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Interventional treatment of keratoacanthoderma: a case report

Dan Mei, Lei Song, Jin-Qi Gao and Jie Wu

Abstract

This current case report describes a 56-year-old male patient with a skin mass on his lip that had been growing for 1 year. The pathological findings demonstrated that the epidermis was characterized by hyperkeratosis, hyperplasia and hypertrophy and was formed in the shape of a crater. The skin on both ends had developed into a ball-like growth that resembled a volcanic cone. There was invasive growth of heterotype squamous epithelium and a small number of inflammatory cells infiltrating the dermis. Immunohistochemistry demonstrated an increase in P16 (the focus, +) and the hot spot Ki-67 index. The diagnosis was of tumour-like hyperplasia, malignancy and moderate-to-severe dysplasia confirming that it was keratoacanthoma. The patient underwent surgical resection and was discharged from hospital, but the tumour returned. Paclitaxel and cisplatin were administered intraoperatively and bilateral lingual artery perfusion chemoembolization was undertaken six times. This procedure led to an excellent postoperative recovery and discharge from hospital. Tumour therapy was regarded as successful. The patient's medical history included acute lymphoblastic leukaemia L1 and long-term immunosuppressant use. After a 6-month period of follow-up, he died from systemic organ failure as a consequence of having too many ailments.

Keywords

Keratoacanthoma, interventional therapy, paclitaxel combined with cisplatin, squamous cell carcinoma

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Introduction

The uncommon, quickly expanding benign skin tumour known as keratoacanthoma (KA), also known as sebaceous molluscum or squamous cell pseudoepithelial tumour, may be a hyperplastic lesion of the

Department of Interventional Therapy, The Second Affiliated Hospital of Dalian Medical University, Dalian, Liaoning Province, China

Corresponding author:
Lei Song, Department of Interventional Therapy, The Second Affiliated Hospital of Dalian Medical University, 467 Zhongshan Road, Shahekou District, Dalian, Liaoning Province, 116023, China.
Email: songlei_1975@126.com

keratinized epithelium of the hair follicle.[1] A solitary, pink or pigmented, spherical nodule is the most typical symptom.[2] KA is similar to squamous cell carcinoma (SCC), but with the potential to progress to malignancy.[3] However, there are several ways to treat KA. In this current case, interventional embolization therapy, a novel approach to treating KA of the oral lip, was explored.

Case report

In March 2020, a 56-year-old male patient presented to the Beijing Cancer Hospital, Beijing, China with a skin mass on his lip that had been growing for 1 year. A sample of grey mucosa measuring $0.5 \times 0.5 \times 0.5$ cm was obtained for pathological and immunohistochemical analyses. The pathological findings revealed that the epidermis was characterized by hyperkeratosis, hyperplasia and hypertrophy and was formed in the shape of a crater. The epidermis at both ends was spherical forming into a ball-like growth that resembled a volcanic cone. In addition, there was invasive growth of heterotype squamous epithelium and a small number of inflammatory cells infiltrating the dermis. The tissue was not thick. Immunohistochemistry demonstrated an increase in P16 (the focus, +) and the hot spot Ki-67 index. The diagnosis was of tumour-like hyperplasia, malignancy and moderate-to-severe dysplasia (Figures 1 and 2). After undergoing tumour removal at Shengjing Hospital affiliated to the China Medical University, Shenyang, Liaoning Province, China, the patient was discharged after making progress. Four months later, the illness relapsed. The patient developed more oral lesions, ulcers of the oral mucosa and degeneration of the ulcerated lesions. He sought treatment at Shengjing Hospital affiliated to the China Medical University. He had treatment with oral capecitabine, laser therapy, liquid nitrogen cryotherapy and traditional Chinese medicine throughout this time, but there was no discernible change.

In April 2021, the patient ultimately presented to the Department of Interventional Therapy, The Second Affiliated Hospital of Dalian Medical University, Dalian, Liaoning Province, China after 3 months as his symptoms had worsened and included ulceration on the surface of the tumour lesion, throat discomfort and trouble feeding. Following multi-departmental discussions, it was agreed to provide bilateral lingual artery perfusion chemoembolization treatment. The patient's overall health has been fine since the sickness started, with no fever, emaciation or any pain. On physical examination, body temperature, pulse rate, heart rate and blood pressure were all

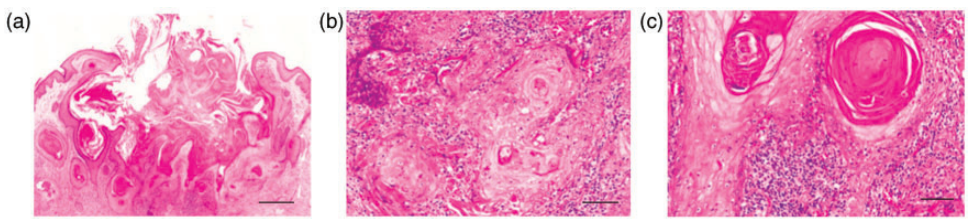

Figure 1. Representative photomicrographs of a histopathological sample of a lesion removed from a 56-year-old male patient that presented with a skin mass on his lip: (a) the epidermis was characterized by hyperkeratosis, hypertrophy and it was crater shaped; (b) the tumour cells demonstrated heteromorphic hyperplasia with histopathological mitosis and (c) basal inflammatory cell infiltration. Haematoxylin and eosin. Scale bar 50 μm. The colour version of this figure is available at: http://imr.sagepub.com.

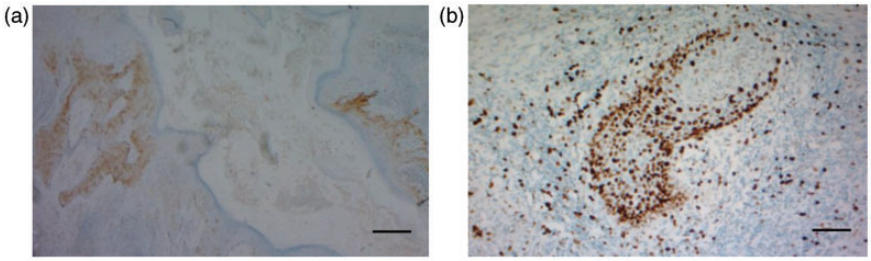

Figure 2. Representative photomicrographs showing the results of an immunohistochemical analysis of a histopathological sample of a lesion removed from a 56-year-old male patient that presented with a skin mass on his lip: (a) P16(+) and (b) hot spot Ki-67. Scale bar 50 μm. The colour version of this figure is available at: http://imr.sagepub.com.

normal. There were no immediately apparent abnormalities in the heart, lungs or abdomen. Routine blood, liver and renal function testing and auxiliary examinations revealed no abnormalities. SCC-related antigen was found on routine blood testing and tumour lesions were detected in maxillofacial enhanced computed tomography (CT). The patient was able to withstand interventional surgery. During the procedure, an 18G puncture needle was introduced first into the right femoral artery and subsequently, through the guiding wire, into the arterial sheath. The catheter received an injection of 20 ml of normal saline and 5000 U of heparin. The growth of the right tongue artery was examined by angiography and the tongue tumour was stained. The right external carotid artery was superselected using a 5F vertebral artery catheter (Figure 3). Blood was provided by the branch artery of the right tongue artery. Tumour staining was verified by angiography after the branch arteries were inserted with a 2.7F microcatheter (Boston Scientific, Marlborough, MA, United States USA). Cisplatin (drug dosage adjusted according to treatment effect and adverse reactions: 90 mg/m^2, 120 mg/m^2 or 60 mg/m^2, for the duration of the operation) and paclitaxel (drug dosage adjusted according to treatment effect and adverse reactions: 270 mg/m^2 or 240 mg/m^2, for the duration of the operation) were both injected into the arteries. After infusion, gelatin sponge embolization was undertaken. After embolization, angiography revealed no tumour staining. There were no difficulties following the operation. After surgery, the patient recovered well. The malignant lesion dramatically reduced (Figure 4). The tumour range was restricted according to the postoperative CT scan. Following interventional treatment, the tumour shrank, and after a few sessions, the tumour's tissue became necrotic and new tissue started to form (Figure 5). After six interventional surgical sessions, the SCC-related antigen (pretreatment level: 9.87 μg/l; post-treatment level: 1.45 μg/l; normal range $\leq$1.5 μg/l) returned to a normal value. The Karnofsky score was 80 points after therapy, which was greater than the score before treatment. It is generally accepted that a Karnofsky score $>$ 80 indicates personal independence or the ability to take care of oneself. A higher score translates into better postoperative status and longer life for patients. After six interventional surgical sessions, the clinical outcome evaluation was recorded as stable disease (i.e. the sum of the largest diameters of the target lesions had decreased) according to the Response Evaluation Criteria in Solid Tumors (RECIST). The clinical efficacy evaluation

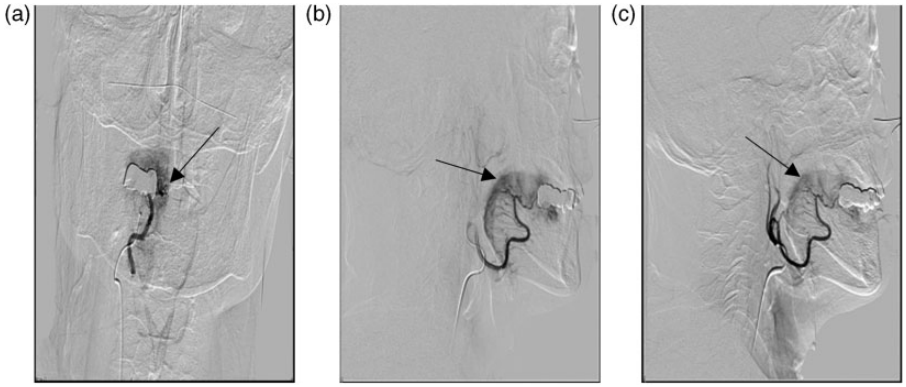

Figure 3. Intraoperative angiography images of the arteries and tumour of a 56-year-old male patient that presented with a skin mass on his lip: (a) anteroposterior radiography of the left tongue arteriography and lip tumour development; (b) right lingual arteriography and tongue tumour development and (c) left tongue arteriography and tongue tumour development. The arrows show the staining of the tumour.

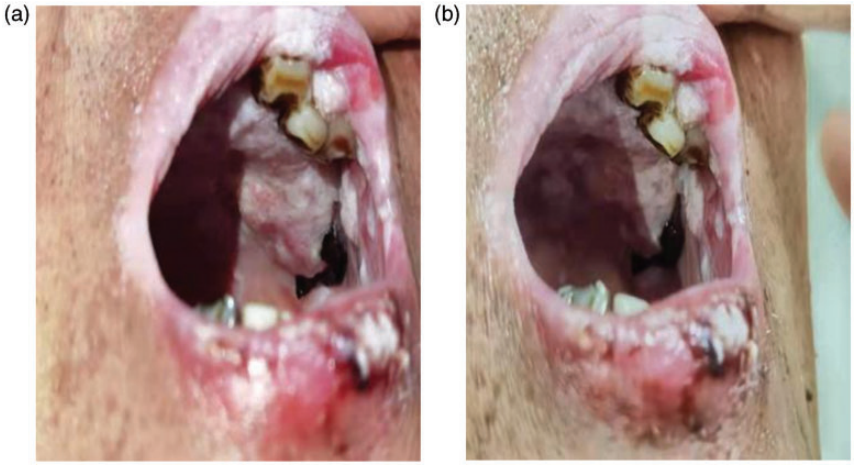

Figure 4. Tumour changes before and after surgery in a 56-year-old male patient that presented with a skin mass on his lip: (a) before surgery and (b) after surgery. The colour version of this figure is available at: http://imr.sagepub.com.

after each intervention treatment was a partial response (i.e. the sum of the largest diameters of the target lesions was reduced by $\geq$30% and maintained for at least 4 weeks) according to RECIST. Previous medical history of the patient included acute lymphoblastic leukaemia L1. After a bone marrow transplant, the patient received long-term oral prednisone, azathioprine and cyclosporine A to manage graft rejection. After a 6-month period of follow-up, the patient died from systemic organ failure as a consequence of having too many ailments with no notable postoperative complications being noted.

The patient and his family provided approval for his therapeutic plan. The patient's family provided approval for the

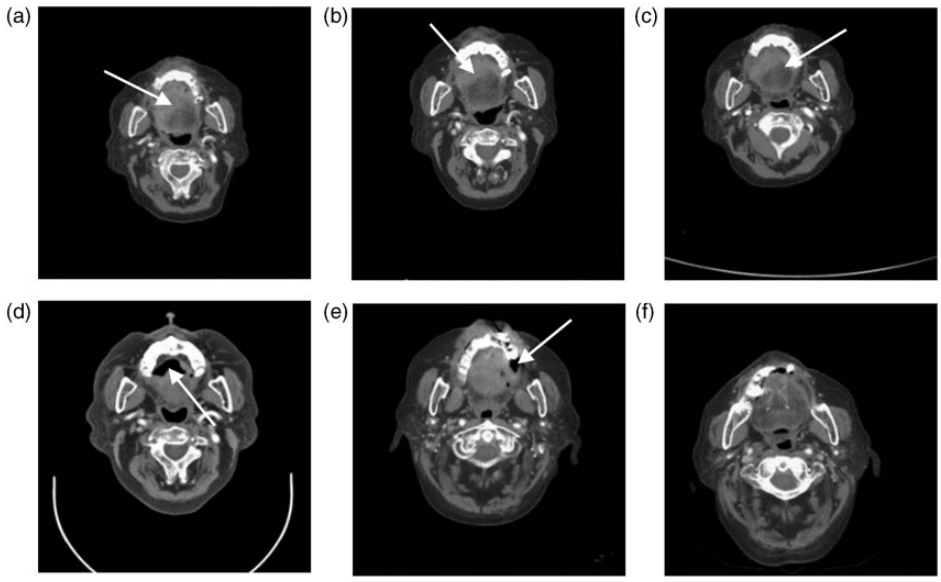

Figure 5. Preoperative and postoperative enhanced computed tomography (CT) images of a 56-year-old male patient that presented with a skin mass on his lip showing that the tumour volume significantly reduced postoperatively. The sequence of images shows the tumour before and then after each operation: (a) CT image of the tumour (arrow) before treatment; (b) the tumour (arrow) slightly widened following a single round of therapy; (c) the extent of the tumour (arrow) was less than it was following the previous therapy; (d) tumour tissue necrosis (arrow) due to embolization; (e) shrinkage of the necrotic cavity (arrow) within the tumour and (f) no necrotic cavity is present.

publication of this case report and the associated images. This study's reporting complies with CARE recommendations.[4]

Discussion

Keratoacanthoma is an uncommon benign skin tumour that develops on the face and other sun-exposed areas, mostly affecting middle-aged and older males.[5,6] The majority of the cases of KA are associated with viral infection.[7] Other reasons include trauma, long-term exposure to carcinogens like asphalt and tar and prolonged sun exposure.[8,9] Research has demonstrated that some people with red tattoos or those that have had laser surgery have experienced the quick development of KA lesions within approximately a month, while some people start developing lesions 9–10 years after getting tattooed.[10–12] As a result, laser therapy and red tattoos might both be contributing factors to keratoacanthoma.[10–12] The development of KA has been linked to certain pharmacological agents such as sorafenib, B-raf protein inhibitors and inhibitors of mutant serine-threonine protein kinases (e.g. dabrafenib).[13] Additionally, research had demonstrated that programmed cell death protein-1 inhibitors can cause KA.[14] A number of hereditary conditions such Muir–Torre syndrome have been associated with KA.[15]

Keratoacanthoma is clinically, histologically and histopathologically similar to SCC.[16] KA is regarded as a low-grade variant of SCC.[17] It can be very difficult to distinguish between SCC and KA.A previous study examined the presence, distribution and activity of plasma cell-like

dendritic cells (PDCs) in KA and SCC using large samples.[18] CD123-positive PDCs are more active in KA than SCC.[19] In contrast to SCC, KA is a benign lesion.[20] KAs are linked to inflammatory infiltration, which includes infiltration with Langerhans cells, interleukin (IL)-27-producing cells, CD8-positive T cells surrounding the tumour, CD3-positive T cells inside the tumour, CD4-positive T cells with IL-2 receptors and CD3-positive T cells.[21,22] The typical histopathological features of KA include the following: (i) a significant number of eosinophilic keratinocytes within the epidermal hyperplasia; (ii) keratin filling the indentation in the centre; (iii) the depressions on both sides of the ball-like growth are filled by tumour edge epidermis that is stretched like a 'lip' or 'arch wall'; (iv) the tumour is clearly separated from the stroma around it; (v) the dermis is infiltrated by a variety of inflammatory cells.[23] The pathological abnormalities observed in the current case were in line with these typical histopathological features and when there were paired with the clinical signs, the diagnosis of KA was confirmed. A recent study used dermoscopy and reflection confocal microscopy (RCM) to effectively detect KA and discovered that KA has unique dermoscopy and RCM features.[24] This approach may serve as a foundation for the early identification of KA.[24]

At present, there is no standard treatment for KA. Although surgical resection is seen to be the best option, it comes with a number of disadvantages, including increased discomfort, a higher chance of infection following the removal of large tumours and scars that can be unsightly. The mainstay of the therapy is intralesional 5-fluorouracil. Previous studies have demonstrated that the tumour might fully disappear in 67–80% of cases when treated with intralesional 5-fluorouracil.[25–27] Following a period of therapy, the surgical resection rate decreased over time and tumours located in aesthetically delicate locations did not leave a scar when treated this way.[25–27] Another study that compared the effectiveness of intralesional methotrexate treatment with surgical resection found that 88% of the lesions were totally cured with intralesional methotrexate treatment and there were no problems during the 6-week follow-up.[28] There was no significant difference between the two treatment modalities, and after surgical resection, the patients fully recovered without recurrence or sequelae.[28] Intralesional methotrexate might be utilized for the early treatment of multitype KAs and isolated KAs.[28] Patients with multitype KAs were given oral acitretin and after receiving therapy for 1 year the tumours fully shrank without recurrence.[29] Large lesions were effectively removed with avitracin in conjunction with surgery.[30] A novel approach to treating KA is called photodynamic therapy (PDT).[31,32] A previous study administered PDT five times to KA that had developed on the top portion of the lips (a sensitive aesthetic location) and this resulted in the entire eradication of the tumour, removal of the scar and the tumour did not recur during the 3-year follow-up.[16]

In this current case, the quantity of KA lesions was significant, the area covered was large and the tumour lesions were growing on the lips and around the corners of the mouth. There were no signs that a surgical resection had taken place. The KA had not been controlled despite the use of laser treatment, liquid nitrogen cryotherapy and conventional Chinese medicine. In order to treat the condition, the current case then received interventional therapy of bilateral lingual arterial chemoembolization. The arterial blood supply to the KA tumour was specifically targeted during interventional therapy to eliminate the tumour with precision and power while minimizing

systemic toxicity and adverse effects. Embolization stops the supply of energy to the KA tumour, which might then cause the tumour to deteriorate owing to ischaemia, hypoxia and nutritional deprivation. When chemotherapy medications are administered concurrently, the curative impact is considerably improved, the local drug concentration is increased and the contact period between the tumour and the drug is prolonged owing to blood flow restriction. One of the more popular medications used in neoadjuvant chemotherapy is paclitaxel. Platinum-containing anticancer medication such as cisplatin has a nonspecific effect on the cell cycle. Cisplatin can have a clear anticancer effect when combined with paclitaxel; and it can also enhance the patient's peripheral blood cell immunity.[33] Tumour cells are effectively killed when paclitaxel and cisplatin are combined.[33]According to research, paclitaxel and cisplatin have a reasonably good efficacy in treating oral cancer patients, boosting their peripheral blood cell immunity and improving their prognosis.[34] In addition, interventional therapy offers the benefits of low trauma, high safety, reduced postoperative infection and no visible scarring. Following interventional therapy, the current patient's health improved, demonstrating the viability of interventional therapy–tongue arterial chemoembolization for the treatment of KA. After several rounds of embolization, the SCC-related antigen level returned to normal. The imaging showed that the tumour did significantly shrink. The efficacy of interventional embolization for KA will need to be confirmed by large clinical trials.

In conclusion, interventional embolization might become a viable therapeutic option for KA lesions that cover a large surface area, present in an aesthetically important location such as the lips and face or when there is no indication for surgical resection.

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Author contributions

The corresponding author Lei Song is responsible for ensuring that the descriptions are accurate and agreed by all authors. The individual contributions were as follows: Jin-Qi Gao, conceptualization, methodology; Dan Mei, data curation, writing (original draft preparation); Jie Wu, methodology; Lei Song, supervision, writing (reviewing and editing).

Declaration of conflicting interests

All authors declare that there are no conflicts of interest.

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ORCID iD

Mei Dan https://orcid.org/0000-0001-5781-5778

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