72314_Auto_Edited.docx

WORD COUNT	2536	TIME SUBMITTED	24-JAN-2022 04:31PM
		PAPER ID	81735190

Name of Journal: *World Journal of Clinical Cases*

Manuscript NO: 72314

Manuscript Type: CASE REPORT

Primary or metastatic lung cancer? Sebaceous carcinoma of the thigh: A case report

Xiao-Lin Wei, Qing Liu, Qiang-Lin Zeng, Hui Zhou

Abstract

BACKGROUND

Sebaceous carcinoma (SC), a malignancy primarily characterized by aggressive growth, affects cutaneous tissues of the periocular region. Extraocular SC is extremely rare, especially in the extremities, as evidenced by only a handful of reported cases.

CASE SUMMARY

A 65-year-old man presented with a rapidly enlarging swelling at left inner thigh, which was initially misdiagnosed as a subcutaneous abscess. The lesion had appeared two months prior to admission. Clinical examination revealed a cauliflower-like swollen content, with ulcerated and infected mass located on his left thigh. At the same time, we observed solitary nodular lesions in his lungs and brain, with biopsy pathology of the lung lesions found to be consistent with the mass in the thigh. The patient received chemotherapy comprising cis-platinum with fluorouracil, followed by targeted therapy with anlotinib hydrochloride and chemotherapy with vinorelbine, implantation of Iodine- 125 seeds in the thigh and pulmonary tumor. The initial stage intervention achieved partial remission. The efficacy of maintenance treatment was evaluated as stable disease after the first 5 cycles, however the patient developed a new brain lesion after the sixth cycle treatment, which resulted the progressive disease and thus, the patient received whole brain gamma knife radiotherapy.

CONCLUSION

We analyzed clinical presentation, imaging feature, pathology and treatment of a rare case of lung, brain and lymph node metastasis of SC located in the thigh. It is evident that cis-platinum combined with fluorouracil, vinorelbine combined with anlotinib hydrochloride may be an effective therapeutic regimen to advanced SC. But brain metastatic lesions should receive early radiotherapy.

INTRODUCTION

A sebaceous gland is a microscopic exocrine gland in the skin, which occurs between the hair follicles and the trichotricus erectus. It opens into a hair follicle and secretes an oily or waxy matter, called sebum, which lubricates the hair and skin in mammals. Sebaceous carcinoma (SC), which is characterized by aggressive growth, is a rare neoplasm that commonly arises in the eyelid and facial skin, and is extremely rare in other body parts[1]. Clinically, SC is typically asymptomatic, although it presents with yellow, red, or grayish-white domed nodules or plaques, accompanied by ulcers or crusts. The lack of specific clinical features often leads to delayed or misdiagnosis. To date, diagnosis and treatment approaches for SC are not well studied due to the rarity of the tumor. Here, we present a case of lung, brain and lymph node metastasis from thigh-located SC, and discuss the clinicopathological features, and treatment, with a brief review of relevant literature.

CASE PRESENTATION

Chief complaints

A 65-year-old man was admitted to the department of Respiratory and Critical Care Medicine, Affiliated Hospital of Chengdu University on March 18, 2020. His primary complaint was a lump over the left inner thigh, over the past 2 mo, and a 1-month-old pulmonary occupation. Two months prior to admission, the patient had developed a nodule on his left inner thigh, about the size of a broad bean, and was experiencing pain

due to local compression, but with no discomforts, such as ulceration or suppuration. The patient had cough but no chest pain, bloody sputum, headache and other discomforts.

History of present illness

He had consulted a local hospital where they performed local incision and drainage as well as pathological biopsy, out of which the condition was considered "suppurative infection". Results from pathological examinations suggested infiltration of malignant tumor with necrosis (Figure 1A) while immunohistochemical findings suggested that Cytokeratin (CK) (+), Epithelial membrane antigen (EMA) (+), protein p63 (P 63) (partial+), Thyroid transcription factor 1 (TTF-1) (-), chromogranin A (CgA) (-), S 100 (-), HMB45 (-), cell differentiation factor 34 (CD 34) and cell differentiation factor 31 (CD 31) (-), Ki- 67 (+, > 50%), in support of poorly differentiated carcinoma, SC should be considered after exclusion of metastasis. The chest CT scan revealed soft tissue shadows in the tip of the left upper lobe, about 19 × 23 × 21 mm, considering peripheral lung cancer. At the same time, the nodules on the patient's inner thigh gradually grew, exhibiting local redness, swelling and bleeding.

History of past illness

Medical records revealed that the patient had neither a history of hypertension nor diabetes, but had an unexplained weight loss of 5 kg in the recent 2 mo. He had a 40-year history of tobacco smoking, although he had stopped in the 2 mo prior to admission. He also occasionally drank alcohol for over 40 years, although he was not addicted to it.

1

Personal and family history

There was no pertinent family history.

Physical examination

There was a lump over the left inner thigh.

Laboratory examinations

Routine blood tests were normal, including erythrocyte sedimentation rate and C-reactive protein. The liver and kidney functions were normal. CA19-9 and CA125 were significantly increased.

Imaging examinations

The patient underwent further examination to assess tumor metastasis. Analysis of plain and enhanced brain magnetic resonance imaging (MRI) images revealed a well-defined mass with a size of about 32 mm × 28 mm × 29 mm in the left parietal lobe. The enhanced chest CT scan showed a lobulated high-density shadow with the size of 23 mm × 21 mm × 25 mm in the upper lobe apex of the left lung, surrounded by spicules. Furthermore, systemic positron emission tomography computed tomography demonstrated the presence of a malignant lesion (peripheral lung cancer) at the tip of the upper lobe of the left lung, single brain metastasis in the left parietal lobe, and lymph node metastasis in the left inguinal region and the inner upper left thigh. No other abnormalities were observed.

FINAL DIAGNOSIS

Left thigh SC with lung, brain, inguinal lymph node metastasis.

TREATMENT

The patient was administered with cisplatin combined with fluorouracil for 6 cycles of chemotherapy. In the first 4 cycles, the patient received intravenous infusion of 40 mg cisplatin from day 1 to day 3, intravenous injection of 250 mg fluorouracil from day 1 to day 4, continuous intravenous pumping of 4000 mg fluorouracil from day 1 to day 4, once every 3 wk. Severe myelosuppression occurred after chemotherapy. Therefore, the subsequent two cycles of chemotherapy were adjusted as follows: intravenous infusion

of 50 mg cisplatin from day 1 to day 2, intravenous injection of 250 mg fluorouracil from day 1 to day 4, continuous intravenous pumping of 4000 mg fluorouracil from day 1 to day 4, once every three weeks, with implantation of Iodine- 125 seeds in the thigh and pulmonary tumor. We recommended brain radiotherapy, and the patient declined. Thereafter, the patient was sustained on a maintenance treatment comprising targeted therapy with anlotinib hydrochloride combined with vinorelbine adjuvant chemotherapy for 6 cycles. The dose of anlotinib hydrochloride was 12 mg once a day, taken orally before breakfast. This medication was continued for 2 wk and withdrawn for 1 wk, i.e., the course of treatment was 3 wk (21 d). Vinorelbine treatment was administered as follows: In the first cycle, 80 mg vinorelbine tartrate soft capsule was given orally on the first day, 100 mg vinorelbine tartrate soft capsule was administered orally on the eightieth day. From the second to the sixth cycles, 100 mg vinorelbine tartrate soft capsule was given orally on the first day and on the eightieth day, once every three weeks.

OUTCOME AND FOLLOW-UP

After the first stage treatment, we observed a significant reduction in the nodule on the medial side of the left thigh, as well as marked improvement of the local ulceration and bleeding as well as reduction in lung and brain metastases. After 6 cycles of early-stage chemotherapy, the patient achieved partial remission partial remission (PR). There were no significant adverse events. After the first 5 cycles of maintenance treatment, efficacy of this maintenance treatment was evaluated as stable disease (SD), the lung and thigh lesions continued to shrink, however, the patient developed a new brain lesion after the sixth cycle of treatment (Figure 2), which resulted progressive disease (PD) in comprehensive efficacy evaluation, and thus, the patient received whole brain gamma knife radiotherapy at a regular dose, and continuing with anlotinib combined with vinorelbine treatment, we will continue to follow up on his condition.

Radiological evaluation of the brain and chest after maintenance treatment confirmed the following: Chest CT scan revealed a lobulated high-density shadow with

the size of 11 mm × 17 mm × 13 mm in the upper lobe apex of the left lung, surrounded by spicules, and focal emphysema. Brain MRI revealed an irregular solid lesion (25 mm × 22 mm) in the left parietal lobe, and an irregular solid lesion (18 mm × 15 mm) in the left occipital lobe. The edges of the lesions seemed to be surrounded by a capsule.

DISCUSSION

SC is a rare malignant tumor that originates from adnexal skin structures. This rare and potentially aggressive sebaceous gland derived malignancy was first described in the salivary glands by Rauch and Masshoff[2]. Typically, clinical manifestations of SC are painless skin nodules, with slow growth, or diffuse thickening of the skin and irregular mass, and often involve the subcutaneous tissue, or distant metastasis, which can easily be misdiagnosed as benign disease and delayed diagnosis, thereby requiring differentiation from cutaneous inflammation, sebaceous cyst and cutaneous malignant tumor[3,4]. Although SC often occurs in the head and neck, about 75% of adenocarcinomas all cases are found around the orbit, especially the eyelid. Notably, only about 25% of these cases originate from the sebaceous glands outside the orbit, such as the neck, scalp, trunk, limbs, and the reproductive system. SC is usually divided into the eye and extraocular areas, and its onset is predominantly in people aged between 60 to 70 years old. Previous studies have found no evidence of significant differences in its incidence between men and women, although it is more common in Asian populations[5,6]. Extraocular sebaceous carcinomas are extremely rare skin cancers, exhibiting diverse clinical and histopathological manifestations, which makes diagnosis difficult, thereby increasing the rate of misdiagnosis and missed diagnosis. In the present study, our patient was a 65-year-old man, and his age was within the average age of people expected to be diagnosed with SC. However, he presented with this extra-ocular type of neoplasm at an atypical location, the thigh. Given that the neoplasm did not cause pain or swelling, it was initially misdiagnosed as a subcutaneous abscess and it was not clear whether it could be considered as skin cancer lung metastasis or lung cancer skin metastasis.

SC has a varied pattern of histopathological manifestations. Microscopically, tumor cells show lobulated or papillary growth, and are arranged into a number of nests or sheets of different sizes by the fibrous stroma. In fact, these present an invasive growth pattern, with varying degrees of pleomorphism and atypia, as well as common cell necrosis and fibrosis. Notably, SC with prevalent cellular pleomorphism and cytologic atypia can exhibit poorly differentiated squamous cell sample sebaceous glands cancer alien, owing to differences in the degree of differentiation, and these are characterized by obvious squamous metaplasia, as evidenced by keratin pearls. Alternatively, they may show basal cell sebaceous glands cancer alien, tumor tissue invade surrounding tissues and cells is less cytoplasm of basaloid cells, arranged in a fence surrounding the form, the central can form "acne" necrosis, nuclear pleomorphism, prominent nucleoli. Therefore, clinicians can employ immunohistochemical studies using oil red-O stain, fat stain, EMA, cytokeratin, CAM 5.2, or BRST- 1 differentiate it from mucoepidermoid carcinoma, poorly differentiated squamous cell carcinoma, basal cell carcinoma and metastatic clear cell renal carcinoma[7-10]. In the present case, results from immunohistochemical analysis revealed that both the primary SC and pulmonary metastasis were positive for EMA, Ki- 67 but negative for TTF- 1, whereas pulmonary metastasis was positive for CAM 5.2 but negative for P 63, Napsin-A, and CEA. Based on these findings, we diagnosed this pulmonary disease as pulmonary metastasis from SC.

SC can be part of Muir-Torre syndrome, an autosomal dominant genetic syndrome characterized by presence of at least one sebaceous adenoma and internal malignancy. Colorectal cancer is the most common internal malignancy[11]. Since the patient in the present study exhibited abnormality in many markers, such as CA19-9 and CA125, we employed gastroscopy to ascertain intestinal polyps. Although pathological biopsy revealed benign lesions, we could not rule out the possibility of them turning into malignant lesions during disease progression. Therefore, we recommend regular follow-up gastroscopy during later stage, as well as health screening of family members.

Currently, surgical resection of early and low-grade tumors are the key treatment strategies for SC, although they are associated with high local recurrence rates after excision[12]. For patients with high-grade and advanced tumors, radiotherapy, chemotherapy, local treatment, and other comprehensive treatment measures are recommended. Anti-angiogenesis and blocking of certain inflammatory pathways are expected to become new treatment targets[13,14]. Previous evidences have recently demonstrated efficacy of platinum in combination with immunotherapy for some patients with postoperative recurrence, Programmed death-1 (PD- 1) or Programmed death-ligand 1 (PD-L 1) inhibitors during SC treatment[15,16]. However, these treatment are mainly for eye area SC, while treatment for the extraocular SC is not well studied. This patient had a short course of disease, but once confirmed, he presented with local lymph node, lung and head metastases, making it impossible to perform early radical surgery. Therefore, we chose comprehensive treatment. Fortunately, the therapeutic effect of cisplatin combined with fluorouracil in the early stage was good. Although severe myelosuppression occurred, the patient's condition improved significantly. During chemotherapy, the patient received iodine- 125 seed implantation in the thigh and lung lesions, and the final therapeutic outcome was designated as PR. For maintenance treatment, targeted anlotinib therapy combined with vinorelbine tartrate soft capsule adjuvant chemotherapy was administered. The response to chemotherapy and targeted therapy was SD in the first 5 cycles. However, the patient developed new brain metastases due to delayed brain radiotherapy after the 6th cycle therapy. The patient is currently continuing to receive anlotinib hydrochloride combined with vinorelbine maintenance treatment. Our treatment significantly reduced the primary lesion in the leg and distant metastases in the lung and lymph node of the patient, indicating that chemoradiotherapy, targeted therapy and early brain radiotherapy may be efficacious in treating lung and head metastasis from thigh located SC with well tolerated toxicity. The subsequent outcome of the brain lesions still needs further observation.

CONCLUSION

SC is a very rare and aggressive malignant tumor. Here, we treated a case of SC originating from the lower extremities, that had initially been misdiagnosed as an abscess with incision and drainage, and obtained relatively satisfactory outcomes. In clinical practice, there is need to pay attention to the differential diagnosis with other tumors in order to avoid misdiagnosis and missed diagnosis. Although, there is no better treatment currently, it is clearly that early and accurate diagnosis and removal of the lesion could benefit these patients. Patients with brain metastases should receive early radiotherapy to the brain. The lack of in-depth experience necessitates further explorations into novel and effective treatment strategies for sebaceous adenocarcinoma, including radiotherapy and targeted therapy.

ACKNOWLEDGEMENTS

The authors thank the patient for permitting them to use his data to complete this article.

72314_Auto_Edited.docx

ORIGINALITY REPORT

7%
SIMILARITY INDEX

PRIMARY SOURCES

1	f6publishing.blob.core.windows.net Internet	50 words — 2%
2	www.ncbi.nlm.nih.gov Internet	46 words — 2%
3	en.wikipedia.org Internet	20 words — 1%
4	El Amin Marnouche, Abdelhak Maghous, Selma Kadiri, Soufiane Berhili et al. "Sebaceous carcinoma of the parotid gland: a case report and review of the literature", Journal of Medical Case Reports, 2016 Crossref	15 words — 1%
5	www.wjgnet.com Internet	15 words — 1%
6	Peters, Sara, and Thomas Olencki. "Unusual Cutaneous Malignancies", Textbook of Uncommon Cancer Raghavan/Textbook of Uncommon Cancer, 2012. Crossref	13 words — 1%
7	www.science.gov Internet	13 words — 1%

EXCLUDE QUOTES ON

EXCLUDE MATCHES OFF

EXCLUDE BIBLIOGRAPHY ON