VIA MEDICA

Case report

NOWOTWORY Journal of Oncology
2019, volume 69, number 3–4, 150–156
DOI: 10.5603/NJO.2019.0028

ISSN 0029–540X
www.nowotwory.edu.pl

# A squamous cell carcinoma arising from scrotal epidermal cyst. A case report and review of 94 cases from the world literature

Abdalla Saad Abdalla Al-Zawi[1], Sadaf Memon[2], Ahmed Shah[2], Soad Eldruki[3], Elizabeth Tan[4], Salem Omar Alowami[2]

[1]*Basildon & Thurrock University Hospital, Essex, United Kingdom*
[2]*Department of Pathology, McMaster University, Hamilton, Ontario, Canada*
[3]*Department of Pathology, Benghazi Medical Centre, Libya*
[4]*King's College Hospital, London, United Kingdom*

Epidermal cysts are a common benign skin abnormality, comprising 85–90% of all excised skin cysts. The term epidermal inclusion cyst refers specifically when the cyst resulted from the implantation of epidermal elements in the dermis. Squamous cell carcinomas (SCCs) are common skin lesions; however, a malignant transformation of an epidermal cyst is very rare with incidence of 0.011–0.045%. Few cases of malignant transformation of an epidermal cyst have been reported in the literature so far. This paper presents a case of squamous cell carcinoma arising from a scrotal epidermal cyst.

NOWOTWORY J Oncol 2019; 69, 3–4: 150–156

**Key words:** epidermal cyst, squamous cell carcinoma, PD-1 blockade, cemiplimab

## Introduction

Epidermal cysts (EC), also known as sebaceous, keratin, follicular infundibular or epidermal inclusion cysts, are extremely common lesions that can occur anywhere in the body. Histologically, they are lined with a thin layer of *squamous epithelium* and develop by buildup of keratin inside the cyst [1].The malignant transformation of an epidermal cyst is very rare clinically. Several neoplasms have been reported to develop in EC including basal cell carcinoma [2], malignant melanoma [3], Merkel cell carcinoma [4], plasmacytoma [5] and squamous cell carcinoma [6].

The development of true squamous cell carcinoma in pre-existing epidermal cysts is a rare event with incidence of 0.011–0.045% [7].

## Case report

A 70-year-old male presented with a left scrotal lesion. The lesion was extra-testicular and solid. The initial clinical impression was lymphoma. A CT of chest, abdomen and pelvis was requested, which showed no evidence of lymphadenopathy or any mass lesion.

The patient underwent surgical excision of the scrotal mass. The pre-operative diagnosis and impression was that of a large sebaceous cyst. Intra-operatively, the cystic mass was accidently punctured and revealed a large amount of sebaceous fluid. The entire cystic mass was carefully dissected. The specimen was sent to Pathology.

Gross examination revealed a partially collapsed cyst measuring 3.0 x 2.0 x 1.8 cm with portion of skin attached to it. The inner lining was smooth with the exception of one white raised area measuring 0.8 x 0.8 x 0.5 cm. The entire specimen was serially sectioned and submitted for microscopic examination. The histo-pathological examination revealed infiltrating nests of atypical squamoid cells with surrounding intense desmoplastic stromal reaction, representing an early invasive well-differentiated carcinoma arising from epidermal scrotal cyst. The resection margins were clear (fig.: 1, 2).

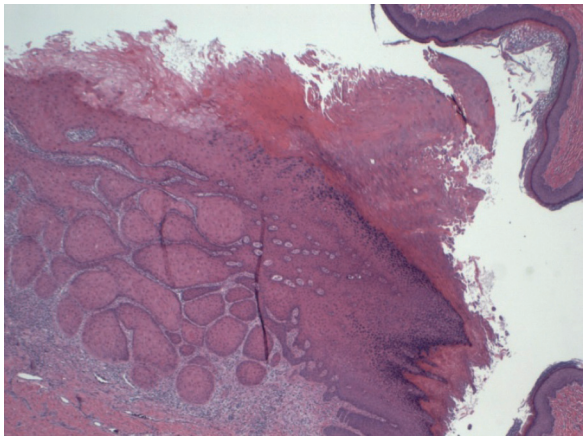

**Figure 1.** Low power view showing atypical squamoid nests arising from wall of scrotal epidermal cyst

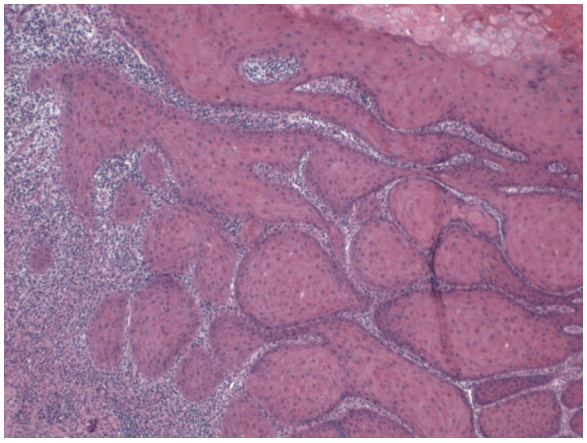

**Figure 2.** High power view showing the infiltrating nests of atypical squamoid cells with surrounding intense desmoplastic stromal reaction

## Discussion

Epidermal cysts are common cutaneous lesions that may occur anywhere on the body. Malignant changes in the epidermal cysts are an uncommon finding.

Among the pre-malignant and malignant neoplasms that have been reported to develop in EC are: basal cell carcinoma [2, 8], malignant melanoma [3], Bowen's disease [9], Paget's disease [10], bowenoid papulosis [11], mycosis fungoides [12], Merkel cell carcinoma [4] and plasmacytoma [5]. All these lesions have a far lesser incidence than squamous cell carcinoma [6]. The development of true squamous cell carcinoma, in a pre-existing cutaneous epidermal cyst, is a rare event with incidence of 0.011–0.045% [7].

SCC also known as epidermoid carcinoma is the second most common skin cancer, after basal cell carcinoma. The rare Merkel cell carcinoma (MCC) is a frequently lethal skin cancer with a higher mortality (33%) than malignant melanoma (MM) (15%) [13]. In contrast, the survival rate for most other non-melanoma skin cancers is excellent. For instance, the 5-year relative survival for basal cell carcinoma (BCC) is 100%, whereas the 5-year relative survival for SCC is slightly less at 95% [14]. Among the above-mentioned skin malignancies, the reports show that the incidence of melanoma has been steadily rising in the recent decades [15].

The literature review revealed that in 1968 McDonald [16] analysed 637 epidermal cysts, but found malignancy in only in 7 (1.1%) cases. Of these, 6 were basal cell carcinomas and only one was a squamous cell carcinoma.

The development of SCC in EC occurs most frequently on the head and neck [17, 18], trunk [19] and thigh. Other reported sites are scrotum [20], perineal regions [7, 21], sublingual gland [22], vulva [23] and breast [24]. After reviewing all reported 94 cases, it was obvious that they are more frequent in males with incidence of 65% (table I). The localization of the lesion was as follows: head and neck (55%), lower limbs (13%), trunk (13%), perineum (8%) and the upper limbs (6%) (figure 3). Malignant transformation of an epidermoid cyst can also occur in the deeper parts of the body other than the skin, such as the intra-cranial region [25] and ovary [26]. It has been reported that the rate of malignant transformation of epidermal cyst into cutaneous squamous cell carcinoma ranges between 0.011% and 0.045% [27, 28]. The documented size of the affected cyst varies between 8 mm and 150 mm. Patients often present with a lesion size between 1 to 4 cm, and the lesion duration ranged from 2 months to 20 years (table I).

The blamed predisposing factors include chronic history, trauma, recurrent infection, chronic sunlight exposure [29, 31], advanced age, skin that is sensitive to ultraviolet radiation, and immunosuppression [32]. Furthermore, chronic inflammation and irritation is classically described to be associated with malignant transformation in lesions behaving similarly to the

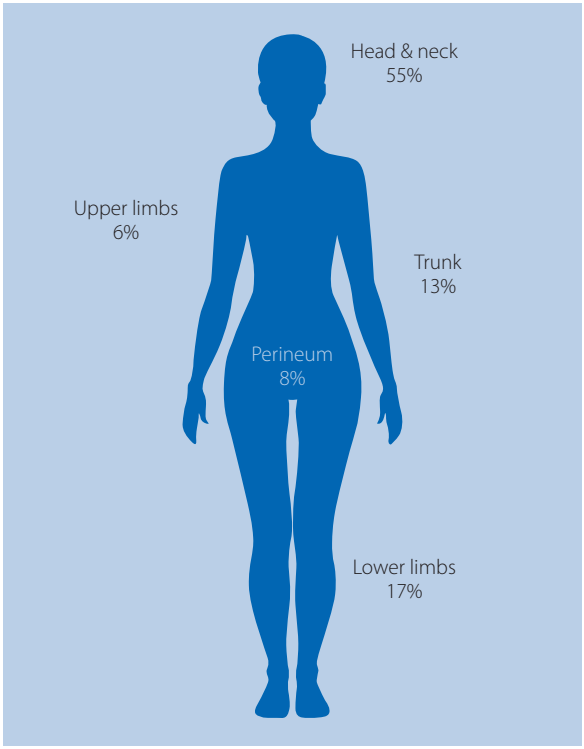


**Figure 3.** Distribution of 94 cases of squamous cell carcinoma developed in subcutaneous epidermoid cysts

**Table I.** Malignant transformation of cutaneous epidermal cyst into squamous cell carcinoma: a review of 95 cases reported in literature

| Author | Year published | Gender | Age | Site | Size (mm) | Histology | Lesion duration/ /months | Symptoms |
|---|---|---|---|---|---|---|---|---|
| Peden: 11 cases [50] | 1948 | F | 43 | scalp | – | SCC | 180 | ↑ size |
| | 1948 | F | 63 | scalp | – | SCC | 180 | – |
| | 1948 | M | 43 | face | – | SCC | 1 | ↑ size |
| | 1948 | F | 64 | forearm | – | SCC | 1 | ↑ size |
| | 1948 | M | 25 | thigh | – | SCC | – | – |
| | 1948 | F | 48 | scalp | – | SCC | 300 | ↑ size |
| | 1948 | F | 63 | shoulder | – | SCC | 24 | ↑ size |
| | 1948 | F | 75 | scalp | – | SCC | 24 | ↑ size |
| | 1948 | F | 53 | scalp | – | SCC | – | – |
| | 1948 | M | 57 | scalp | – | SCC | 48 | ↑ size |
| | 1948 | M | 79 | ear | – | SCC | 18 | – |
| Latimer: 2 cases [51] | 1949 | M | 40 | face | 40 | SCC | 24 | ulcer |
| | 1949 | F | 5 | face | 10 | SCC | – | ↑ size |
| McDonald [8] | 1963 | F | 43 | sternum | – | | – | – |
| Davidson [52] | 1976 | M | 52 | ear | – | SCC | 2 | – |
| Bauer [53] | 1980 | M | 68 | preauricular | 30 | WD-SCC | – | inflammation |
| Miler [54] | 1981 | M | 34 | scalp | 30 | WD-SCC | 240 | ↑ size |
| Yaffe [55] | 1982 | M | 58 | ear | 25 | SCC | 132 | ↑ size |
| Arianayagam [16] | 1987 | F | 59 | thigh | 25 | WD-SCC | 3 | ↑ size, pain |
| Sagi [81] | 1988 | F | 60 | scalp | – | WD-SCC | 120 | ulcer |
| Shah [56] | 1989 | F | 55 | buttock | 90 | WD-SCC | 6 | – |
| Davies [57] | 1994 | M | 32 | index finger | – | WD-SCC | 120 | ulcer |
| Malone [58] | 1999 | F | 92 | forehead | 35 | PD-SCC | – | ↑ size |
| Lopez-Rios: 8 cases [23] | 1999 | M | 68 | preauricular | 50 | SCC | 4 | – |
| | 1999 | M | 66 | preauricular | 15 | WD-SCC | 2 | – |
| | 1999 | M | 58 | ear | 25 | SCC | 132 | – |
| | 1999 | M | 52 | ear | 20 | SCC | 132 | – |
| | 1999 | M | 34 | retro-auricular | 80 | SCC | – | – |
| | 1999 | M | 32 | index finger | – | SCC | 120 | – |
| | 1999 | F | 59 | thigh | 50 | WD-SCC | 3 | – |
| | 1999 | F | 55 | buttock | 100 | | 6 | – |
| Wong [77] | 2000 | M | 57 | buttock | 60 | WD-SCC | 240 | ↑ size |
| Morgan: 5 cases [34] | 2001 | 3M | 21–80 (mean 56.7) | trunk | – | WD-SCC | – | – |
| | | 2F | | neck | – | WD-SCC | – | – |
| | | | | face | | | | |
| Debaize [78] | 2002 | F | 38 | buttock | 200 | SCC *in-situ* | 240 | ↑ size |
| Lin [37] | 2002 | M | 68 | axilla | 65 | WD-SCC | 2 | ↑ size |
| Cameron [59] | 2003 | M | 67 | temple | 30 | PD-SCC | 48 | ↑ size, inflamed |
| Kume [60] | 2004 | M | 55 | sacrum | – | SCC | 48 | – |
| Nemoto [61] | 2006 | F | 48 | abdominal wall | 92 | PD-SCC | 120 | ↑ size, pain |
| Chiu [27] | 2007 | M | 47 | thigh | 130 | WD-SCC | 480 | ↑ size, bleeding |
| Jehle [48] | 2007 | M | 48 | gluteal area | 50 | WD-SCC | 336 | ↑ size, trauma |

| Author | Year published | Gender | Age | Site | Size (mm) | Histology | Lesion duration/ /months | Symptoms |
|---|---|---|---|---|---|---|---|---|
| Bhatt [22] | 2008 | F | 64 | sublingual gland | – | SCC | 144 | ↑ size |
| Kuvat [31] | 2009 | M | 48 | scalp | 60 | SCC | 156 | ulcer |
| Ziadi [28] | 2010 | M | 50 | head | 15 | SCC | 3 | no change |
| Antón-Badiola [38] | 2010 | M | 65 | retro-auricular | 20 | MD-SCC | 2 | ulcer |
| Pusiol: 2 cases [35] | 2010 | M | 88 | face | 7 | SCC | – | – |
| | 2010 | M | 96 | ear | 15 | SCC | 12 | |
| Kshirsagar [39] | 2011 | M | 72 | buttock | 100 | WD-SCC | 120 | ↑ size, ulcer |
| Shabbir [62] | 2011 | M | M | ear | 12 | SCC | – | – |
| Moritt: 4 cases [33] | 2011 | M | 48 | leg | – | SCC | – | ↑ size |
| | 2011 | M | 68 | back | – | SCC | 72 | ↑ size, inflamed |
| | 2011 | F | 72 | scalp | – | SCC | 240 | ↑ size, ulcer |
| | 2011 | F | 60 | face | – | SCC | 3 | ↑ size |
| Anastasios [63] | 2012 | F | 69 | face | 9 | MD-SCC | 18 | ↑ size |
| Terada [42] | 2012 | F | 76 | nasal | | SCC | – | cosmetic |
| Sumi [64] | 2012 | F | 76 | labia majora | 125 | WD-SCC | – | ↑ size |
| Sinha [65] | 2012 | M | 65 | scalp | | WD-SCC | 72 | ↑ size |
| Pusiol: 4 cases [35] | 2012 | M | 88 | face | – | SCC | – | – |
| | 2012 | M | 96 | ear | 15 | SCC | – | – |
| | 2012 | M | 67 | hallux | 8 | SCC | – | ulcer |
| | 2012 | F | 86 | perineum | 15 | SCC | – | – |
| Tokunaga [30] | 2013 | M | 65 | neck | 90 | PD-SCC | 420 | ↑ size, bleeding |
| Yeh [20] | 2013 | M | 86 | scrotum | 41 | WD-SCC | 276 | discharge |
| Cappello [47] | 2013 | M | 63 | nasal skin | 20 | WD-SCC | 36 | pain, discharge |
| Skroza [66] | 2014 | M | 63 | scalp | 30 | SCC | 24 | – |
| Hasegawa [67] | 2014 | M | 75 | buttock | 60 | SCC | – | – |
| Fujita [68] | 2015 | M | 48 | pre-sacral | 120 | SCC | 1 | pain |
| Satoh [69] | 2015 | M | 76 | pre-sacral | 70 | SCC | 36 | ↑ size |
| Sridevi [21] | 2015 | M | 68 | submandibular | 60 | WD-SCC | 12 | ↑ size |
| Suhani [24] | 2015 | F | 60 | breast | 50 | | 6 | – |
| Sakamoto [17] | 2015 | M | 41 | thumb | 20 | SCC | – | ulcer |
| Veenstra: 3 cases [70] | 2016 | F | 46 | thigh | 20 | WD-SCC | 12 | – |
| | 2016 | F | 89 | supra-pubic | 40 | WD-SCC | 1 | pain, discharge |
| | 2016 | M | 61 | thigh | 12 | WD-SCC | 6 | ↑ size |
| Sze [23] | 2016 | F | 65 | vulva | 50 | MD-SCC | 240 | ↑ size |
| Lee [71] | 2016 | M | 62 | face | 25 | WD-SCC | – | ↑ size |
| McAllister [36] | 2017 | M | 73 | ear | – | SCC | 2 | ulcer |
| Rathna [72] | 2017 | M | 30 | forehead | 20 | SCC *in-situ* | 36 | |
| Sirvastava [73] | 2016 | M | 28 | neck | 65 | SCC | 7 | ↑ size |
| Suzuki [74] | 2017 | M | 56 | perineum | 43 | SCC | 540 | ↑ size |
| Frank [18] | 2018 | F | 64 | neck | 4 | WD-SCC | 48 | ↑ size |
| Zanguoie [29] | 2018 | F | 77 | neck | large | SCC | 240 | ↑ size |
| Park [7] | 2018 | M | 51 | perineal | 150 | SCC | 360 | ↑ size |
| Bears [75] | 2019 | M | 44 | thigh | 15 | WD-SCC | 5 | ↑ size |

| Author | Year published | Gender | Age | Site | Size (mm) | Histology | Lesion duration/ /months | Symptoms |
|---|---|---|---|---|---|---|---|---|
| Kim [76] | 2019 | M | 46 | nasal alar | 9 | SCC | – | – |
| Daisley [6] | 2019 | M | 67 | abdominal wall | 150 | WD-SCC | 300 | ↑ size, pain, ulcer |
| Niimi [46] | 2019 | F | 71 | buttock | 100 | WD-SCC | 12 | ↑ size, pain |
| Kasahara [79] | 2019 | M | 50 | scrotum | 48 | WD-SCC | 24 | firm |
| Lopez [80] | 2019 | M | 83 | peri-coccygeal | 61 | MD-SCC | 10 | ↑ size, pain |
| Shah [81] | 2019 | M | 37 | scalp | 70 | PD-SCC | 4 | ↑ size, pain |
| This case | 2019 | M | 70 | scrotum | 8 | WD-SCC | – | ↑ size |

WD – well differentiated, MD – moderately differentiated, PD – poorly differentiated

epidermal cyst, such as *pilonidal sinus*, *hidradenitis suppurativa* and *chronic osteomyelitis* [33].

HPV-associated malignant transformation of the epidermal cyst in head and neck area, and the perineum has been reported before. Previous studies looked to the aetiological relation of HPV to the malignant transformation of the EC, however the limited number of cases prevents complete exoneration of HPV as an aetiological factor [29, 30, 34–36].

In the malignant transformation of the EC, the squamous cell carcinoma arises from the lining cells of the epidermal inclusion cyst. The malignancy may be associated with a sudden development of suspicious features in a sebaceous cyst, which has been present for a long time. These signs and symptoms may include the cyst changing into a firmer mass, pain, discharge, inflammation, ulceration, bleeding, rapid increase in size, inflammation or infection not responding to conservative treatment. Such findings may alert the clinician to excise the lump and examine it [7, 31, 37, 38].

Histologically, the lumen of the EC is filled with laminated keratin, and the specimen may reveal scattered islands of severely atypical neoplastic squamous epithelium arranged in small nests or sheets with marked nuclear irregularity, nuclear hyperchromasia, pleomorphism, absence of intracellular bridges, increased mitotic figures and an infiltrative growth pattern [39].

The immunohistochemistry may show positivity of the tumor cells for p53 protein, a tumor marker which is positive in malignancies including SCCs [40–42]. CK5/6 is a cytokeratin marker used to identify breast basal/myoepithelial cells [43] and together with p63+ identify squamous origin in poorly differentiated metastatic carcinomas [42, 44]. CAM 5.2 "commonly used antibody to cytokeratins 8 and CK7", is positive in most epithelial cells as in SCC [30, 45]. The suppressor protein p16 marker may also be present in SCCs [23]. Serum markers, such as SCC-related antigen level, helps in diagnosis and detection, and its upper normal is 1.5 ng/dl [26, 46]. Cytokeratin AE1/AE3 "pancytokeratin" marker, which detects most of the epithelial tissue is also found to be positive in a such cases [42, 45].

The treatment of choice in localized disease is radical surgical excision. Disease free margin specimens are recommended to avoid residual disease or recurrences. Fortunately, despite malignant transformation distant metastatic disease is rare [47]. SCC can metastasize to the regional lymph nodes and lungs [48].

Most of the cases are cured with surgery. In a small percentage of patients, the tumor reaches an incurable stage due to metastatic disease or locally advanced progression, and thus is no longer amenable to surgery or radiation therapy. At this stage palliative systemic chemotherapy or immunotherapy with PD-1 blockade using cemiplimab is indicated [32, 49].

Prognostic factors of local recurrence, metastasis, and disease-specific death, include tumor size larger than 2 cm, gender, preceding lesions, rapid tumor growth, degree of the differentiation and tumor location.

## Conclusion

The malignant transformation of an epidermal cyst is a rare condition; this case illustrates the importance of patho-morphological examination of the excised epidermal cysts. Moreover, potential malignancy should be suspected in patients with chronic sebaceous cysts, and the cyst exhibits suspicious features. The most frequently affected region is the head and neck.


## Acknowledgment

We are extremely thankful to Mrs. Sarah Colquhoun, Senior library assistant, Basildon Healthcare Library – Basildon University Hospital for her invaluable support in preparing this paper.

We would like to thank Miss Rihana Saad Abdalla from the BMAT STEM Academy in Harlow-England for her extraordinary work to prepare the included figure.

**Conflict of interests:** none declared



**Abdalla Saad Abdalla Al-Zawi**
*Basildon & Thurrock University Hospital*
*Essex, United Kingdom*
*e-mail: abdalasaad@gmail.com*



*Received: 23 Jul 2019*
*Accepted: 27 Aug 2019*

## References


1. Fromm LJ. https://emedicine.medscape.com/article/1061582-overview
2. Viewed 24/06/2019
3. Udovenko ODO, Guo Y, Connelly T et al. Basal-Cell Carcinoma Occurring in Cutaneous Infundibular Cysts: report of 2 cases and review of the literature. *Am J Dermatol.* 2015; 37 ( 8): 635–638 .
4. Bajoghli A et al. Melanoma arising from an epidermal inclusion cyst. *J Am Acad Dermatol.* 2013; 68 (1): 6–7.
5. Aljufairi E, Alhilli F. Merkel cell carcinoma arising in an epidermal cyst. *Am J Dermatol.* 2016; 39 (11).
6. Komen N, Mertens M. A (malignant) sebaceous cyst. *Tijdschrift voor Geneeskunde.* 2010; 66 (17): 830–832
7. Daisley Jr H, Rampersad A, Acco O et al. Squamous cell carcinoma developing in an epidermal squamous cell carcinoma developing in an epidermal inclusion cyst. *Dermatology Online Journal.* 2019; 10 (2): 166–169.
8. Park BS, Shin DH, Kim SH et al. Perineal squamous cell carcinoma arising from an epidermal cyst: a case report. *World J Surg Oncol*. 2018; 16 (1): 155.
9. McDonald LW. Carcinomatous change in cysts of the skin. *Arch Dermatol.* 1968; 37: 208–211.
10. Shelley WB, Wood MG. Occult Bowen's disease in keratinous cysts. *Br J Dermatol.* 1981; 105 (1): 105–8.
11. Stephenson TJ, Cotton DW. Paget's disease in an epidermal cyst. *Dermatologica.* 1987; 174 (4): 186–90.
12. Masessa JM, Schwartz RA, Lambert WC .Bowenoid papulosis in a penile epidermal inclusion cyst. *Br J Dermatol.* 1987; 116 (2): 237–239.
13. Aloi F, Tomasini C, Pippione M. Mycosis fungoides and eruptive epidermoid cysts: a unique response of follicular and eccrine structures. *Dermatology.* 1993; 187: 273–277.
14. Al Zawi ASA, Prodromou A, Chicken W et al. Merkel cell carcinoma: literature review. *Nowotwory Journal of Oncology.* 2017; 67 (1): 127–131.
15. Survival statistics for non-melanoma skin cancer.www.cancer.ca. Visited on 20 Jul 2019.
16. Al-Zawi ASA, Osayi K, Eades M. Breast metastasis from a malignant melanoma – a case report. *Int J Radiol Radiat Ther.* 2017; 3 (3): 230–232.
17. Arianayagam S, Jayalakshmi P. Malignant epidermal cyst: a case report. *Malays J Pathol.* 1987; 9: 89–91.
18. Skamoto A, Shiba E, Hisaoka M. Squamous cell carcinoma arising from an epidermal cyst in the thumb. *J Surg Case Rep Int.* 2015; 11: 37–39.
19. Frank E, Macias D, Hondorp B et al. Incidental squamous cell carcinoma in an epidermal inclusion cyst: a case report and review of the literature. *Case Rep Dermatol.* 2018; 10 (1): 61–68.
20. Handa U, Kumar S, Mohan H. Aspiration cytology of epidermoid cyst of terminal phalanx. *Diagn Cytopathol.* 2002; 26 (4): 266–267.
21. Yeh L-P, Liao K-S. Squamous cell carcinoma arising from an epidermal cyst of the scrotum. *Tzu Chi Medical Journal.* 2013; 25: 117–118.
22. Sridevi HB, Shariff MH, Pushpalatha Pai K. Squamous cell carcinoma arising in an epidermal cyst. *Indian J Cancer.* 2015; 52: 335–336.
23. Bhatt V, Evans M, Malins THE. Squamous cell carcinoma arising in the lining of an epidermoid cyst within the sublingual gland – a case report. *Br J Oral Maxillofac Surg.* 2008; 46: 683–685.
24. Sze S, Richmond I, Bickers A et al. Squamous cell carcinoma arising from a vulval epidermal cyst. *J Obst Gynaecol.* 2016; 42(11): 1623–1626.
25. Suhani, Aggarwal L, Meena K et al. Squamous cell carcinoma arising in epidermal inclusion cyst of the breast: a diagnostic dilemma. *Breast Disease.* 2015; 35 (1): 25–27.
26. Roh TH, Park YS, Park YG et al. Intracranial squamous cell carcinoma arising in a cerebellopontine angle epidermoid cyst – a case report and literature review. *Medicine.* 2017; 96 (51): 9423.
27. Agarwal S, Pandey P, Ralli L et al. Squamous cell carcinoma arising from an epidermoid cyst of the ovary and metastasizing to the uterus: report of an unusual case with review of literature. *Journal of Gynecologic Surgery.* 2016; 33 (4).
28. Chiu MY, Ho ST. Squamous cell carcinoma arising from an epidermal cyst. *Hong Kong Med J.* 2007; 13: 482–484.
29. Ziadi S, Trimeche M, Hammedi F et al. Squamous cell carcinoma arising from an epidermal inclusion cyst: a case report. *N Am J Med Sci.* 2010; 2 (1): 46–47.
30. Zanguoie M. Squamous cell carcinoma arising from the sebaceous cyst. *JST.* 2018; 6 (2): 71–72.
31. Tokunaga M, Toya M, Endo Y et al. A case of an undifferentiated squamous cell carcinoma arising from an epidermal cyst. *Case Rep Dermatol Med*. 2013; 2013: 469516.
32. Kuvat SV. Squamous cell carcinoma arising from a sebaceous cyst, case report. *Istanbul Tip Dergrsi.* 2009; 1: 109–110.
33. Migden MR , Rischin D , Schmults CD et al. PD-1 blockade with cemiplimab in advanced cutaneous squamous-cell carcinoma. *N Engl J Med.* 2018; 379: 341–351.
34. Moritt AN, Tiffin N, Brotherston TM. Squamous cell carcinoma arising in epidermoid cysts: rerport of four cases and review of the literature. *Journal of Plastic, Reconstructive & Aesthetic Surgery.* 2012; 65 (9): 1267–1269.
35. Morgan MB, Stevens GI, Somach S et al. Carcinoma arising in epidermal cyst; a case series and aetiological investigations of human papilloma virus. *BJD.* 2001; 145 (3): 505–506.
36. Pusiol T et al. Squamous cell carcinoma arising in epidermal cyst and human papillomavirus associated cyst. *Pathologica.* 2010; 102 (3): 88–92.
37. McAllister P, Affleck A, Manickavasagam J et al. Aggressive cutaneous squamous cell carcinoma arising from a human papillomavirus-infected epidermoid cyst of the conchal bowl. *Clinical and Experimental Dermatology.* 2017; 43 (2).
38. Lin C-Y, Jwo S-C. Squamous cell carcinoma arising in an epidermal inclusion cyst. *Chang Gung Med J.* 2002: 25: 279–82.
39. Antón-Badiola I, San Miguel-Fraile P, Peteiro-Cancelo A et al. Squamous cell carcinoma arising on an epidermal inclusion cyst: a case presentation and review of the literature. *Actas Dermosifiliogr.* 2010; 101 (4): 349–53.
40. Kshirsagar AY, Sulhyan SR, Deshpande S et al. Malignant change in an epidermal cyst over gluteal region. *J Cutan Aesthet Surgery.* 2011; 4: 48–50.
41. Al-Zawi ASA, Lazarevska A, Omer MM et al. Metastatic breast cancer to the cervix presenting with abnormal vaginal bleeding during chemotherapy: a case report and literature review. *Chirurgia.* 2018; 113 (4): 564–570.
42. Khodaeiani E, Fakhrjou A, Amirnia M et al. Immuno-histochemical evaluation of p53 and Ki67 expression in skin epithelial tumors. *Indian J Dermatol.* 2013; 58 (3): 181–187.
43. Terada T. Squamous cell carcinoma originated from an epidermal cyst. *Int J Clin Exp Pathol.* 2012; 5 (5): 479–481.
44. Al-Zawi ASA, Ratajczak A, Idaewor P et al. Primary lung cancer with metastasis to the ipsilateral breast – a case report. *Int J Res Med Sci.* 2018; 6 (1): 334–339.
45. Kaufmann O, Fietze et al. Value of p63 and Cytokeratin 5/6 as Immunohistochemical markers for the differential diagnosis of poorly differentiated and undifferentiated carcinomas. *Am J Clin Pathol.* 2001; 116: 823–830.
46. Asaad A, Al-Zawi ASA, Idaewor P et al. Breast metastasis as a presentation of malignant melanoma. *Chirurgia.* 2018; 113 (5): 712–718.
47. Niimi Y, Takeuchi M, Isono N. Squamous cell carcinoma following epidermal cyst in the buttock. *Plast Reconstr Surg Glob Open.* 2019; 7: e2069.
48. Cappello ZJ, Kasdan ML, Augenstein ACet al. Squamous cell carcinoma in an epidermoid cyst. *www.ePlasty.com, Interesting Case.* 2013, April 26.
49. Jehle KS, Shakir AJ, Sayegh ME. Squamous cell carcinoma arising in an epidermoid cyst. *Br J Hosp Med.* 2007; 68: 446.
50. Potenza C, Bernardini N, Balduzzi V et al. A review of the literature of surgical and nonsurgical treatments of invasive squamous cells carcinoma. *Biomed Res Int.* 2018; Apr 2; 2018: 9489163.
51. Peden JC Jr. Carcinoma developing in sebaceous cysts. *Ann Surg.* 1948; 128 (6): 1136–1147.
52. Latimer EO, Spicer DD. Epidermoid carcinoma in sebaceous cysts. *Q Bull Northwest Univ Med Sch.* 1949; 23 (1): 61–63.
53. Davidson TM, Bone RC, Kiessling PJ. Epidermoid carcinoma arising from within an epidermoid Inclusion Cyst. *Ann Otol Rhinol Laryngol.* 1976; 85 (3 pt 1): 417–418.
54. Bauer BS, Lewis VL Jr. Carcinoma arising in sebaceous and epidermoid cysts. *Ann Plast Surg.* 1980; 5 (3): 222–226.
55. Miller JM. Squamous cell carcinoma arising in an epidermal cyst. *Arch Dermatol.* 1981; 117: 683.
56. Yaffe HS. Squamous cell carcinoma arising in an epidermal cyst. *Arch Dermatol.* 1982; 118: 691.
57. Shah LK, Rane SS, Holla VV. A case of squamous cell carcinoma arising in an epidermal cyst. *Indian J Pathol Microbiol.* 1989; 32 (2): 138–140.
58. Davies MS et al. Squamous cell carcinoma arising in a traumatically induced epidermal cyst. *Injury.* 1994; 25 (2): 116–117.
59. Malone JC, Sonnier GB, Hughes AP et al. Poorly differentiated squamous cell carcinoma arising within an epidermoid cyst. *Int J Dermatol.* 1999; 38 (7): 556–558.
60. Cameron DS, Hilsinger Jr RL. Squamous cell carcinoma in an epidermal inclusion cyst: case report. *Otolaryngol Head Neck Surg.* 2003; 129 (1): 141–143.
61. Kume M. Squamous cell carcinoma arising in an epidermal cyst on the sacrum. *Skin Cancer (Japan).* 2004; 19: 112–115.
62. Nemoto I. Aggressive squamous cell carcinoma developing in a giant epidermal cyst of the abdomen. *Int J Dermatol.* 2006; 45, 1446–1447.

63. Shabbir A, Loss L, Bogner P et al. Squamous cell carcinoma developing from an epidermoid cyst of the ear. *Dermatol Surg.* 2011; 37 (5): 700–703.
64. Anastasios K, Alexandra G, Anthony K et al. Malignant transformation in a typical epidermal cutaneous cyst .*J Med Cases.* 2012; 3 (4): 254–256.
65. Sumi Y, Yamamoto N, Kiyosawa T. Squamous cell carcinoma arising in a giant epidermal cyst of the perineum: a case report and literature review. *J Plast Surg Hand Surg.* 2012; 46: 3–4.
66. Sinha P, Lingegowda JB et al. Malignant transformation in sebaceous cyst – a case report. *Int J Med Health Sci.* 2012; 1 (2): 63–65.
67. Skroza N, Proietti I, Tolino E et al. Isotretinoin for the treatment of squamous cell carcinoma arising on an epidermoid cyst. *Dermatol Ther.* 2014; 27 (2): 94–96.
68. Hasegawa Y, Yokota K et al. A case of squamous cell carcinoma occurred in an epidermal cyst on the buttock. *Skin Cancer (Japan).* 2014; 28 (3): 292–296.
69. Fujita R, Takebayashi S, Sekikawa Z et al. A giant pelvic epidermoid cyst with malignant transformation to squamous cell carcinoma. *Edorium J Radiol.* 2015; 1: 1–5.
70. Satoh M et al. Squamous cell carcinoma arising from a presacral epidermoid cyst in an adult. *Jpn J Gastroenterol Surg.* 2015; 48 (2): 145–151.
71. Veenstra JJ, Choudhry S, Krajenta RJ et al. Squamous cell carcinoma originating from cutaneous cysts: the Henry Ford experience and review of the literature. *J Dermatol Treat.* 2016; 27: 1, 95–98.
72. Lee J-W, Shin J-Y, Roh S-G et al. Squamous cell carcinoma arising from an epidermal inclusion cyst. *APS.* 2016; 43: 112–114.
73. Rathna S, Desai KR, Lal Mishra K. Epidermal cyst with malignant transformation: a case report. *J Diagn Pathol Oncol.* 2017; 2 (1): 13–14.
74. Srivastava A et al. Malignant changes in twin epidermoid cysts in neck: a rare case report. *Otolaryngology Online Journal.* 2017; 7 (1): 146.
75. Suzuki M, Hashimoto KA Case of squamous cell carcinoma arising in atheroma of the perineum. *Yamaguchi Medical Journal.* 2017; 66 (1): 37–14.
76. Beers P, Vincek V. Atypical proliferating epidermoid cyst with xanthomatous reaction. *Human Pathology: Case Reports Volume 15*. 2019; 37–40.
77. Kim J-W, Kang C-S, Lee JH et al. Squamous cell carcinoma identified in a thick-walled epidermal cyst with a recurrent ulcer. *Arch Plast Surg.* 2019; 46: 94–95.
78. Wong TH, Khoo AKM, Tan PH et al. Squamous cell carcinoma arising in a cutaneous epidermal cyst – a case report. *Ann Acad Med Singapore.* 2000; 29: 757–759.
79. Debaize S, Gebhart M, Fourrez T et al. Squamous cell carcinoma arising in a giant epidermal cyst: a case report. *Acta Chir Belg.* 2002; 102: 196–198.
80. Kasahara R, Tajiri R, Kobayashi K et al. Squamous cell carcinoma developing from a testicular epidermal cyst: a case report and literature review. *Case Reports in Urology.* 2019; Article ID 9014301.
81. Lopez L, Schoeniger L, Zhou Z. Squamous cell carcinoma arising in a peri-coccygeal – rectal epithelial inclusion cyst with adjacent benign notochordal cell tumor: first case report and review of the literature. *Pathology and Laboratory Medicine International.* 2019; 11: 1–5.
82. Shah A, Aram J et al. Cystic poorly differentiated squamous cell carcinoma of the scalp, a rare scalp tumor: aase report and literature review. *International Journal of Surgery Case Reports.* 2019; 60: 21–24.