

This would seem a logical hypothesis, then massive misdiagnosed tumours would have a greater risk of metastasis; however, in addition to this theory, deep or perineural invasion and bone involvement should be considered as a possible cause of the spread.

This third event was observed in our cases.

In fact in patient N°1 the histological evaluation showed a bone invasion in twelve superficial fragments scheduled as BCC: this patient developed metastatic disease to the lungs in the successive months. In case N°2 the bone invasion was not present and no metastatic disease was reported during five years of follow-up.

Surgery is considered treatment of choice for BCCs and it should also be indicated for BSCs, however, the ideal treatment for this pathology has not been elicited to date because of the paucity of data on the subjects [19].

According to Costantino et al. currently the standard of care treatment is a wide local excision with evaluation of both local nodal basins and distant sites for evidence of metastasis [22].

It is very important to identify prognostic indicators of recurrence which should include: positive surgical margins, perineural or lymphatic invasion, bone involvement and size greater than of 3 cm in diameter. A close radiological and clinical follow-up should be mandatory in presence of one of these factors [17] but it appears necessary also in patients with a positive diagnosis of BSC even in absence of indicators. In addition we think that more attention should be paid for all tumours diagnosed as BCC but with aggressive histological features and involvement of deep structures (bone, nerves, blood and lymphatic vessels and others).

As reported by Dudic et al. adjunctive radiation therapy has been used in presence of high-risk lesions (deep invasion, positive margins, intravascular spread, perineural involvement after surgical excision) [19] but the absence of a standardized approach and/or lesions too near to radio-sensible organs (such as our first patient) may limit this management.

Treatments of metastatic disease are palliative [23]. Regimens using radiation, surgery or chemotherapy have been employed with disappointing results.

Conclusion

BSC is a rare clinical entity that arises principally in head and neck district with propensity to metastasize. Unfortunately BSC is clinically indistinguishable from BCC and diagnosis is possible only by an accurate histological evaluation of specimens. Wide local surgical excision with negative tissue margins together with a long term follow-up is the treatment of choice. A particular attention should be reserved also in cases diagnosed as BCC but characterized by bone invasion or deep tissue involvement. These forms could hide a BSC and the Otolaryngologists should keep in mind this insidious possibility during the diagnostic evaluation.

In fact our experience suggests that a deep biopsy is often necessary to discover a BSC that appears as BCC but with local aggressive features. It is very important to emphasize that the BSC features can be present only in the deep layers of the lesion near to bone, nerves or vessels.

At present an early detection of BSC and a wide local excision with free-disease margins represent the only gold standard of treatment for the patients affected by this tumour.

Authors’ contributions/Wkład autorów

Alessandro De Stefano – concepted, wrote and reviewed the study, Francesco Dispensa – wrote the study, Anna Grazia Petrucci – analyzed data and the English text, Leonardo Citraro – collected data, Adelchi Croce – reviewed the paper.

Conflict of interest/Konflikt interesu

None declared.

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