Synchronous Axillary Intranalod SCC And Scalp SCC Case Report – Skip Nodal Metastasis Or Malignant Transformation Of An Intranalod Squamous Cyst?

Jun Xian Jeffrey Hing (✉ hing.jun.xian@singhealth.com.sg)
Changi General Hospital Department of General Surgery  https://orcid.org/0000-0003-4215-4932

Tee Sin Lee
CGH: Changi General Hospital

Anjarwalla Salim M
CGH: Changi General Hospital

Sze Hwa Tan
CGH: Changi General Hospital

Chien Sheng Tan
CGH: Changi General Hospital

Su-Ming Tan
CGH: Changi General Hospital

Case report

Keywords: Isolated axillary, synchronous axillary nodal

DOI: https://doi.org/10.21203/rs.3.rs-409907/v1

License: ☑️ ☛️ This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License
Abstract

Background

Isolated axillary SCC nodal metastasis from a head and neck primary is a highly unusual presentation. Different possibilities include that of a skipped nodal metastasis bypassing the cervical region, or an axillary SCC of a separate unknown primary (SCCUP), or even malignant transformation of a preexisting intranodal squamous cyst. To date, there has been no report of isolated SCC nodal metastases from a scalp primary and even rarer, a case of malignant transformation of an intranodal squamous cyst.

Case presentation

We present a successful management of a synchronous axillary nodal SCC and scalp SCC through curative surgery in a 73-year-old gentleman with extensive psoriasis and a history of immunosuppression from methotrexate use.

Conclusion

We reviewed the literature of this rare entity of an axillary SCCUP, discussed its optimal investigations and management, and the three distinct possible explanations for this unusual presentation.

Background

Isolated axillary SCC nodal metastasis from a head and neck primary is a highly unusual presentation. [1] Different possibilities include that of a skipped nodal metastasis bypassing the cervical region, or an axillary SCC of a separate unknown primary (SCCUP), or even malignant transformation of a preexisting intranodal squamous cyst. To date, there has been no report of isolated SCC nodal metastases from a scalp primary and even rarer, a case of malignant transformation of an intranodal squamous cyst. [2, 3]

Case Presentation

A 73-year-old gentleman presented with isolated painful progressive right axillary swelling of 2-months duration (Fig. 1). He had extensive psoriasis for which he is on intermittent methotrexate 10mg twice weekly for past 20 years. Computed tomography (CT) demonstrated a 7-cm conglomerate necrotic axillary lymph node mass, (Fig. 2.) for which core biopsy showed squamous cell carcinoma (SCC). Further examination revealed an irregular 2cm posterior scalp nodule, whereupon punch biopsy established moderately differentiated SCC. He had neither arsenic, chronic sun exposure nor smokes. Panendoscopy of the aerodigestive tract did not reveal any source of primary. Fused whole body positron emission tomography (PET) - CT demonstrated only two exclusive hypermetabolic areas: the posterior scalp and the right axilla. After discussion at the multidisciplinary meeting, the decision was for wide excision of the scalp SCC and right axillary clearance followed by adjuvant radiotherapy to the axillary nodal basin (Fig. 3). Final histology revealed a moderately differentiated scalp SCC 11mm wide and
4.5mm deep, extending to subcutis with adjacent actinic keratosis. There was no lymphovascular or perineural invasion. The right axillary clearance specimen revealed a 9cm moderately differentiated keratinising SCC tumour within soft tissue but not connected to the overlying skin. (Fig. 4). There was a suggestion of a pre-existing squamous cyst but this could not be confirmed (Fig. 5). There was also some adjacent lymphoid tissue and two other involved nodes. The patient subsequently declined radiotherapy. At 6 months follow up, CT showed no evidence of disease recurrence and the patient remains in remission.

**Discussion**

This case illustrates an exceedingly rare instance of isolated axillary SCC without truncal nor extremity primary. Several possible explanations exist. Based on clinical and radiological findings, there were only two exclusive sites of disease. Hence, the scalp SCC could be the primary site, metatrasizing to the right axillary nodal basin. However, the argument against this is the discordant presentation of a small innocuous primary scalp lesion and a massive axillary nodal metastasis, which seems to exhibit a more aggressive tumour biology. Although small superficial SCC can metastasize, it is uncommon to spare the intervening nodal basin [1]. Since axillary lymph nodes are not considered regional nodes, metastasis to them is presumably via haematogenous route. To our knowledge, scalp SCC with isolated axillary nodal metastasis has not been reported. More common regional metastasis are parotid or cervical lymph nodes and distant sites being lung. [2, 3, 4]

The second possibility is that the axillary SCC is a metastasis not from the scalp SCC but from an unknown primary. The scalp SCC developed as a result of sun exposure, actinic keratosis, compounded by chronic immunosuppression from methotrexate use, albeit intermittently over the past two decades. The axillary SCC is a metastatic SCC from an unknown primary. However, unlike head and neck SCC metastasis of unknown primary site (SCCUP), there is paucity of data on the approach and management to patients with SCCUP of the axilla [7]. Besides excluding a primary from the head and neck, aerodigestive tract, a primary breast pathology was excluded with an unremarkable mammogram and ultrasound. Full dermatological survey revealed extensive psoriatic plaques but no other suspicious lesions. The sensitivity of PET-CT has been reported to be more than 95% in SCC detection, with limitations in detecting occult disease of < 5mm [8]. A cohort of metastatic SCC treated at Memorial Sloan Kettering Cancer Centre recorded 33 axilla lymphadenectomies over 25 years, of which 12 were classified as unknown primary origin. Their 5-year survival analysis did not show significant difference between known and unknown origin [9]. Another occult skin primary may be present among the psoriatic plaques. While this theory was most plausible, there was no clinical or imaging evidence to support this.

The last possibility entertained was a malignant transformation of a pre-existing squamous cyst or an intranodal squamous inclusion cyst in the axillary lymph node. This is illuminated by the pathological finding of a foci suggestive of a squamous cyst with adjacent lymphoid tissue -the latter finding raising the possibility of intranodal origin. While heterotopic squamous inclusions within a lymph node, although described in literature, it is an uncommon finding [5]. They are also always benign, singular, and may
present with history of previous breast biopsy, pre-sentinel lymph node massage [6]. The presence of these squamous cysts in subcapsular area of lymph node may suggest mechanical carriage of inclusions. Other likelihoods are embryological dislodgment or squamous metaplasia of already present glandular epithelium [5, 6]. Extensive psoriasis has not been described as a possible association with squamous inclusion cyst. The argument against this explanation, is the rarity of a malignant intranodal squamous cyst and that the large axillary nodal SCC was not the only node involved. Although high-risk features (large size and poor differentiation) were present, but there was no perineural or lymphovascular invasion to account for how the adjacent nodes could be involved. The authors postulate that the squamous inclusion cyst could have undergone malignant transformation de novo and acquired further metastatic capability to involve other adjacent nodes.

The approach to isolated axillary SCC nodal metastasis has not been well described in literature. The best treatment outcomes in patients with nodal metastases from SCC are achieved with surgery and radiotherapy. [9] Psoriasis has been associated with increased risk of cutaneous malignancy due to the immunosuppressive effects of its treatment and the presence of chronic inflammatory state [2]. For this patient, the authors suggest active surveillance for recurrent SCC together with cessation of immunosuppressive medications such as methotrexate or topical steroids. Instead, topical emollients, vitamin D analogs or systemic retinoids may be considered for psoriasis management [10, 11]. The authors propose the use of PET-CT for surveillance in view of the difficulty and limited sensitivity of clinical examination in presence of such extensive psoriasis. Lastly, this diagnostic dilemma of whether the nodal SCC represents distant metastasis or isolated locoregional disease also posed a challenge in determining the exact stage and prognosis of the condition.

Conclusion

This case demonstrates the successful management of a patient with scalp SCC and giant axillary SCC who has chronic psoriasis on immunosuppression. There is a paucity of literature on this rare and poorly understood axillary SCCUP, hence we proposed three distinct possible explanations for this presentation, including the possibility of a unique histopathological diagnosis.

Abbreviations

| Abbreviation | Description |
|--------------|-------------|
| SCCUP        | Squamous cell carcinoma of unknown primary |
| PET-CT       | Positron emission tomography – computed tomography |

Declarations

Ethics approval and consent to participate – N/a

Consent for publication - The authors have sought written and signed consent to publish the individual person's data in any form (including individual details, images or videos) from the patient prior to
submission. The consent form can be made available to the Editor if requested, and will be treated confidentially.

Availability of data and materials – N/a

Competing interests – Nil

Funding – Nil

Authors’ contribution – JXJH, TSL, SMT took part in the care of the patient. ASM, SHT and CST were responsible for the pathology review. JXJH and SMT were responsible for the literature review, design, writing, completion and critical review of the manuscript.

We confirmed that all authors have approved the manuscript for submission

We confirmed that the content of the manuscript has not been published, or submitted for publication elsewhere

References

1. Dona E, Veness MJ, Cakir B, Morgan GJ. Metastatic cutaneous squamous cell carcinoma to the parotid: the role of surgery and adjuvant radiotherapy to achieve best outcome. ANZ J Surg. 2003;73(9):692–6. doi:10.1046/j.1445-2197.2003.02737.x.

2. Alam M, Ratner D. (2001). Cutaneous Squamous-Cell Carcinoma. New England Journal of Medicine, 344(13), 975–983. doi:10.1056/nejm200103293441306.

3. Howle JR, Morgan GJ, Kalnins I, Palme CE, Veness MJ. Metastatic cutaneous squamous cell carcinoma of the scalp. ANZ J Surg. 2008 Jun;78(6):449 – 53. doi:10.1111/j.1445-2197.2008.04533.x. PMID: 18522564.

4. Beydoun N, Graham PH, Browne L. Metastatic Cutaneous Squamous Cell Carcinoma to the Axilla: A Review of Patient Outcomes and Implications for Future Practice. World J Oncol. 2012 Oct;3(5):217–26. doi:10.4021/wjon503w. Epub 2012 Oct 28. PMID: 29147309; PMCID: PMC5649899.

5. Agorogiannis E, Rana M, Mahler-Araujo B, Meredith P, Metaxas G. (2012). Recurrent axillary lymphadenopathy with benign squamous epithelial inclusions in a female with no breast pathology. Journal of Clinical Pathology, 65(12), 1146–1147. doi:10.1136/jclinpath-2012-201034.

6. Fellegara G, Carcangi ML, Rosai J. Benign epithelial inclusions in axillary lymph nodes: report of 18 cases and review of the literature. Am J Surg Pathol. 2011 Aug;35(8):1123–33. doi:10.1097/PAS.0b013e3182237985. PMID: 21753696.

7. Maghami E, Ismaila N, Alvarez A, Chemock R, Duvvuri U, Geiger J, Gross N, Haughey B, Paul D, Rodriguez C, Sher D, Stambuk HE, Waldron J, Witek M, Caudell J. Diagnosis and Management of Squamous Cell Carcinoma of Unknown Primary in the Head and Neck: ASCO Guideline. J Clin Oncol. 2020 Aug 1;38(22):2570–2596. doi: 10.1200/JCO.20.00275. Epub 2020 Apr 23. PMID: 32324430.
8. Escott EJ. (2013). Role of Positron Emission Tomography/Computed Tomography (PET/CT) in Head and Neck Cancer. Radiologic Clinics of North America, 51(5), 881–893. doi:10.1016/j.rcl.2013.05.002.

9. Wach MM, van Beek E, Ayabe R, Ruff S, Brown Z, Goldman DA, Zambirinis CP, Gholami S, Pulitzer M, Hernandez J, Coit D. Metastatic squamous cell carcinoma of known and unknown primary origin treated with axillary or inguinal lymphadenectomy. Am J Surg. 2018 Nov;216(5):963–8. doi: 10.1016/j.amjsurg.2018.06.006. Epub 2018 Jun 20. PMID: 30143231; PMCID: PMC7545876.

10. Mason AR, Mason J, Cork M, et al. Topical treatments for chronic plaque psoriasis. Cochrane Database Syst Rev 2013;:CD005028.

11. Menter A, Gelfand JM, Connor C, Armstrong AW, Cordoro KM, Davis DMR, Elewski BE, Gordon KB, Gottlieb AB, Kaplan DH, Kavanaugh A, Kiselica M, Kivelevitch D, Korman NJ, Kroshinsky D, Lebwohl M, Leonard CL, Lichten J, Lim HW, Mehta NN, Paller AS, Parra SL, Pathy AL, Prater EF, Rahimi RS, Rupani RN, Siegel M, Stoff B, Strober BE, Tapper EB, Wong EB, Wu JJ, Hariharan V, Elmets CA. Joint American Academy of Dermatology-National Psoriasis Foundation guidelines of care for the management of psoriasis with systemic nonbiologic therapies. J Am Acad Dermatol. 2020 Jun;82(6):1445–86. doi:10.1016/j.jaad.2020.02.044. Epub 2020 Feb 28. PMID: 32119894.

Figures
Figure 1

Clinical photograph of the isolated axillary mass on a background of extensive psoriasis (top) front view, (middle) side view, (bottom) arms abducted view
Figure 2

Clinical photograph of a 1.5cm fleshy nodule on the posterior scalp which yielded squamous cell carcinoma on biopsy
Figure 3

CT image showing right axillary conglomerate necrotic mass measuring 6.9cm by 5.2cm two months prior to surgery
Figure 4

Specimen photograph depicting the axilla post axillary clearance with preservation of the axillary vein, thoracodorsal bundle and the long thoracic nerve (top), a 9 by 9 cm axillary clearance specimen (bottom)
Figure 5

Histopathology slide showing foci suggestive of a squamous cyst (indicated by ^) as well as some adjacent lymphoid tissue (indicated by *)