ISSN : (Online): 3008-038X
Abbreviation: J Derm Cse Rep
DOI: 10.61705/jdcr.19.2.2026.54.60

Journal of Dermatological Case Reports

Keratoacanthoma with Extensive Perineural Invasion: A Case Report

Caitlin Wenske[1], Alexandra Smith[2], Natasha Bray[3], Todd Mollet[4]
[1]BS Oklahoma State University College of Osteopathic Medicine at the Cherokee Nation Office of Medical Student Research 19592 E Ross St Tahlequah, OK 74464, USA Email: caitlin.ball@okstate.edu ORCID: 0009-0008-8000-8884
[2]BS Oklahoma State University College of Osteopathic Medicine at the Cherokee Nation Office of Medical Student Research 19592 E Ross St Tahlequah, OK 74464, USA Email: alexandra.m.smith@okstate.edu ORCID: 0009-0001-1849-0736
[3]MSEd, DO Oklahoma State University College of Osteopathic Medicine at the Cherokee Nation Office of Medical Student Research 19592 E Ross St Tahlequah, OK 74464, USA Email: natasha.bray@okstate.edu ORCID: 0000-0002-6140-1962
[4]MD Skin Surgery Center of Oklahoma 13100 N Western Ave #301 Oklahoma City, OK 73114, USA Email: Todd.mollet@gmail.com ORCID: 0009-0005-0562-5784

Corresponding Author

Caitlin Wenske
BS Oklahoma State University College of Osteopathic Medicine at the Cherokee Nation Office of Medical Student Research 19592 E Ross St Tahlequah, OK 74464, USA Email: caitlin.ball@okstate.edu

Keywords:

Atypical, Cancer, Invasion, Keratoacanthoma, Perineural, Tumor

Abstract:

Keratoacanthoma (KA), a typically less aggressive squamous cell carcinoma (SCC) subtype, is characterized by rapid growth with potential spontaneous resolution. Rarely, KA exhibits aggressive features including perineural invasion and vascular involvement. The authors report a 56-year-old female with a 2.5 cm papule on her right nasal supratip at initial presentation. Pathology revealed a well-differentiated squamous cell carcinoma, keratoacanthoma type. A gene expression profile test revealed a class 1 result. The papule grew rapidly into a 5 x 3.5 cm tumor by the time of Mohs surgery 4 weeks later. During Mohs, extensive perineural invasion was discovered. While peripheral margins were cleared, deep margin clearance proved impossible due to the inability to obtain adequate local anesthesia at the nasal bone. The patient was subsequently referred to an academic head/neck cancer clinic for further management. This case demonstrates that KAs can exhibit aggressive behavior, particularly in head/neck locations.

Received : 26-03-2026 **Revised : 14-04-2026** **Accepted: 18-04-2026** **Published : 20-04-2026**

Introduction

Keratoacanthoma (KA), a less aggressive subtype of squamous cell carcinoma (SCC), remains underreported in the United States due to its usually limited progression and inconsistent pathological classification. Australian data indicates an incidence rate of 409 individuals per 100,000 person-years (2020) [1]. Keratoacanthoma typically manifests as a rapidly growing, dome-shaped nodule with a central keratinous plug [2], affecting individuals across all age groups with peak incidence in the fifth and sixth decades. Risk factors include lightly pigmented skin, ultraviolet light exposure, skin trauma, chemical carcinogens, and human papillomavirus [1]. Keratoacanthomas are

ISSN : (Online): 3008-038X
Abbreviation: J Derm Cse Rep
DOI: 10.61705/jdcr.19.2.2026.54.60

Journal of Dermatological Case Reports

associated with several genetic syndromes, including Muir-Torre syndrome (Lynch Syndrome variant), xeroderma pigmentosum, and Ferguson-Smith disease [3].

Unlike other cutaneous malignancies, KA exhibits a distinctive growth pattern – rapid growth for 6-8 weeks, a 2–6-week dormancy period, and occasional spontaneous regression [4]. Despite this self-resolving potential, treatment remains standard due to KA's histological similarity to well-differentiated SCC. Treatment options include standard excision or electrodesiccation and curettage for smaller lesions [2]. Though topical chemotherapy agents (imiquimod, 5-fluorouracil) effectively treat actinic keratoses and SCC in situ, evidence for KA treatment remains limited [5, 6]. Mohs surgery is preferred for larger, aggressive lesions, particularly in cosmetically sensitive areas and head/neck lesions. Radiation is utilized in some cases. In addition to therapeutic interventions, gene expression profiling (GEP) may be utilized in unique cases as this test analyzes RNA in tumor-containing tissue and assesses individual risk for metastasis and recurrence [7]. More specifically, the 40-gene expression profile (40-GEP) identifies patients diagnosed with a higher-risk cutaneous SCC who are at increased risk for local recurrence and metastasis, despite negative margins after surgical resection [8].

While KAs can follow an indolent course, untreated lesions can develop aggressive features including perineural invasion and intravascular involvement [9-11]. This case report demonstrates how a rapidly growing KA with extensive perineural invasion presented challenges during Mohs surgery, and necessitated interdisciplinary management.

Case Synopsis

A 56-year-old Fitzpatrick III, immunocompetent female with no personal history of cutaneous cancer presented with a tender, intermittently ulcerating papule on her right nasal supratip. Her history included extensive UV exposure and a paternal melanoma history. She reported rapid lesion growth, consistent sunscreen use, denied smoking, and reported no previous chemotherapy or radiation. Initial examination revealed a tan-gray, slightly raised, indurated tumor measuring 2.5 cm **(Figure 1)**. Shave biopsy demonstrated hyperkeratosis, parakeratosis, and glassy acanthosis with crateriform architecture, basal keratinocytes atypia, and chronic dermal inflammation. Histopathology confirmed well-differentiated SCC, keratoacanthoma type. The 40-GEP test revealed a low-risk, class 1 result. Classification stratifies risk of metastasis over a 3-year period as follows: Class 1 (low risk ≈ 6%), Class 2A (moderate risk ≈ 20%), or Class 2B (high risk ≈ 50%) [12, 13].

Given the head/neck location, the patient was referred for Mohs surgery. By the time of surgery, the tumor had expanded to 5 x 3.5 cm with no lymphadenopathy **(Figure 2)**. Standard Mohs protocol was followed using local infiltration and infraorbital nerve block. The surgeon initially debulked the clinically apparent tumor with a #15 blade, then harvested clinically normal tissue with a 2 mm margin. Histopathology of the frozen section revealed residual tumor with atypical keratinocytes cells extending into muscle with perineural invasion **(Figure 3)**. The peripheral margin was cleared with 5 stages of Mohs surgery.

Deep margin clearance was hindered by underlying bone and anesthetic challenges. Some nasal bone was removed with double action nail nippers during stage 4, but deep margin excision was halted in stage 5 due to the inability to obtain adequate anesthesia. The final defect measured 8.5 x 6 cm **(Figure 4)**.

Given the extensive nature of the defect and inability to definitively clear the deep margin, the patient was referred to the local academic head and neck cancer clinic for evaluation. A computed tomography of the head/neck was negative. Adjuvant radiation followed by reconstruction was recommended. The patient declined additional treatment.

Two months later, she scheduled another consultation and requested reconstruction. Her wound had healed completely by second intention **(Figure 5)**. The patient again declined radiation. We recommended a referral for a prosthesis versus definitive reconstruction after a 12-month observation period. At 6 months post-op, the patient has no evidence for recurrence clinically and on CT.

ISSN : (Online): 3008-038X
Abbreviation: J Derm Cse Rep
DOI: 10.61705/jdcr.19.2.2026.54.60

Journal of Dermatological Case Reports

She plans to have definitive reconstruction after the observation period.

Case Discussion

Keratoacanthoma typically presents as a sporadic, solitary lesion, with multiple KAs generally suggesting inherited familial syndromes [14]. Our patient presented with a single lesion. The rapid expansion observed in our patient – from 2.5 cm at initial presentation to 5 x 3.5 cm at surgery – highlights the unpredictable biological behavior of some KAs.

Perineural and vascular invasion in KA is rarely documented. This case demonstrates that while the external lesion expands, internal invasion can extend along nerves beyond clinically apparent boundaries. This aggressive behavior challenges the conventional understanding of KA's typically indolent nature and highlights the importance of thorough histological examination and appropriate surgical management. Perineural invasion can be identified and tracked histologically using Mohs surgery. Clinically and histologically, nerve involvement is statistically associated with highly aggressive cutaneous cancers [9, 14]. Similarly, vascular involvement, although rare in KAs, indicates a much more aggressive cancer. Recent literature suggests that KAs may possess more aggressive characteristics than previously recognized [9, 16].

This patient's gene expression profile (GEP) test for cutaneous SCC (cSCC) revealed a Class 1 result, suggesting a lower-risk tumor. However, considering the extensive perineural invasion, invasion beyond subcutaneous fat, and size larger than 2 cm, her cancer is high-risk. Some tumors with high-risk clinical and histologic features may have low-risk gene expression profiles. On the other hand, some tumors with low-risk clinical features may have high-risk histologic features or gene expression profiles. Lastly, some tumors with low-risk histologic features may have high-risk clinical features or gene expression profiles. This case supports evaluating clinical, histologic, and genetic features when determining risk for KAs and SCCs. The authors do not advocate ordering genetic testing for all cutaneous squamous cell carcinomas but believe the tests are helpful when high-risk clinical and/or histologic features are present.

Additionally, the occasional extension of KAs to bone and need for adjuvant radiation therapy challenge the classification of KA as a low-risk cancer. We propose that KA may exist on a biological spectrum, with some cases exhibiting aggressive features that warrant treatment strategies typically reserved for higher risk SCC [17].

Conclusion

This case exemplifies a favorable GEP test combined with high-risk clinical and histologic features. Patients with such presentations require aggressive treatment and close follow-up. We recommend combining clinical, histologic, and genetic features when risk stratifying cSCC. Neither GEP tests, clinical features, or histologic features alone identify all tumors with recurrent or metastatic potential. While GEP testing remains a contested topic among dermatologists, providers should follow current and future evidence-based medicine to make informed decisions for each individual patient. Further research is needed to determine optimal combinations of clinical, histologic, and genetic features to improve risk stratification.

Conflicts of interest: The authors declare no conflicts of interest.

Ethical Statement: Informed consent was obtained from the patient for the publication of this case report, including any accompanying images. The identity of the patient has been protected to ensure confidentiality.

Funding: None

References

1. Claeson M, Pandeya N, Dusingize JC, Thompson BS, Green AC, Neale RE, Olsen CM, Whiteman DC. Assessment of incidence rate and risk factors for keratoacanthoma among residents of Queensland, Australia.

ISSN : (Online): 3008-038X
Abbreviation: J Derm Cse Rep
DOI: 10.61705/jdcr.19.2.2026.54.60

Journal of Dermatological Case Reports

JAMA Dermatol. 2020;156(12):1324-1332. doi:10.1001/jamadermatol.2020.4097.
2. Zito PM, Scharf R. Keratoacanthoma. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2026 Jan–. 2023 Aug 8. PMID:29763106.
3. Dobre A, Nedelcu RI, Turcu G, Brinzea A, Struna I, Tudorache G, Ali A, Hulea I, Balasescu E, Fertig TE, Gherghiceanu M, Harwood C, Ion DA, Forsea AM. Multiple keratoacanthomas associated with genetic syndromes: narrative review and proposal of a diagnostic algorithm. *Am J Clin Dermatol.* 2025;26(1):45-59. doi:10.1007/s40257-024-00900-0.
4. American Osteopathic College of Dermatology. Keratoacanthoma [Internet]. [cited 2025 Mar 31]. Available from: https://www.aocd.org/page/Keratoacanthoma
5. Gray RJ, Meland NB. Topical 5-fluorouracil as primary therapy for keratoacanthoma. *Ann Plast Surg.* 2000;44(1):82-85. doi:10.1097/00000637-200044010-00015.
6. Patel GK, Goodwin R, Chawla M, Laidler P, Price PE, Finlay AY, Motley RJ. Imiquimod 5% cream monotherapy for cutaneous squamous cell carcinoma in situ (Bowen's disease): a randomized, double-blind, placebo-controlled trial. *J Am Acad Dermatol.* 2006;54(6):1025-1032. doi:10.1016/j.jaad.2006.01.055.
7. LeQuang JA. Using gene expression profiling to personalize skin cancer management. *J Clin Aesthet Dermatol.* 2022;15(11 Suppl 1):S3-S15.
8. Ratner D, Arron ST, Kim YJ, Hurton LV, Ng E, Martin BJ, et al. The 40-gene expression profile test identifies patients with National Comprehensive Cancer Network high-risk cutaneous squamous cell carcinoma at high risk of poor outcomes to inform management decisions. *J Skin.* 2025;9(4):2426-2443. doi:10.25251/mvr2rn83.
9. Basoglu Y, Metze D, Nashan D, Ständer S. Keratoacanthoma with perineural invasion: an indicator for aggressive behavior? *J Dtsch Dermatol Ges.* 2008;6(11):952-955. doi:10.1111/j.1610-0387.2008.06739.x.
10. Melato M, Cecovini G, Perazza L, Grandi G. Perineural invasion in solitary keratoacanthoma: a malignant feature? *Acta Dermatovenerol Alp Pannonica Adriat.* 1995;4(2):60-62.
11. Rossi AM, Park B, Qi B, Lee EH, Busam KJ, Nehal KS. Solitary large keratoacanthomas of the head and neck: an observational study. *Dermatol Surg.* 2017;43(6):810-816. doi:10.1097/DSS.0000000000001080.
12. Wysong A, Newman JG, Covington KR, Kurley SJ, Ibrahim SF, Farberg AS, Bar A, Cleaver NJ, Somani AK, Panther D, et al. Validation of a 40-gene expression profile test to predict metastatic risk in localized high-risk cutaneous squamous cell carcinoma. *J Am Acad Dermatol.* 2021;84(2):361-369. doi:10.1016/j.jaad.2020.04.088.
13. Ibrahim SF, Kasprzak JM, Hall MA, Fitzgerald AL, Siegel JJ, Kurley SJ, Covington KR, Goldberg MS, Farberg AS, Trotter SC, et al. Enhanced metastatic risk assessment in cutaneous squamous cell carcinoma with the 40-gene expression profile test. *Future Oncol.* 2022;18(7):833-847. doi:10.2217/fon-2021-1277.
14. Kwiek B, Schwartz RA. Keratoacanthoma (KA): an update and review. *J Am Acad Dermatol.* 2016;74(6):1220-1233. doi:10.1016/j.jaad.2015.11.033.
15. Cernea CR, Ferraz AR, de Castro IV, Sotto MN, Logullo AF, Bacchi CE, et al. Perineural invasion in aggressive skin carcinomas of the head and neck: potentially dangerous but frequently overlooked. *ORL J Otorhinolaryngol Relat Spec.* 2009;71(1):21-26. doi:10.1159/000165171.
16. Gottfarstein-Maruani A, Michenet P, Kerdraon R, Bonneau C, Heitzmann A, Estève E, Rémy RC. Kératoacanthome: deux cas avec emboles vasculaires [Keratoacanthoma: two cases with intravascular spread]. *Ann Pathol.* 2003;23(5):438-442.
17. Godbolt AM, Sullivan JJ, Weedon D. Keratoacanthoma with perineural invasion: a report of 40 cases. *Australas J Dermatol.* 2001;42(3):168-171. doi:10.1046/j.1440-0960.2001.00508.x.

ISSN : (Online): 3008-038X
Abbreviation: J Derm Cse Rep
DOI: 10.61705/jdcr.19.2.2026.54.60

Journal of Dermatological Case Reports

Figure Legends

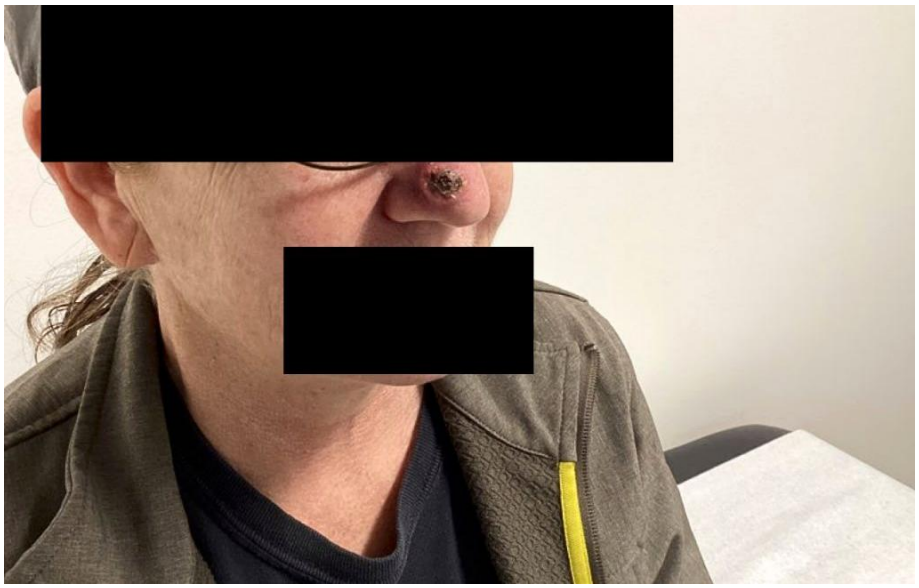

Figure 1. Mohs surgery consult appointment. Two weeks after shave biopsy. Tan-gray, slightly raised, indurated tumor measuring 2.5 cm.

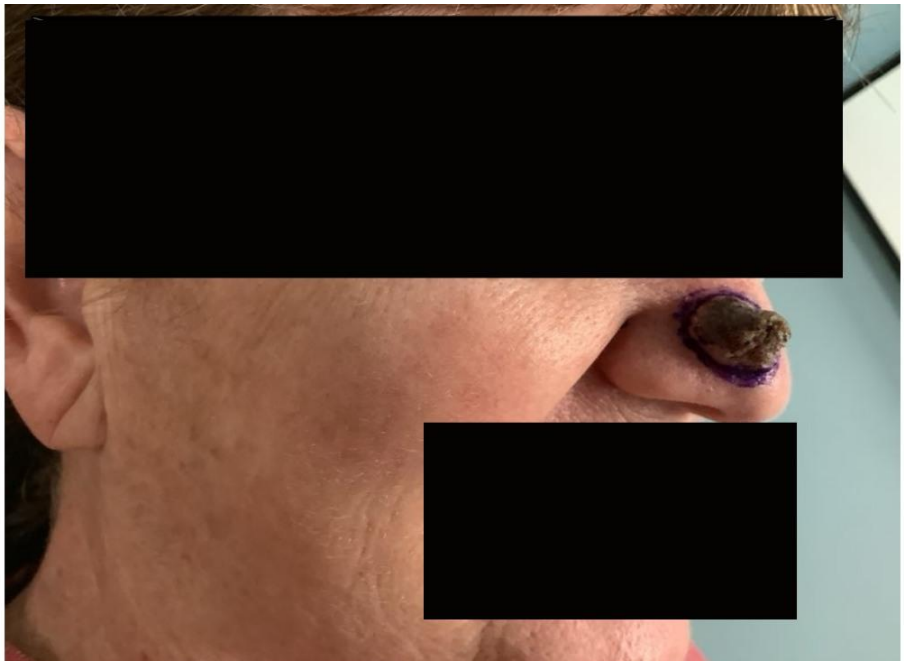

Figure 2. Marked size increase of right-sided nasal supratip lesion with cutaneous horn. Approximately 6 weeks after shave biopsy.

ISSN : (Online): 3008-038X
Abbreviation: J Derm Cse Rep
DOI: 10.61705/jdcr.19.2.2026.54.60

Journal of Dermatological Case Reports

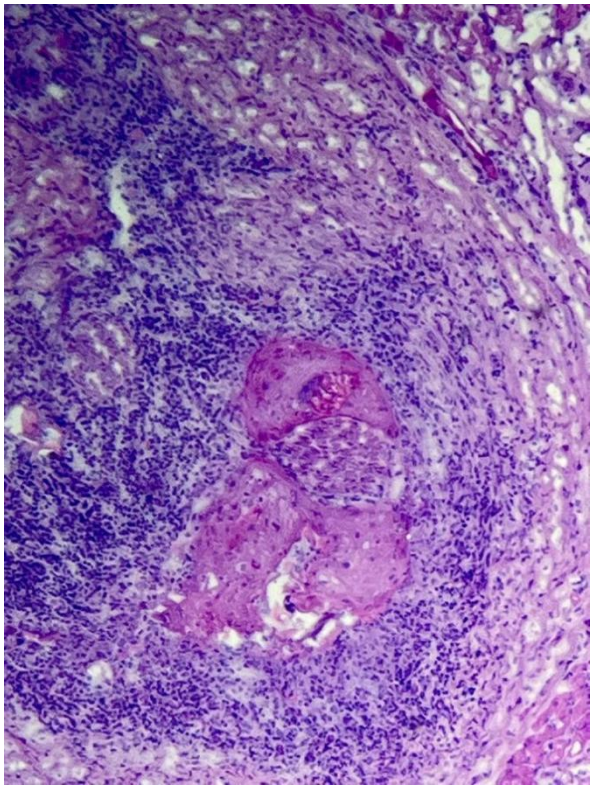

Figure 3. Atypical Keratinocytes extending into muscle with perineural invasion, observed in 2nd stage of Mohr Surgery (50x magnification).

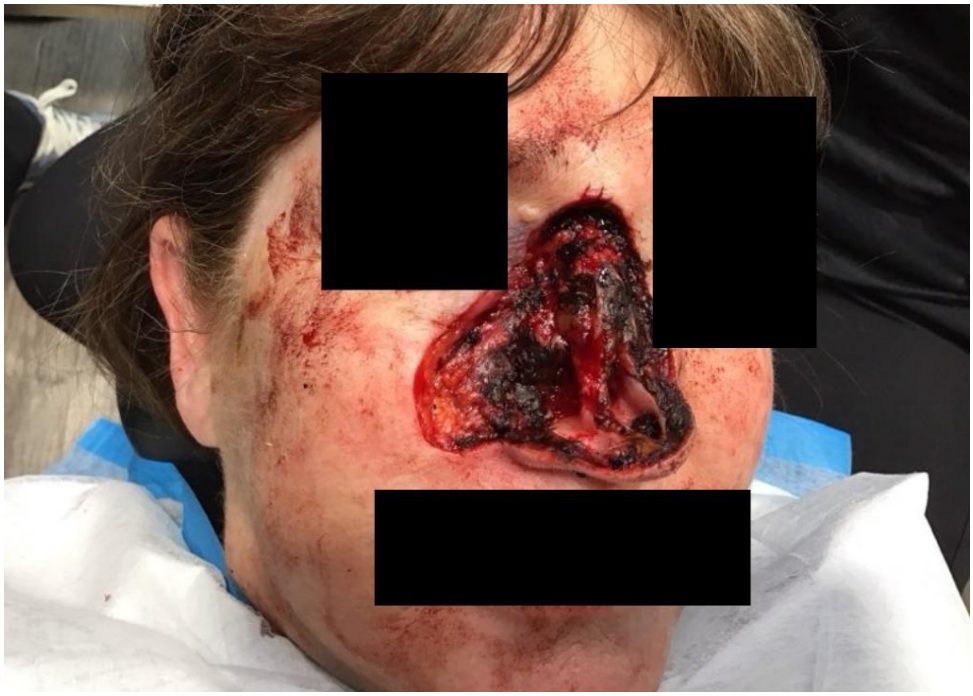

Figure 4. Final defect after laterally cleared surgical margins. Deep margins remained positive. Referral to head/neck cancer clinic for further evaluation

ISSN : (Online): 3008-038X
Abbreviation: J Derm Cse Rep
DOI: 10.61705/jdcr.19.2.2026.54.60

Journal of Dermatological Case Reports

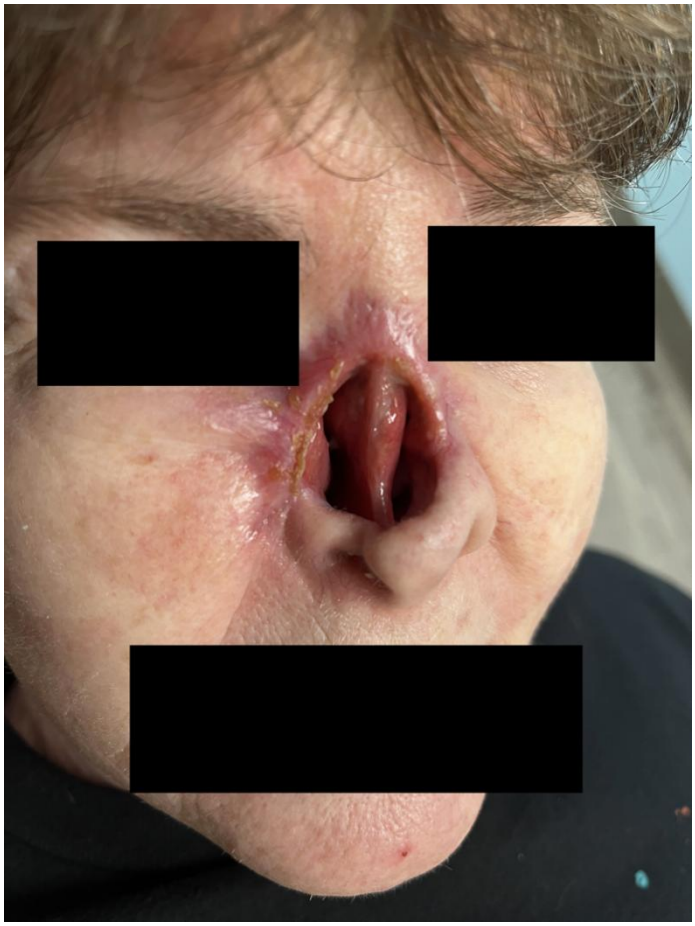

Figure 5. The follow-up consultation showed the defect was completely healed by second intention.