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Published in:
Clinical Case Reports

DOI:
10.1002/ccr3.575

Publication date:
2016

Document Version
Publisher's PDF, also known as Version of record

Clinical Case Reports

Open Access

CASE REPORT

Metastatic basal cell carcinoma caused by carcinoma misdiagnosed as acne – case report and literature review

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Funding Information
No sources of funding were declared for this study

Received: 27 January 2016; Revised: 24 March 2016; Accepted: 15 April 2016

Clinical Case Reports **2016; 4(6): 601–604**

doi: 10.1002/ccr3.575

Key Clinical Message

Basal cell carcinoma can be misdiagnosed as acne; thus, carcinoma should be considered in treatment-resistant acne. Although rare, neglected basal cell carcinoma increases the risk of metastasis.

Keywords

Basal cell carcinoma, metastatic basal cell carcinoma, review, survival, treatment.

Introduction

Basal cell carcinoma (BCC) is the most common type of skin cancer. It grows slowly and originates from the basal layer of epidermis and hair follicles. Initially, it grows in the epidermis and superficial dermis, but when neglected, invasive growth and local tissue destruction may occur [1]. BCCs are treated with curettage, excision, radiotherapy, or other topical/dermatological treatment [2, 3]. Metastatic basal cell carcinoma (MBCC) is very rare with a reported incidence between 0.0028% and 0.5% [4]. The true incidence is, however, probably even lower, since the frequency of BCC is considered to be substantially underreported [5]. The mortality associated with BCC is below 1% [6]. In MBCC, average survival is reported to be 3.6 years in patients with metastases to lymph nodes, while metastasis to bone, liver, or lungs only convey an average survival about 8–14 months [4, 7]. Acne is a common skin disease characterized by blockage and/or inflammation of hair follicles and their sebaceous gland. Severe acne presents comedones and abscesses that may persist for months and even longer if untreated. Acne is typically localized in the skin surface of the face, but the chest, back, and upper extremities are often involved as well [8]. Treatment options for acne include topical anti-acne preparations, lasers, lights, tetracyclines, and isotretinoin. The similarities in presentation and localization between BCC and acne may cause misdiagnosis. However, in contradiction to BCC, acne usually respond to the treatment at least to some extent [8]. We present a case of MBCC to the right axillary lymph nodes 6 years following excision of primary tumor initially mistaken as acne.

Case Report

In April 2014, a 53-year-old Caucasian male presented with a subcutaneous swelling in his right axilla, which had been progressing over a 6-month period. Blood tests were unremarkable. He had a long history of multiple small BCCs in the face and torso. Treatments had varied from x-ray therapy, surgery, and curettage. The patient's father and older brother had also been treated for multiple BCCs. The patient had a Fitzpatrick skin type 1. The patient was otherwise healthy and had no environmental risk factors such as immunosuppression, exposure to X-ray, arsenic or excessive sun use.

An ultrasound-guided needle biopsy of the enlarged lymph node was performed and the pathology report concluded MBCC. The patient was referred to our plastic surgery department where a skin examination showed no suspicious tumors and the remaining lymph node stations were without clinical pathology. Full body positron emission tomography (PET) with 18-Flouro-dexocyglucosen (FDG) and computer tomography (CT) only showed a marginally enlarged FDG-positive lymph node in the right axilla measuring 11 × 9 mm. This was consistent with the clinical presentation and pathology report. A right axillary lymph node dissection was performed, and the pathology report confirmed MBCC in three of the 23 excised lymph nodes.

As mentioned, the patient had a history of multiple minor BCCs, and especially one episode of cutaneous BCC located on the right pectoral region was interesting and was considered as the BCC, which later metastasized. This BCC had clinically been diagnosed as acne in 2006. The patient developed the acne at the age of 45 years and was treated successfully with systemic isotretinoin by a dermatologist for a period of 18 months. The patient did not receive X-ray treatment for the acne. However, an element on the right pectoral region did not respond to the treatment as the only one. A biopsy was taken from the element, which at the time measured 30 × 20 × 9 mm and histological examination determined infiltrative BCC. The carcinoma was excised with an 8-mm margin including some subcutaneous fat, but this excision was not radical. Re-excision with an additional 5-mm margin and in depth to the muscle fascia was found with free margins. The wound was closed directly, and no further treatment was indicated at that time.

We believe that this BCC in the right pectoral region was the one that spread to a lymph node in the right axilla. Since the patient had a history of multiple BCCs, we can of course not be absolutely certain of this; however, none of the previous BCCs had been at a substantial size like the one in question, and none had been in the right pectoral/dorsal region (or right side of the neck), which would be expected due to the drainage pattern to the right axilla.

Because of the family predisposition to BCCs, the patient was now offered genetic testing for the Basal Cell Nevus Syndrome (#109400, http://www.omim.org/), but the patient declined.

Currently, the patient is followed with full skin examination and clinical evaluation of the lymph node basins quarterly, and after 2 years biannually for a total of 5 years. PET/CT scans performed 3 and 9 months postoperatively was unremarkable. The patient remains free from recurrence 18 months after surgery.

Discussion

We reviewed the past 10 years of scientific literature and identified 15 cases of MBCC (Table 1). As shown in Table 1, the most common metastatic sites were lymph nodes (n = 12), lungs (n = 2), and bones (n = 2), which confirms the findings of Ganti and colleagues, who in 2011 presented a systematic review [9]. The majority of primary BCCs that metastasize have been reported to originate from the head and neck [10]. Contrary, as presented in Table 1, we found five cases with primary tumor on head and neck, while six cases had primary tumor on the truncus as in the current case. Increased risk of metastasis is associated with large size of primary tumor, infiltrating type of BCC, recurrent and neglected tumors, and perineural invasion [4]. Snow et al. [11] reported an association of increased risk of MBCC originating from neglected BCC misdiagnosed as acne, which was exactly the situation for our case.

In the literature, the median duration between the diagnosis of the primary tumor and the occurrence of metastasis was 18 month (range 1–48 months, N = 9). Two patients had metastases at the time of diagnosis [12, 13]. In our case, the metastasis occurred approximately 6 years after diagnosis of the primary tumor. This correlates well with previous cases [7, 12]; an MBCC review found the estimated median interval from tumor appearance to metastasis to be 9 years [9].

The reported median disease free survival from MBCC of reviewed cases (n = 9) was 18 month. Our patient has been free of recurrence for 18 months so far. Ganti et al. [9] reported that the prognosis of patients with MBCC was poor with an average survival time of approximately 3.6 years in patients with regional lymph nodes metastases, and 10 months in those with hematogenous metastases (bone, lungs, and other internal organs). Surgery is still considered the first line of treatment [14, 15] (Table 1). Our review is presented in Table 1; six patients had surgery, two patients underwent surgery and radiotherapy, while one patient received surgery and chemotherapy. Two patients underwent all treatment modalities. Additionally, two patients received chemotherapy alone, one of which refused surgery, while the other patient, who died within 6 months, had such an extended progression of disease that surgery was not indicated. One patient received vismodegib after surgery and chemotherapy due to insufficient effect of chemotherapy. The molecule vismodegib is an inhibitor of the Hedgehog pathway and was approved in January 2012 by the US Food And Drug Administration. The use of vismodegib is recommended for the treatment of adults with metastatic BCC, or with locally advanced BCC, which has recurred following surgery or which is not eligible for surgery or radiation therapy [16].

Table 1. Reported cases of metastatic basal cell carcinoma.

Author	Year	Age (yrs)	Sex	Location of primary	Location of metastasis	Histological Type	Tumor size (cm)	Interval between primary and metastasis (month)	Treatment (chemotherapy = CT, surgery = S, radiotherapy = RT)	Disease free survival (months)
Kurian et al. [18]	2014	68	M	Head/neck	Intraparotid lymph nodes and parotid gland	Infiltrative	3 × 2	13	S and RT	12
Di Lernia et al. [19]	2013	66	M	Truncus	Inguinal lymph nodes, lung, liver, bone marrow, and bone metastasis	Infiltrative	11 × 6	1	CT (carboplatin and docetaxel)	Died from disease 6 months after treatment
Moser et al. [2]	2013	64	F	Head/neck	Cervical lymph nodes	Infiltrative	6.5 × 4	NR	S	NR
Stewart et al. [20]	2013	51	M	Truncus	Bone and axillary lymph node	NR	NR	NR	S	NR
Pham et al. [9]	2013	46	M	Truncus	Bone marrow	Infiltrative	8 × 7	Metastatic at diagnosis	S, CT (cisplatin, paclitaxel) Vismodegib initiated due to insufficient effect of CT	3
Galioto et al. [21]	2012	1:89 2:80	1:F 2:M	1: Head/neck 2: Head/neck	1: Regional mandibular bone and submandibular gland 2: Regional bone, submandibular gland and cervical lymph nodes	Infiltrative	1:2.5 × 3.5 2:3 × 3	1:15 2:18	S	NR
Nakamura et al. [22]	2012	66	F	Foot	Inguinal lymph nodes	Infiltrative	3 × 4	30	S	NR
Gropper et al. [23]	2012	63	M	Head/neck	Cervical lymph nodes and parotid gland	Infiltrative	5 × 5	36	S, RT and CT (carboplatin, 5-fluorouracil, leucovorin)	32
Dai et al. [7]	2012	1:60 2:71	NR	Scrotum	1: Inguinal lymph nodes 2: Lung	Infiltrative	1:5 × 5 2:3 × 3	1:48 2:21	1:S 2:S, CT (cyclophosphamide, cisplatin, doxorubicin)	1:9 2:36
Grekin et al. [6]	2011	51	M	Truncus	Cervical and axillary lymph nodes	NR	NR	NR	S, RT and CT (cisplatin)	18
Khan et al. [24]	2010	65	F	Truncus	Cervical lymph nodes	Infiltrative	1 × 1.5	24	S	36
Ozgediz et al. [13]	2008	52	M	Truncus	Axillary Lymph nodes	Infiltrative	5 × 6	Metastatic at diagnosis	S and RT	24
Soleymani et al. [25]	2008	44	M	Truncus	Right upper extremity skin metastasis and edema, and axillary lymph nodes	Infiltrative	NR	NR	CT and palliative treatment with acitretin and imiquimod (refused surgery)	7

Marghoob et al. [17], found that patients diagnosed with BCC had a 45.2% risk of developing another BCC within 5 years. This correlates with the NCCN guidelines stating that 30–50% of patients with BCC will develop another BCC within 5 years [15]. Less than 1% of BCCs spread to another site in the body. In such cases, prolonged or lifelong follow-up care including regular skin screening and PET/CT is recommended [14, 15].

Conflict of interest

None declared.

Consent

Written informed consent was obtained from the patient for publication of this Case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

References

1. Cotran, R. S. 1961. Metastasizing basal cell carcinomas. Cancer 14:1036.
2. Moser, S., J. Borm, D. Mihic-Probst, C. Jacobsen, and A. L. K. Gujer. 2014. Metastatic basal cell carcinoma: report of a case and review of the literature. Oral Surg. Oral Med. Oral Pathol. Oral Radiol. 117:79–82.
3. Lo, J. S., S. N. Snow, G. T. Reizner, F. E. Mohs, P. O. Larson, and G. J. Hruza. 1991. Metastatic basal cell carcinoma: report of twelve cases with a review of literature. J. Am. Acad. Dermatol. 24:715–719.
4. Ting, P. T., R. Kasper, and J. P. Arlette. 2005. Metastatic basal cell carcinoma: report of two cases and literature review. J. Cutan. Med. Surg. 9:10–15.
5. Perera, E., N. Gnaneswaran, C. Staines, A. K. Win, and R. Sinclair. 2015. Incidence and prevalence of non-melanoma skin cancer in Australia: a systematic review. Australas. J. Dermatol. 56:258–267.
6. Grekin, S. J., C. K. Bichakjian, M. S. Sabel, D. B. Chepeha, and D. R. Fullen. 2011. Metastatic basal cell carcinoma from a small tumor with lymphatic invasion. J. Am. Acad. Dermatol. 65:16–17.
7. Dai, B., Y. Y. Kong, D. W. Ye, X. W. Xu, X. D. Yao, and S. L. Zhang. 2012. Basal cell carcinoma of the scrotum: clinicopathologic analysis of 10 cases. Dermatol. Surg. 38:783–790.
8. Lynn, D. D., T. Umari, C. A. Dunnick, and R. P. Dellavalle. 2016. The epidemiology of acne vulgaris in late adolescence. Adolesc. Health Med. Ther. 7:13–25.
9. Ganti, A. K., and A. Kessinger. 2011. Systemic therapy for disseminated basal cell carcinoma: an uncommon manifestation of a common cancer. Cancer Treat. Rev. 37:440–443.
10. Rubin, A. I., E. H. Chen, and D. Ratner. 2005. Basal-cell carcinoma. N. Engl. J. Med. 353:2262–2269.
11. Snow, J. S., and W. Sahl. 1994. Metastatic basal cell carcinoma: report of five cases. Cancer 73:328–335.
12. Pham, C. M., A. A. Syed, H. A. Siddiqui, R. A. Keller, and C. Kowalewski. 2013. Case of metastatic basal cell carcinoma to bone marrow, resulting in myelophthisic anemia. Am. J. Dermatopathol. 35:34–36.
13. Ozgediz, D., E. B. Smith, J. Zheng, J. Otero, Z. L. Tabatabai, and C. U. Corvera. 2008. Basal cell carcinoma does metastasize. Dermatol. Online J. 14:5.
14. Mc Loone, N. M., J. Tolland, M. Walsh, O. M. Dolan. 2006. Follow-up of basal cell carcinomas: an audit of current practice. J. Eur. Acad. Dermatol. Venereol. 20:698–701.
15. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Basal Cell Skin Cancer, Version 1. 2015. NCCN. Available at http://www.nccn.org/professionals/physician_gls/pdf/nmsc.pdf. Accessed: Jan 26, 2016.
16. Fecher, L. A., and W. H. Sharfman. 2015. Advanced basal cell carcinoma, the hedgehog pathway, and treatment options - role of smoothened inhibitors. Biologics 9:129–140.
17. Marghoob, A., A. W. Kopf, R. S. Bart, L. Sanfilippo, M. K. Silverman, P. Lee, et al. 1993. Risk of another basal cell carcinoma developing after treatment of a basal cell carcinoma. J. Am. Acad. Dermatol. 28:22–28.
18. Kurian, R. R., S. Di Palma, and A. W. Barrett. 2014. Basal cell carcinoma metastatic to parotid gland. Head Neck Pathol. 8:349–353.
19. Di Lernia, V., C. Ricci, I. Zalaudek, and G. Argenziano. 2013. Metastasizing basal cell carcinoma. Cutis 92:244–246.
20. Stewart, N. C., B. O'Brien, L. Francis, D. Graham, and S. Yang. 2013. Metastasis of basal cell carcinoma in a patient with basal cell carcinoma syndrome. Pathology 45:200–202.
21. Galioto, S., M. Lucioni, M. Pastori, A. Arecchi, and A. di Petrillo. 2012. Metastatic basal cell carcinoma: two cases involving the maxillofacial area. Int. J. Dermatol. 51:1097–1100.
22. Nakamura, Y., Y. Ishitsuka, K. Ohara, and F. Otsuka. 2012. Basal cell carcinoma on the dorsum of the foot with inguinal and pelvic lymph nodes metastases. Int. J. Dermatol. 51:1068–1073.
23. Gropper, A. B., S. D. Girouard, L. P. Hojman, S. J. Huang, X. Qian, G. F. Murphy, et al. 2012. Metastatic basal cell carcinoma of the posterior neck: case report and review of the literature. J. Cutan. Pathol. 39:526–534.
24. Khan, M. K., S. Powell, N. Cox, A. Robson, and N. Murrant. 2010. Cervical in-transit metastasis from a truncal basal cell carcinoma. BMJ Case Rep. 21:2010.
25. Soleymani, A. D., N. Scheinfeld, K. Vasil, and M. A. Bechtel. 2008. Metastatic basal cell carcinoma presenting with unilateral upper extremity edema and lymphatic spread. J. Am. Acad. Dermatol. 59(2 Suppl 1):1–3.