Giant Basal Cell Carcinoma: Clinicopathological Analysis of 51 Cases and Review of the Literature

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Abstract. *Background: Giant basal cell carcinoma (GBCC) is an aggressive malignant neoplasm. Because of the rarity of the tumor and its recognized high risk of recurrence, there are no guidelines for its treatment. Patients and Methods: Published articles in PubMed Central were carefully reviewed. Data from 48 patients obtained from 30 individual articles were added to our 3 cases, producing a total number of 51 cases of GBCC. A clinical database was established in order to define the behavior of this tumor, prognostic factors and optimal treatment. Results: GBCC mostly occurs in elderly male patients, with a peak incidence in the seventh decade of life. It develops as long-standing dermal tumor with mean disease duration of 14.5 years and is most commonly located on the back, followed by the face and upper extremity. The most common histological subtype is nodular. The average size at presentation is 14.77 cm in its largest diameter. The presence of metastasis at the time of presentation represents the most significant adverse prognostic factor. Local recurrence or metastasis develops in 38.3% of patients despite optimal therapy. The overall reported cure rate is 61.7% by a mean follow-up of 2 years. Wide local excision of the tumor with or without postoperative radiochemotherapy represents the optimal treatment. Conclusion: Optimal management of GBCC consists of wide local excision with histologically confirmed tumor-free margins, frequently followed by adjuvant therapy. In cases of lymphatic spread, a regional lymphadenectomy is also necessary. In addition, consideration should be given to a close and long-term follow-up because of the high rate of locoregional recurrence.*

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Basal cell carcinoma (BCC) is the most common skin malignancy of Caucasian populations and is only rarely seen in pigmented races. It generally grows slowly and behaves in a relatively benign, less aggressive fashion.

Giant BCC (GBCC) is, on the contrary, a rare skin malignancy characterized by an aggressive biological behavior, deep tissue invasion with infiltration of the dermis and involvement of extradermal structures such as bone, muscle and cartilage, as well as by metastasis and frequently carries a poor prognosis.

According to the American Joint Committee on Cancer (1), GBCC is defined as a tumor with a diameter larger than 5 cm. Only 1% of all BCCs achieve this size (2). Since its first description by Eckoff (3) in 1951, data originating from large clinical series are rare in the literature, due to the rarity of GBCC. Consequently, reliable conclusions cannot be drawn from isolated case reports with regard to clinical and histological presentation of the tumor, prognostic factors and treatment strategy.

The purpose of this article was to collect and summarize the data on GBCC from numerous case reports published since 1969. Additionally, the data of 3 patients with GBCC, who were treated in our Institute, are presented and analyzed.

Patients and Methods

Data presented in 30 published case reports in Medline and PubMed Central since 1969 were reviewed. These account for 48 cases in total. We have also reported 3 new cases (in total 51 cases), establishing a database for a better understanding of the biological behavior of GBCCs.

The main criterion for the inclusion of an isolated case report in the collective database was the presence of adequate data regarding its description. The data collection referred, in particular, to the age and sex of the patient, tumor location and size, histological subtype of the tumor, stage of the disease on presentation, age of the lesion, primary management and outcome. Table I summarizes the data collected from reviewing 30 articles, as well as the data arising from our patients. Prognostic factors influencing outcome have been

defined and the statistical significance of each factor was assessed using a χ^2 test, as well as regression analysis.

A short presentation of the additional 3 cases, presented for treatment at our Institute follows.

Case Report 1

A 65-year-old Caucasian female presented with a complaint of an invasive, non-healing ulcerative lesion, measuring 11.5×7 cm in diameter, located on her back (Figure 1). A punch biopsy of the lesion confirmed the diagnosis of a nodular BCC. There was no clinical lymph node involvement.

Magnetic resonance imaging (MRI) showed infiltration of the paravertebral muscles and part of the vertebral spines, especially at the level of T12-O3 vertebral spine processes. There was also significant iron deficiency anemia and hypoalbuminemia.

The therapeutic approach was multidisciplinary, with wide local resection of the tumor, including a part of the vertebral spine processes. For the reconstruction of the wide defect, both myocutaneous latissimus dorsi flaps, as well as the left fasciocutaneous gluteal flap were mobilized (Figure 2). Postoperative radiotherapy was also administered. Eight months after the surgery, the patient underwent a percutaneous cyphoplasty because of recurrence of the neoplasia in the region of the vertebral spines.

Case Report 2

A 63-year-old Caucasian man presented with a large ulcerated tumor on his right anterior chest wall, measuring 20x15 cm with necrotic areas and a sclerotic border. There was a history of tumor resection one year earlier, which was followed by recurrence of the lesion. There was no evidence of lymph node involvement. Laboratory examination revealed hypochromic microcytic anemia and low albumin serum level. Biopsy of the lesion was compatible with adenoid BCC with invasion of the dermis and subcutis, and squamous metaplasia (Figure 3). MRI showed thickening of the subcutaneous layer with infiltration of the ribs of the anterior chest wall area. The lesion extended posteriorly into the anterior mediastinum (Figure 4). In consultation with thoracic surgeons, the patient underwent an extensive excision for the recurrent tumor with resection of 4 ribs.

Reconstruction was performed with a tranverse rectus abdominis myocutaneous flap (TRAM) and synthetic mesh. Because of partial necrosis of the myocutaneous flap (zone II, IV), the subsequent defect was completely covered by using an ipsilateral pedicled latissimus dorsi flap.

The patient received postoperative adjuvant radiotherapy. Five months after initial treatment, the patient is in good condition and free of disease.

Case Report 3

A 76-year-old Caucasian man was referred to our Institute with a large vegetative tumor, measuring about 7x4.5 cm, involving the posterior scalp region (Figure 5). The lesion had been present for many years, during which time it had progressively increased in size, although the patient had otherwise been in good health. The core biopsy confirmed the diagnosis of a nodular BCC and the radiological examination revealed bone invasion. He underwent wide resection of the tumor and repair with a pedicled trapezius myocutaneous flap (Figure 6). Radiotherapy was also necessary postoperatively. The patient was seen over the next 3 months with well-healed flaps and no signs of locoregional recurrence being documented.

Results of Literature Survey

We have reviewed 30 articles presenting the clinical and pathological data arising from 48 patients treated for GBCC since 1969. By adding 3 cases of our own to the above population, a group of 51 patients was created.

There were 34 men with a mean age of 66.7years (range 47-82 years) and 17 women with a mean age of 68.6 years (range 43-84 years). The male: female ratio being 2:1 demonstrates a clear gender predilection. A peak occurrence in the seventh decade of life was identified in both genders.

With the exception of 2 cases, all patients were Caucasians.

There was a previous history of burn in 1 case (2.0%) and of X-ray exposure in 3 (5.9%), whereas a recurrence of a BCC after previous treatment was present in 5 patients (9.8%).

Alcohol abuse was noted in 4 patients (7.8%) and common clinical findings such as hypoalbuminemia and iron deficiency anemia were noted in 15.7% and 35.3% of patients respectively.

The primary sites of GBCCs were the back (14 patients, 27.5%), the face (12 patients, 23.5%), and upper extremity (7 patients, 13.7%). In the remaining cases, the tumor was located on the abdominal wall (3 patients, 9.8%), on the scalp or genitalia region (2 patients, 5.9%) as well as on the anterior chest wall, lower extremity or scapula region (1 patient, 3.9%).

The mean size of the tumor in its largest diameter was 14.77 cm (average 5-40 cm), while the duration of tumor presence was 14.57 years, on average.

The histological subtype of the tumor was reported in 42 patients. Twenty-three patients had nodular lesions (54.7%), 8 patients presented with an infiltrating subtype (19%), 2 patients (4.76%) with superficial GBCCs, 1 patient had the keratotic subtype (2.3%), whereas 4 patients (9.5%) had metatypical or morpheaform lesions respectively.

The stage of the disease was reported in 50 patients. Six patients (12%) had regional lymphadenopathy at presentation.

Three patients had systemic metastatic disease at presentation (6%), and the remaining 41 had localized disease (82%).

There were 41 node-negative patients. Wide local excision and reconstruction with grafting or flaps, with intent to cure was offered to 27 of the 41 patients. Local excision in combination with adjuvant treatment was given to 6 patients, radiotherapy or chemotherapy alone to 2 patients, cryotherapy to one patient and no therapy at all to 5 patients. In 2 patients without treatment, the outcome was not reported. From this group, 7 patients died (17.07%) and 5 patients (12.19%) developed local recurrence, whereas 25 patients (60.9%) are reported as being alive.

There were 9 patients with metastases (6 node-positive and 3 patients with distant metastases). Radiotherapy with excision was used in 3 patients and excision alone was employed in 2 patients of this group, while 1 was not treated and three patients underwent chemoradiotherapy alone. From this group, 3 patients (37.5%) died of the disease, 2 patients (25%) developed distant metastases and 3 patients (37.5%) are still alive after a mean follow-up of 2 years. In one patient of this group, the outcome was not mentioned.

The Mann-Whitney test shows that there was no significant difference in the follow-up time between patients with good and poor outcome and this measures approximately 2 years (ranges 0.75-72 months). The sex and age of the patients, anatomical site, duration of the disease, size and histological subtype of the lesion were examined for their influence on overall prognosis but they have failed to show any statistical correlation. The presence of metastasis was found to be a negative prognostic factor for the outcome, as the χ^2 test shows (p=0.041). The regression analysis shows that the presence of metastasis multiplied the risk for a poor outcome by three-fold (OR=3.612).

The treatment administered was also statistically significant. Excision of the lesion and reconstruction of the defect in combination or not with adjuvant treatment gave a better outcome and the patients had a better prognosis compared to those patients who were treated palliatively (radiotherapy or chemotherapy alone) or who received no therapy at all. The examination of these relations was possible with χ^2 test (p=0.004), in which one person who was treated with cryotherapy was not included.

Discussion

GBCCs are infrequently reported in the literature, representing a quite rare oncological entity. Only occasional case reports are usually published. According to Betti *et al*. (2), the occurrence rate is approximately 0.5%-1% out of all types of BCCs.

GBCC is defined as a tumor with a diameter larger than 5 cm. By the TNM classification, these tumors are characterized as T3 (42). According to other authors, however, tumors measuring 10 cm or more were designated as giant (18).

BCC is considered to arise from the pluripotential epithelial cells of the epidermis and hair follicles. Although Ono *et al*. (43) have shown that generally BCC grows at a rate of 1 mm in diameter on average per year; when BCC existσ for a long period of time, this tumor may grow to a large size and in an aggressive manner.

The primary cause of BCC is exposure to ultraviolet radiation. It also occurs in association with specific disease entities such as basal cell nevus syndromes, xeroderma pigmentosum, albinism and nevous sebaceous. It has also been described in association with trauma (chronic leg ulcers, vaccination scars), immunosuppression and exposure to arsenic, X-rays and coal-tar derivatives (44).

The causes of GBCC are not clearly defined. Sahl *et al*. (18) regard neglect as the primary cause of GBCC resulting in continuous growth of the tumor over a period of 10 to 20 years. It is usually reported among people with a poor socioeconomic status, physical or psychiatric disability that impedes judgment or access to health care providers. According to Randle *et al*. (42), neglect is an important factor in BCC achieving a large size, but they considered the most important variable in development of such large tumors to be inadequate treatment of smaller tumors and the resulting local recurrence.

In the present review, long-standing tumors were the rule and neglect for a long time period was the main cause. A history of inadequate initial treatment was noticed in only 5 cases. Chronic alcoholism is also said to be associated with the development of GBCCs, due to a defect in the host immune response. This was confirmed in only 7.8% of the patients in this study.

The present review demonstrates that the average age of patients at presentation is approximately 67 years, with a clear male predomination. These demographic data are in full accordance with previously published reports (22, 42).

In general, BCCs are most usually located at the head and neck area due to sun exposure (80%), whereas 10% occur on the trunk (44). The anatomical distribution of GBCCs is different, with predominance on the trunk, especially on the back, where they go unnoticed by the patient, such as in the case of our first patient. The hereby reported distribution of GBCCs is in accordance with already published reports (18, 22). Lesions found on the face or neck cannot be readily hidden and patients seek treatment early in the course of the disease. GBCCs located on the anterior chest wall, as in the case of our second patient are quite rare. More recently, one case of non-operable chest wall GBCC has also been reported (29).

The size of these tumors is usually related to their duration rather than to an unusually rapid growth, although in patients younger than 35, the tumor may demonstrate a highly aggressive development (46). In the present review, the mean size of the lesion was 14.77 cm in its greatest diameter.

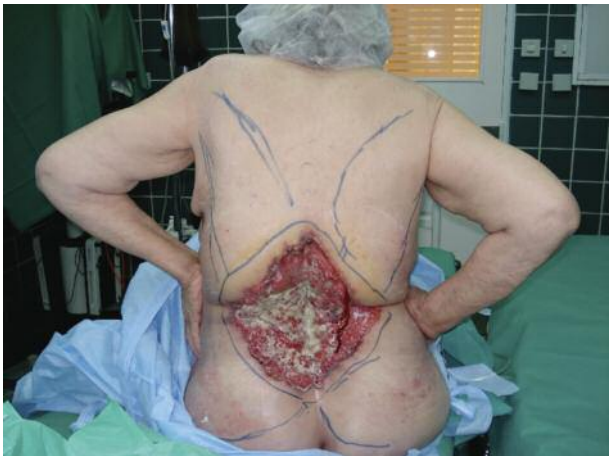

Figure 1. *Giant basal cell carcinoma of the back.*

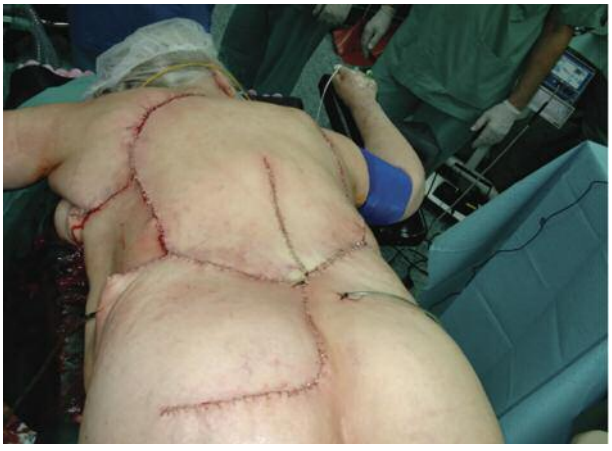

Figure 2. *The tumor was excised and the defect was repaired with mobilization of both myocutaneous latissimus dorsi flaps and left fasciocutaneous gluteal flap.*

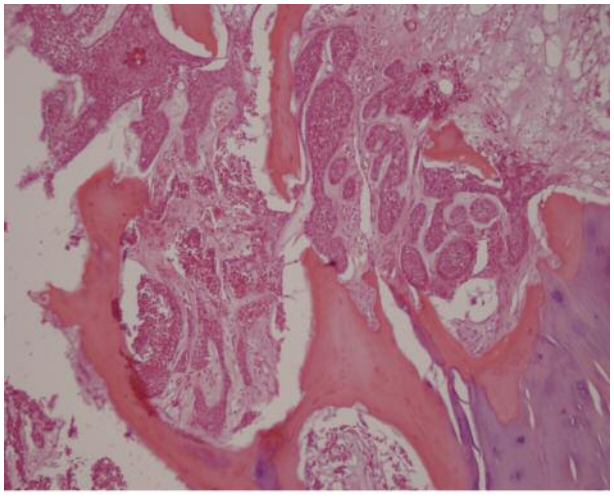

Figure 3. *BCC infiltrating the ribs (H-E, ×100).*

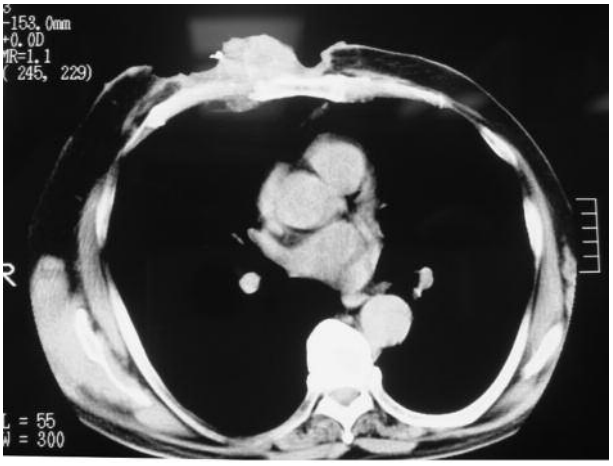

Figure 4. *Preoperative CT showing the infiltration of the ribs and invasion of the deep ulcerating lesion into the anterior mediastinum.*

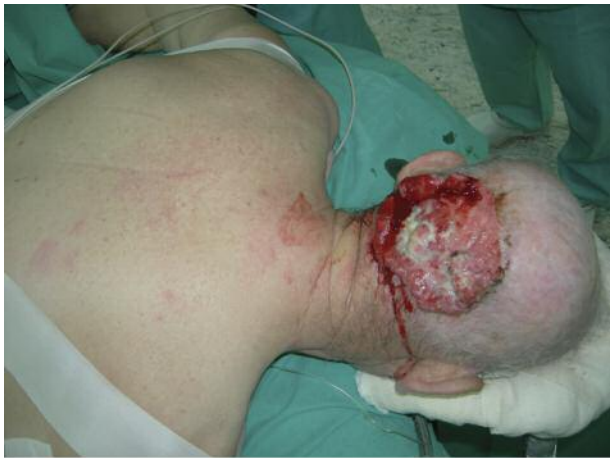

Figure 5. *Large nodular BCC involving the occipitum.*

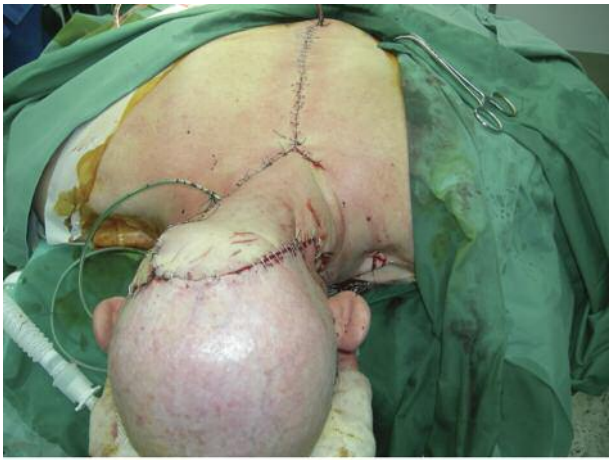

Figure 6. *Excision of the tumor and repair with a pedicled trapezius myocutaneous flap.*

Common clinical findings in patients with GBCCs are reported to be iron deficiency anemia and hypoproteinemia, probably due to intermittent bleeding of the tumor and serum loss (47).

Up to 27 different types of BCCs have been described histologically (35). The histological subtype of the tumor is said to be another factor in the development of GBCC and some histological subtypes have been associated with an aggressive course. Accordingly, GBCCs can be grouped as non-aggressive *i.e.* nodular and superficial subtypes and aggressive *i.e.* morpheaform, micronodular and metatypical (42, 49). Randle and associates (42) found that about 72% of all GBCCs were either micronodular or infiltrative. The classification made by the World Health Organisation (49), which is currently used, is the one most acceptable from the point of view of simplicity and good reproducibility. This classification contains the nodular, superficial and infiltrative types. Furthermore, it sets apart the micronodular, fibroepithelial, metatypical and keratotic types.

Metastasis of BCC is rare with an incidence established to be 0.1% , whereas GBCCs with metastasis are reported even more infrequently (5). BCCs metastasize most frequently to lymph nodes but also spread hematogenously to parenchymatous organs and bones (50) and can result in myelophthisic anemia (11) and secondary amyloidosis of the kidney, spleen and intestines (7). In our review, metastasis was observed in 17.6% of patients at the time of presentation.

GBCCs have a greater propensity to metastasize, particularly after they reach a critical size of 10 cm (42). Lo *et al*. (51) reported that large lesions and deep invasion account for 75% of all metastatic BCCs. Snow *et al*. (16) stated that in tumors larger than 10 cm in diameter, the incidence of metastasis and/or fatal outcome was 45% and in BCCs having a diameter larger than 10 cm, the average duration of the tumor was 22 years. It is now considered that there is no correlation between the histological subtype and the occurrence of metastasis (50). Mean survival following metastatic spread of GBCC is only 8 to 10 months.

Treatment of GBCCs, as for any other BCC, is wide surgical excision with free margins, but only few records of GBCCs supply details of resection margins. For most small <1 cm primary lesions a clinical margin of 2-4 mm represents an adequate excision, whereas larger lesions, which have a higher incidence of subclinical extension, require clinical margins of 3-5 mm. For the treatment of GBCCs, a wide surgical excision is required, usually combined with split-thickness graft or free flap for covering the defect. The histological margin control plays a major role in reducing the potential of recurrence, while the cure rate with Moh's micrographic surgery is reported to be 99% (52). Breuninger *et al*. (53) showed that in cases of surgical resection of a BCC, the possibility of tumor residue increases for larger tumors. The risk of tumor residue in cases of GBCCs with a diameter larger than 5 cm is 68% , while for BCCs with a diameter smaller than 2 cm or 1 cm it is 14% and 4% respectively (42). GBCCs can also threaten the extremities, necessitating an amputation and limb loss as the only surgical option (22). In addition, in cases of regional lymphadenopathy, a radical regional lymph node dissection is usually indicated.

Destructive methods (electrodessication and curettage) have a cure rate that increases with smaller tumor. Radiotherapy and topical chemotherapy is used only in elderly patients or poor surgical candidates (23, 54).

The presence of metastasis at the time of presentation carries an ominous prognosis. By itself, metastatic disease is an adverse prognostic factor. This is especially illustrated in the reports of Beck *et al*. (7) and Schwartz *et al*. (11). In these well-documented reports, treatment failed to achieve disease control and death quickly ensued. The poor overall results of treatment for patients with regional or systemic disease underline the importance of early recognition and prompt surgical management.

The treatment strategy used seems to be an important prognostic factor, as complete surgical excision with or without adjuvant therapy is associated with low local recurrence and longer survival. It is evident that resection on microscopically tumor-free margins is of paramount importance for long-term survival in the case of GBCC. Chemotherapy or radiotherapy alone appears to be ineffective in achieving local control. There are a few reports, such as those from Rossi *et al*. (23) and Copcu *et al*. (30), where chemoradiotherapy was quite effective for disease control. In these reports, however, the follow-up time was either not stated or was shorter than a year.

Due to the paucity of adequate data addressing long-term follow-up, in the elderly population, it is difficult to interpret data regarding overall mortality from disease of all stages. The follow-up time was reported in only 34 cases from the present database and ranged from 3 weeks to 72 months.

As depicted in this clinicopathological analysis, 17% of patients died of the disease, 38.3% developed recurrence of the tumor or distant metastases and 61.7% of the patients reported as being alive had been followed up for approximately 2 years.

Conclusion

Collected data from the present review show that early recognition of a suspicious skin lesion in combination with an aggressive surgical treatment and a close long-term follow-up for cancer surveillance may help to obtain a better prognosis of the disease.

When considering a treatment strategy for GBCC, the following factors should be kept in mind: i) This tumour behaves aggressively and needs to be recognised and treated early. ii) Adequate margin of clearance (probably at least

Table I. *Data of patients with giant basal cell carcinoma, as sourced from Medline and PubMed Central.*

Authors	Patient's age (years)	Gender (M/F)	Alcoholism	Anemia	Hypoalbuminemia	History	Histology	Location of tumor	Size (cm)	Duration of tumor presence (years)	Metastasis	Treatment	Outcome	Follow-up (months)
Gaughan *et al.* (1969) (4)	68	F	No	No	No	Burn	Nodular	Upper extremity (forearm)	5×4	1.5	No	Excision	Alive	NS
Costanza *et al.* (1973) (5)	73	M	No	No	No	No	Nodular	Lower extremity (thigh)	8×6	10	Nodes	Radiotherapy, excision, grafting	Metastasis on nodes, lungs	10
Curry *et al.* (1977) (6)	43	F	No	Yes	Yes	No	Morpheaform	Back	28×26	20	Nodes	Chemoradiotherapy	Metastasis on bone, lungs	36
	72	F	No	Yes	No	No	Nodular (adenoid)	Back	15×12	20	No	Excision and grafting	Alive	12
	72	M	No	Yes	No	No	Nodular (adenoid)	Back	12×8	20	No	Excision and grafting	Alive	NS
	67	M	No	Yes	No	No	Nodular (adenoid)	Back	12×12	25	No	Excision and grafting	Recurrence at 2 years	24
Beck *et al.* (1983) (7)	59	F	No	Yes	Yes	No	Nodular (cystic)	Back	40×30	24	Nodes	No therapy	Death from renal amyloidosis	2
Dudzinski *et al.* (1984) (8)	84	F	No	No	No	No	Infiltrative	Genitalia (vulva)	10×6	50	No	Excision	Alive	NS
O' Brien *et al.* (1984) (9)	57	M	No	Yes	No	No	NS	Scapula (shoulder)	14	20	No	Resection of shoulder girdle	Alive	12
Love *et al.* (1985) (10)	64	M	No	No	No	No	Nodular (adenoid)	Back	5x5	3	No	Excision	Alive	NS
Schwartz *et al.* (1986) (11)	51	M	Yes	Yes	No	Resection	Morpheaform	Scalp	NS	8	Nodes, bone marrow	Chemoradiotherapy, excision	Death	NS
Bianchini *et al.* (1987) (12)	70	M	No	No	No	Radiotherapy, resection	Metatypical	Face	NS	22	No	Radiotherapy, excision	Recurrence, death	48
D'Hermies *et al.* (1989) (13)	69	M	No	No	No	No	Nodular	Face (eyelid)	6	8	No	Excision	Alive	NS
Canterbury *et al.* (1990) (14)	64	M	No	No	No	No	NS	Back	15×22	NS	No	Excision and grafting	Alive	60
Ko *et al.* (1992) (15)	61	M	No	No	No	No	Nodular	Scalp, face	17×12	6	No	No therapy	Death	0.75
	70	F	No	No	No	No	NS	Face	20x15	7	No	Radiotherapy, excision, grafting	Recurrence, death	70
	82	F	No	No	No	No	NS	Face	NS	15	No	Excision, grafting	Recurrence, death	60
Snow *et al.* (1993) (16)	62	M	No	No	No	Radiotherapy, resection	Morpheaform	Face	5.5×6	30	No	Excision	Recurrence at 3 years	66
Warthan *et al.* (1994) (17)	84	F	No	No	No	No	NS	Back	15×4	15	No	Excision	Alive	NS
Sahl *et al.* (1994) (18)	75	M	Yes	Yes	Yes	No	Infiltrative	Abdomen (upper)	18×12	20	NS	Radiation	Death from rupture of abdomen	24
	61	M	Yes	No	No	Curettage, radiation	Nodular	Scapula	10	30	No	Mohs micrographic surgery and flap	Alive	NS
Mc Elroy *et al.* (1996) (19)	56	M	No	No	No	No	Nodular (adenoid)	Upper extremity (shoulder)	7×5	15	No	Excision and grafting	Alive	24
Betti *et al.* (1997) (3)	83	F	No	No	No	No	Superficial	Abdomen	13×6	NS	No	Cryotherapy	NS	NS
	59	F	No	No	No	No	Nodular	Scalp	12×14	5	No	Excision	Alive	24
	72	M	No	No	No	No	Nodular	Face	8×9	4	No	No therapy	Death from pancreatic tumor	NS
	82	M	No	No	No	No	Nodular	Face (cheek)	12×10	8	No	Radiotherapy, excision	Alive	24
Berking *et al.* (1998) (20)	62	F	No	Yes	No	No	Nodular	Abdomen	10×12	15	No	Excision and grafting	Recurrence at 5 months	14

Table I. *continued*

Table I. *continued*

Authors	Patient's age (years)	Gender (M/F)	Alcoholism	Anemia	Hypoalbuminemia	History	Histology	Location of tumor	Size (cm)	Duration of tumor presence (years)	Metastasis	Treatment	Outcome	Follow-up (months)
Sherman *et al*. (2001) (21)	74	M	No	Yes	No	No	NS	Face	6	27	No	No therapy	NS	NS
Vandeweyer *et al*. (2002) (22)	63	M	No	No	No	No	Metatypical	Upper extremity (forearm)	17×14	45	No	Excision and grafting	Alive	10
Rossi *et al*. (2002) (23)	66	M	No	Yes	No	No	Nodular	Upper extremity (shoulder)	10×7	13	Nodes	Radiotherapy	Alive	12
Kikuchi *et al*. (2002) (24)	63	M	No	No	No	No	Infiltrative	Abdomen (lower) genitalia, inguin	40×20	8	Nodes	Excision and fillet thigh flap	Alive	10
Takemoto *et al*. (2003) (25)	70	M	No	Yes	No	No	Nodular	Face (eyelid)	9×7	13	No	Excision, free flap reconstruction	Alive	12
Piteiro *et al*. (2003) (26)	47	M	No	No	No	No	Infiltrative	Abdomen	28×25	7	No	Excision, fascia lata flap	Alive	6
Misago *et al*. (2004) (27)	61	F	No	No	No	No	Keratotic	Pubis	7.1×5.0	NS	No	Excision and pedicle grafting	Alive	36
Northington *et al*. (2004) (28)	64	M	Yes	No	No	No	Infiltrative	Back	20×30	20	No	No therapy	Death of unknown causes	NS
Lorenzini *et al*. (2005) (29)	81	M	No	No	No	No	Infiltrative	Anterior chest wall	6×2	4 months	No	No therapy	NS	NS
Copcu *et al*. (2005) (30)	62	F	No	No	No	No	Nodular (adenoid)	Face	55×45	11	Lung, parotid	Chemo-radiotherapy	NS	6
Handa *et al*. (2005) (31)	74	M	No	No	No	No	Superficial	Genitalia (scrotum)	5.5×2.0	10	No	Excision	Alive	59
Skroza *et al*. (2006) (32)	70	F	No	Yes	Yes	No	Metatypical	Back	20×25	10	No	Excision, grafting	Alive	24
Araco *et al*. (2006) (33)	69	F	No	No	No	No	Infiltrative	Back	20	2	No	Excision, flap reconstruction	Alive	NS
Caloglu *et al*. (2006) (34)	67	M	No	No	No	Resection	Nodular	Face	8×5	18	Bones	Excision, radiotherapy	Death from heart attack	7
Anwar *et al*. (2006) (35)	53	M	No	No	No	Resection	Nm	Upper extremity (forearm)	10×8	NS	No	Shoulder disarticulation	Alive	NS
Kopp *et al*. (2006) (36)	81	M	No	No	No	No	Infiltrative	Upper extremity (elbow)	15×20	NS	No	Excision, flap reconstruction	Alive	NS
Arnaiz *et al*. (2007) (37)	73	F	No	No	No	No	Metatypical	Lower extremity (leg)	17×26	2	No	Below-knee amputation	Alive	6
Fresini *et al*. (2007) (38)	72	M	No	Yes	Yes	No	Nodular (adenoid)	Back	30×20	7	No	Radiotherapy	Alive	NS
Naumann *et al*. (2007) (39)	65	M	No	No	No	Resection	NS	Face	7×8	15	No	Excision	Recurrence at 6 years	72
Dunning *et al*. (2007) (40)	80	M	No	Yes	No	No	NS	Upper extremity (arm)	NS	NS	Nodes	Amputation	Alive	30
Affleck *et al*. (2007) (41)	52	M	No	No	No	No	Morpheaform	Back	NS	2	No	Chemo-radiotherapy	Hepatic metastasis, death	4
Current study	65	F	No	Yes	Yes	No	Nodular (adenoid)	Back	11.5×7	NS	No	Excision, flap, radiotherapy	Recurrence at 8 months	8
Current study	63	M	No	Yes	Yes	Resection	Nodular (adenoid)	Anterior chest wall	20×15	NS	No	Excision, flap, radiotherapy	Alive	5
Current study	76	M	No	Yes	Yes	No	Nodular	Scalp	7×4,5	NS	No	Excision, flap, radiotherapy	Alive	3

NS, Not stated.

2.5-3 cm) must be obtained. iii) Histological margin control is important in reducing the risk of recurrence. iv) Radiotherapy and chemotherapy offer only palliative treatment in the case of elderly patients or of systemic disease. v) Because of the high risk of recurrence, previously treated patients need long-term follow-up for life.

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