

Malignancy Arising in Seborrheic Keratosis: A Report of Two Cases

W M Yap,*^{MBBS, MPath, MRCPATH}, P H Tan,*^{FAMS, MBBS, FRCPA}, B H Ong,**^{MBBS, DCP}

Abstract

We describe the pathological features of two cases of malignant transformation occurring in seborrheic keratosis. The lesions affected elderly individuals: a 79-year-old Chinese lady and a 79-year-old Chinese gentleman, both of whom had long-standing seborrheic keratoses with recent increase in size. Histologically, the malignancies identified were invasive well-differentiated squamous cell carcinoma and Bowen's disease (squamous carcinoma in situ), respectively. Pre-existing seborrheic keratoses demonstrating a zone of transition into the malignant foci were present. Aetiologic factors that have been proposed to explain these exceedingly rare occurrences have included prolonged sun damage and chronic low dose radiation exposure.

Ann Acad Med Singapore 1997; 26:235-7

Key words: *Bowen's disease, Elderly, Malignant transformation, Squamous cell carcinoma, Transition zone*

Introduction

Maligancies arising in seborrheic keratoses are uncommon occurrences.¹ Most cases of malignancy purportedly developing from seborrheic keratosis were based on clinical diagnoses of long-standing skin lesions thought to be seborrheic keratoses in which recent ulceration or rapid growth in size had occurred; and on excision, disclosed a malignant lesion histologically. Most of these cases did not show microscopic evidence of a residual seborrheic keratosis. This has been attributed to the destruction of the seborrheic keratosis by the malignant tumour. Even if the initial benign lesion was present, it was unusual for a zone of transition to be microscopically demonstrated between the malignancy and the seborrheic keratosis. The malignancies reported to be associated with seborrheic keratosis are Bowen's disease, invasive squamous cell carcinoma and basal cell carcinoma.

We wish to document a case of invasive squamous cell carcinoma and a case of Bowen's disease that had developed from long-standing seborrheic keratoses. Residual seborrheic keratoses and the zones of transition are noted in both cases.

Case Reports

Case 1

A 79-year-old Chinese woman had a long-standing skin lesion, clinically a seborrheic keratosis, on the left side of her abdomen. She sought medical attention

because of recent increase in size. An excision biopsy was performed. The macroscopic specimen consisted of a rounded piece of skin measuring 11 cm in the largest dimension, with a central 6.0 × 4.5 cm ulcerated pigmented lesion. Microscopic examination confirmed the presence of an invasive well-differentiated squamous cell carcinoma, with broad anastomosing trabeculae of polygonal cells containing vesicular pleomorphic nuclei, distinct nucleoli and pink cytoplasm. Keratin pearls were seen (Fig. 1). Interestingly, an adjacent acanthotic seborrheic keratosis was present at the edge, demonstrating a transition into the squamous cell carcinoma (Fig. 2).

Case 2

A 75-year-old Chinese man complained of increasing size, ulceration and oozing of a long-standing warty skin lesion on the chest. An excision biopsy was performed. The gross specimen comprised an ellipse of skin measuring 7 × 4 cm with a fungating lesion on the surface that measured 6 × 3 cm. Histologically, there was a squamous cell carcinoma in situ or Bowen's disease, composed of intraepidermal malignant cells with moderate nuclear atypia and ample eosinophilic to clear cytoplasm, affecting the full thickness of the epidermis. Many abnormal mitoses were seen. No invasion into the dermis was detected. The tumour appeared continuous with a hyperkeratotic variant of seborrheic keratoses (Figs. 3 & 4).

* Senior Registrar

** Visiting Consultant

Department of Pathology

Singapore General Hospital

Address for Reprints: Dr Tan Puay Hoon, Department of Pathology, Singapore General Hospital, 1 Hospital Drive, Singapore 169608.

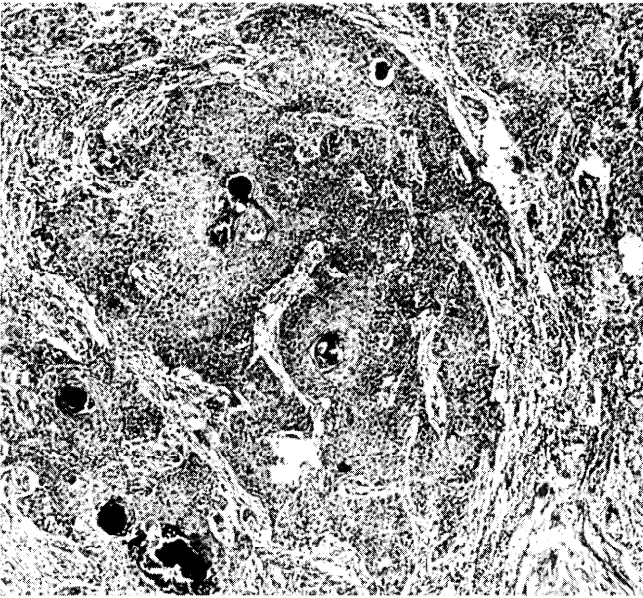


Fig. 1. Invasive well-differentiated squamous cell carcinoma, comprising anastomosing islands of malignant squamous cells with scattered keratin pearls. (Haematoxylin and eosin, x40)

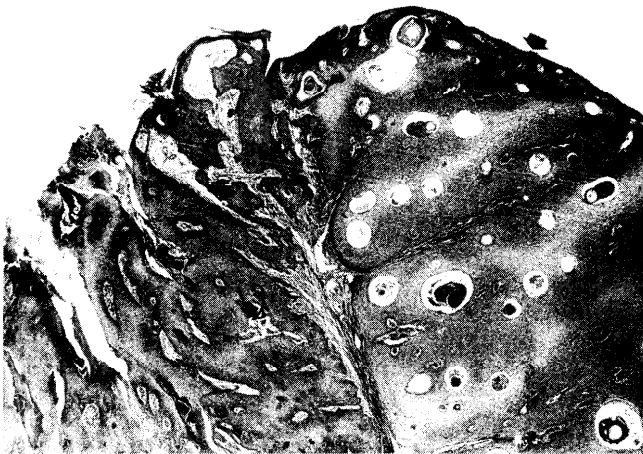


Fig. 2. Acanthotic seborrheic keratosis (arrow) demonstrating a transition into the well-differentiated squamous cell carcinoma. (Haematoxylin and eosin, x20)

Discussion

Seborrheic keratoses are not uncommon lesions and are seen in 20% of middle-aged and elderly persons.² The most common presentation is that of a verrucous cutaneous growth which may be frequently multiple. Internal malignancies are sometimes associated with the sudden appearance of multiple seborrheic keratoses. This uncommon phenomenon constitutes the sign of Leser-Trelat.³ Seborrheic keratoses often occur on the face, arms and upper trunk. Clinically, these may be mistaken for a melanocytic lesion if hyperpigmentation is present.

Histologically, seborrheic keratosis is characterised by proliferation of basaloid cells with some degree of squamous differentiation as evidenced by the presence



Fig. 3. Hyperkeratotic seborrheic keratosis (upper field) with zone of transition into Bowen's disease. (Haematoxylin and eosin, x40)

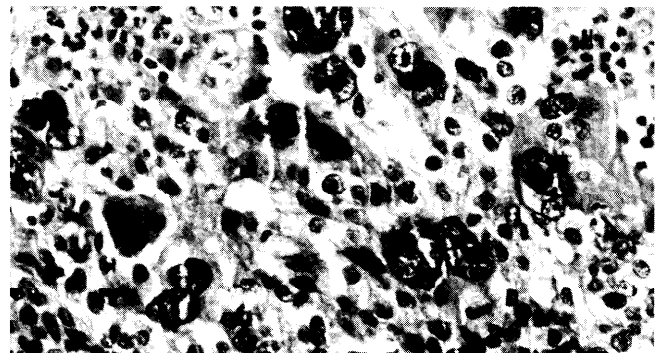


Fig. 4. High magnification of the malignant cells in Bowen's disease, demonstrating pleomorphic nuclei and prominent nucleoli. (Haematoxylin and eosin, x400)

of horn cysts. Hyperkeratosis, acanthosis and papillomatosis are generally present. A mononuclear inflammatory infiltrate is frequently present in the underlying dermis. There are several variants of seborrheic keratoses, including the hyperkeratotic, adenoid, acanthotic, reticulated and clonal variants, as well as the irritated seborrheic wart and melanoacanthoma.

The irritated form of seborrheic keratoses is characterised by numerous squamous eddies which may resemble the keratin pearls of a well-differentiated squamous cell carcinoma. However, squamous eddies are smaller, more numerous and circumscribed, compared to the keratinised foci of a well-differentiated squamous cell carcinoma.⁴

The clonal variant of seborrheic keratoses may resemble basal cell carcinoma and Bowen's disease. In this variant, well-defined nests of cells are present in the epidermis, disclosing small and dark staining nuclei resembling those found in basal cell carcinoma, erroneously referred to as the intraepidermal epithelioma of Borst-Jadassohn.⁴ The epidermal nests may also resemble that seen in Bowen's disease although in the latter, the cells have more nuclear atypia and cytoplasmic contents with occasional mitoses.

Of the different variants, the acanthotic pattern has been associated with bowenoid transformation.⁴

Malignancies arising in seborrheic keratoses are uncommon events. In a prospective study of 4310 cases clinically diagnosed as seborrheic keratoses, 60 (1.4%) were found to be squamous cell carcinoma in situ histologically.⁵ The authors concluded that seborrheic keratoses located in the head and neck regions of the elderly were more frequently associated with malignant transformation, possibly related to cumulative solar damage. No mention, however, was made of whether histological evidence of residual seborrheic keratosis was noted.

Of Kwittken's series of 19 cases of seborrheic keratoses with malignant change, 14 showed squamous cell carcinoma in situ, while 5 were basal cell carcinomas.⁶ A similar predilection for the head and neck region of the elderly was found. Almost all of the basal cell carcinomas in his series arose from seborrheic keratoses with a predominant acanthotic pattern, while most of the cases of carcinoma-in-situ developed within the hyperkeratotic variant. Solar elastosis, a measure of sun damage, was seen in 45% of his cases.

Bloch's case of seborrheic keratosis which transformed into Bowen's disease showed a transitional zone. He held that transformation to Bowen's disease from seborrheic keratosis could not be deduced solely from their topical relationship. The proof of transformation lay in the presence of a transitional zone between the benign lesion and the malignancy. As such, he believed that malignant transformation in seborrheic keratosis might be over-reported as there was not enough documentation to allow a firm diagnosis of transformation. Pseudobasalomatous hyperplasia^{7,8} or pseudoepitheliomatous hyperplasia of seborrheic keratoses could be mistaken for malignant change. Nevertheless, he recognised that a transitional zone might not be readily observed in late lesions.

Suvarna⁹ reported a case of squamous cell carcinoma arising within a seborrheic keratosis in a patient who had received occupational exposure to radiation. In this case, it was postulated that the malignant transformation was linked aetiologically to the chronic low dose radiation received. In another case described by Kwittken, the invasive squamous cell carcinoma arose from a seborrheic keratosis present on the forearm of a 76-year-old man.¹⁰ No aetiological factor was discussed.

In our two cases, histological transition from the benign component of the seborrheic keratoses to malignant lesions was detected. Both patients had no history of occupational exposure to radiation. Although prolonged sun damage might be cited as a possible trigger

for malignant transformation in the chest lesion of case 2, it is less clear what are the likely aetiological factors involved in the malignant change of the abdominal seborrheic keratosis in case 1.

Conclusion

Cases of malignancies arising in seborrheic keratoses have been reported although histological proof of transition between the benign and malignant components is exceedingly rare. Most are clinically diagnosed seborrheic keratoses in which a malignancy is observed microscopically. This is believed to be due to the destruction of the pre-existing seborrheic keratosis by the malignancy. Our two cases showed histological transformation of seborrheic keratoses into a well-differentiated squamous cell carcinoma and Bowen's disease respectively, adding to the increasing evidence that seborrheic keratoses may, in rare instances, undergo malignant change after a long period of time^{1,2,6,8-15}

REFERENCES

1. Bloch P H. Transformation of seborrheic keratosis into Bowen's disease. *J Cutan Pathol* 1978; 5:361-7.
2. Baer R L, Garcia R L, Partsalidou V, Ackerman A B. Papillated squamous cell carcinoma in situ arising in a seborrheic keratosis. *J Am Acad Dermatol* 1981; 5:561-5.
3. Holdiness M R. The sign of Leser-Trelat. *Int J Dermatol* 1986; 25:564-72.
4. Lever W F, Schaumburg-Lever G. Tumours and cysts of the epidermis. In: Lever W F, Schaumburg-Lever G, editors. *Histopathology of the Skin*. Philadelphia: JB Lippincott Co, 1990:528-32.
5. Sloan J B, Jaworsky C. Clinical misdiagnosis of squamous cell carcinoma in situ as seborrheic keratosis. A prospective study. *J Dermatol Surg Oncol* 1993; 19:413-6.
6. Kwittken J. Malignant changes in seborrheic keratosis. *Mt Sinai J Med* 1974; 41:792-801.
7. Gottron H A. Karzinomentwicklungen in der Haut. *Deutsche medizinische Wochenschrift* 1957; 82:761-4.
8. Braun-Falco O. Zur Frage der Entartung von Verrucae seborrhoicae seniles. *Hautarzt* 1964; 15:645-50.
9. Suvarna S K. Radiation-induced squamous carcinoma arising within a seborrheic keratosis. *Br J Dermatol* 1993; 128:443-7.
10. Kwittken J. Squamous cell carcinoma arising in seborrheic keratosis. *Mt Sinai J Med* 1981; 48:61-2.
11. Monteagudo J C, Jorda E, Terencio C, Llombart-Bosch A. Squamous cell carcinoma in situ (Bowen's disease) arising in seborrheic keratosis: three lesions in two patients. *J Cutan Pathol* 1989; 16:348-52.
12. Rahbari H. Bowenoid transformation of seborrheic verrucae (keratoses). *Br J Dermatol* 1979; 101:459-63.
13. Civatte J. Un cas de verrue seborrhoique cancerisee. *Bull Acad Natl Med* 1954; 138:30-1.
14. Marshall S F, Ronan S G, Massa M C. Pigmented Bowen's disease arising from pigmented seborrheic keratoses. *J Am Acad Dermatol* 1990; 23:440-4.
15. Cascajo C D, Reichel M, Sanchez J L. Malignant neoplasms associated with seborrheic keratoses. *Am J Dermatopathol* 1996; 18:278-82.