

MOLLUSCUM SEBACEUM (KERATO-ACANTHOMA)

ITS AETIOLOGY AND RELATIONSHIP TO EARLY SQUAMOUS CARCINOMA, WHETHER SELF-HEALING OR NOT

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In the last decade considerable interest has been directed at a lesion of the skin variously called molluscum sebaceum or kerato-acanthoma or even self-healing squamous carcinoma of the skin. This condition resembles squamous carcinoma histologically, but may resolve spontaneously—which no other malignant tumour has been known to do. In fact, references to such a skin lesion have been noted for a much longer period, although attention to the condition was less general. Smith¹ described a case of multiple, primary, squamous-cell carcinoma of the skin in a young man, with spontaneous healing. This patient from the age of 16 had multiple papular lesions on legs, thighs, face and ears. Most of the lesions lasted approximately 6 months from start to finish, but many for longer periods. The lesions were described as papules about the size of a millet grain with great down-growth of epidermis with a central horny plug. They exhibited a whorled structure. Many epithelial cells penetrated the tissue spaces. The author considered 2 out of 5 such growths as active and malignant. These sections were seen by such eminent histopathologists as the late Professors Sir Robert Muir and J. Shaw Dunn who were unanimous about the histological malignancy.

These lesions generally healed spontaneously, but ultimately the patient refused further medical help and returned only after many years, when Smith² reported that in some of the untreated lesions extensive soft-tissue destruction occurred necessitating the wearing of a prosthesis of nose. McCormack and Scarff³ reported a series of 10 cases having similar, but not identical, features. Their cases show:

1. A small hemispherical nodule, 2.5 cm. in diameter, with an adherent scale of the crown.
2. A history of development over a period of 4-6 weeks.
3. There was never more than one lesion present.
4. The lesions were found on the middle area of face or nose.
5. The tumour was usually firm with occasional central degeneration.
6. All patients were over 60 years of age.
7. The sexes were equally affected.

The histological appearance was of a cystic structure generally similar to the lesions in Smith's case. McCormack and Scarff³ thought the lesions were due to hypertrophic

changes in a sebaceous cyst, and called the lesion molluscum sebaceum.

Somerville and Milne⁴ described a further case of multiple, familial, primary, self-healing squamous carcinoma of the skin. They stressed the familial incidence of this multiple lesion condition and emphasized the impossibility of early histological diagnosis. While the lesions healed in their patients, these authors considered that there was no histological distinction from early squamous carcinoma.

Grzybowski⁵ described a case with hundreds of papules, histologically squamous carcinoma, but self-healing. Each papule had a life history of 4-8 months. He suggested an infectious aetiology, but was unable to reproduce the tumour by inoculating scarified rabbits.

Musso⁶ gave a lucid account of the characteristic clinical history and histological appearance of molluscum sebaceum. This patient was a woman of 52 with an 11-week history of a red, painless pimple the size of a pin head, on the right side of the neck. It enlarged over 6 weeks to become an umbilicated mass with a keratotic centre and a hard, rolled edge. It then shrank to a small lesion, 0.3 cm. in diameter, and then fell off. His description of the histology is as follows:

'On section epidermis is intact and except for one tiny area of union is separated from the lesion by a small band of connective tissue. Essentially there is a central mass of hyperkeratosis and papillomatosis surrounded by epithelium which for the greater part consists of an acanthotic stratum malpighii with slight atypicality of the cells.

'In places the basal layer is missing and in parts the epidermal border of the acanthotic stratum malpighii is being disintegrated and invaded by round cells and at times eosinophils. The corium on the sides and deep aspects of the lesion is oedematous together with an infiltrate of inflammatory round cells and some eosinophils.'

Gordon⁷ stated that he had a number of similar cases, diagnosed by R. A. Willis as squamous carcinomata, and said it seemed there was not general pathological agreement that molluscum sebaceum could be differentiated from squamous carcinoma.

Charteris⁸ reported another case of multiple self-healing squamous carcinomata of forearms and face having the

general histological structure of a tumour of definite malignancy. He suggested that this is a true neoplastic condition in which the mechanisms of the body succeed in overcoming the lesion.

Witten and Zak⁹ suggested that the multiple self-healing squamous carcinomata took origin from hair follicles.

Beare¹⁰ pointed out that although molluscum sebaceum is commonly situated on the face, the ears, neck, forearms and buttocks may occasionally be affected. He maintains that the diagnosis can readily be made clinically and histologically, but insists that a biopsy should be done in all cases. He then goes on to state that the best treatment, where the clinical diagnosis is reasonably certain, is cutting off the tumour flush with the surface of skin and not excision. He draws attention to the fact that molluscum sebaceum is a very common tumour. In contradistinction to McCormack and Scarff² he found cases at ages from 23 to 83, although the average was 55 years. Beare¹⁰ suggested as the possible aetiology:

1. Hypertrophy and inflammation of a sebaceous cyst, or

2. A virus. The arguments against this cause are (a) that there is no positive proof, (b) the lesions are usually single, and (c) no transference of lesion has been noted. Beare¹⁰ disagrees with Fouracres and Whittick,¹¹ who maintain that molluscum sebaceum and 'self-healing' squamous carcinoma are similar conditions. These latter authors argue that the lesions are closely similar histologically and that there is no acceptable record of spontaneous regression of a squamous carcinoma of the skin. Beare¹⁰, on the other hand, rightly points out the multiplicity of lesions and family history in case of 'self-healing' squamous carcinoma of skin. In this connection it is relevant to recall Smith.² In his case, which was of undoubted multiple squamous carcinomata, some of the carcinomata were self-healing and some were progressively destructive. Fouracres and Whittick¹¹ say that with adequate size of biopsy and an experienced pathologist the diagnosis can be made from early squamous carcinoma, particularly in association with typical clinical appearance and a history of rapid growth over a period of 4-8 weeks. They say that the size and rate of growth would mean lymphatic involvement if it were really due to carcinoma. Willis¹² takes a different view stating that 'distinction of molluscum sebaceum from true squamous carcinoma is often difficult or impossible on purely histological grounds'.

Lever¹³ categorically maintained that the histological appearance is of a grade 1 well-differentiated, keratinizing squamous carcinoma.

CLINICAL AND HISTOLOGICAL EVALUATION OF A SERIES OF CASES

The patients examined were accumulated over a period of 3 years in a private pathological practice having in addition consultant appointments to South African Railways (employees and families) and to Provincial Hospitals. All patients seen were Europeans. When a patient with clinical or histological features suggestive of molluscum sebaceum was studied, further information was sought (if not already available) regarding the age of patient, his or her sex, the length of the history, the family history or history of a similar lesion, and whether the lesion was single or multiple.

Generally this information was obtained, but in a few cases further information could not be obtained, e.g. from patients who were many hundreds of miles away, casual patients with whom contact had been lost by practitioner or surgeon, etc. During the histological study points particularly looked for were:

1. Whether marked basophilic degeneration of upper dermal collagen was present thus suggesting, particularly in the younger age-groups, undue exposure to sunlight.

2. Whether a clear histological distinction between molluscum sebaceum and early squamous carcinoma could be made. This was correlated with a clinical assessment of the case.

3. A search was made for intracellular inclusions which might indicate an infectious aetiology. (No such inclusions were found.)

The condition was accepted basically as described by McCormack and Scarff² and by Musso.⁶ My own histological description of a classical molluscum sebaceum, as seen in this series, is thus:

The lesion is generally flask-shaped (Fig. 1), with a central keratinous core. The walls of the flask are proliferating, convoluted, squamous epithelium. The overall shape of the lesion tends to be round, particularly the base of the lesion, whereas a squamous carcinoma, no matter how well differentiated, tends to have a flattish growing margin. Mitotic figures are usually not frequent, but 1-2 per high-power field may be noted (Fig. 2). More than this excites suspicion of definite carcinoma. Dyskeratosis at advancing edge of tumour is likewise a sign suspicious of carcinoma (Fig. 3). There is usually an exudate of round cells and occasional eosinophils in the dermis. Upper dermal collagen, as found in this series, shows basophilic degeneration. One point to be remembered is that the 'flask'-shaped appearance of the condition will vary

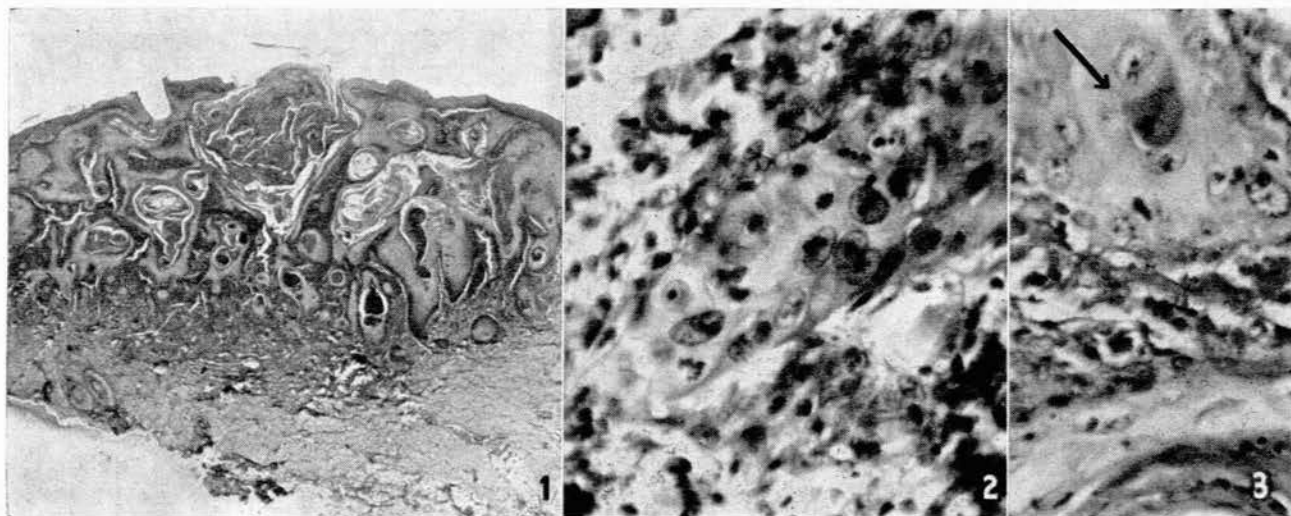


Fig. 1. Clinical molluscum with a 4-week history. 'Roundness' moderately well marked. Note keratinous core and convoluted edge.

Fig. 2. Mitotic figures and nuclear irregularity at growing edge of lesion.

Fig. 3. This was a definite squamous carcinoma which closely resembled molluscum sebaceum in many respects. The arrow points to dyskeratosis at growing edge.

TABLE I. CASE ANALYSIS

Case	Age	Sex	Site of lesion	Length of history	Previous similar lesion	Similar lesion in family	Basophilic degeneration of dermal collagen	Purely histological distinction from squamous carcinoma	Combined clinical and histological distinction from squamous carcinoma
1.	35	F	Face	8 weeks	None	None	Moderate	Certain	Certain
2.	49	M	Nose	2 weeks	None	None	Marked	Impossible	Probable
3.	64	M	Temple	8 weeks	None	None	Slight	Probable	Probable
4.	79	M	Nose	28 weeks	None	None	Marked	Probable	Probable
5.	34	F	Nose	4 weeks	None	None	Marked	Certain	Certain
6.	65	M	Dorsum of hand	12 weeks	Yes	None	Marked	Probable	Probable
7.	75	F	Dorsum of hand	30 weeks	None	None	Moderate	Probable	Possible
8.	58	M	Back of neck	4 weeks	None	None	Marked	Probable	Probable
9.	22	F	Forehead	4 weeks	None	None	None	Probable	Certain
10.	40	M	Dorsum of hand	52 weeks	None	None	Marked	Certain	Probable
11.	40	M	Face	8 weeks	None	None	Moderate	Probable	Probable
12.	38	M	Neck	12 weeks	None	None	Moderate	Certain	Certain
13.	62	F	Cheek	2 weeks	None	None	Marked	Certain	Certain
14.	42	M	Neck	10 weeks	Yes	None	Moderate	Certain	Certain
15.	50	M	Pinna of ear	6 weeks	None	None	Marked	Probable	Certain
16.	56	M	Cheek	32 weeks	Yes	None	Marked	Probable	Possible
17.	45	M	Face	3 weeks	None	None	Marked	Probable	Certain

The following cases have incomplete clinical information

18.	—	M	Ear	—	—	—	Marked	Probable	Probable
19.	—	M	Dorsum of hand	—	None	—	Marked	Probable	—
20.	—	M	Face	—	None	—	Marked	Certain	Certain
21.	60+	M	—	—	—	—	Marked	Certain	—
22.	—	M	Neck	—	—	—	Marked	Probable	—

Definite squamous carcinoma closely resembling molluscum sebaceum

23.	52	M	Dorsum of hand	24 weeks	Yes	Yes	Marked	Squamous carcinoma	Squamous carcinoma
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according to the age of the lesion and the plane of section—the central keratinous plug being less conspicuous in some sections.

The main results of the clinical and histological study are seen in Table I.

Case 10 was of particular interest in so far as the history was very long (52 weeks), but the histological features were typical of molluscum and there was no cytological irregularity to indicate squamous carcinoma. This case was regarded as probably a regressing molluscum sebaceum.

Case 18, histologically, could be a molluscum sebaceum or a well-differentiated squamous carcinoma of sebaceous duct. This case stimulated the speculation that some of the healing cases may be well-differentiated squamous carcinomata of sebaceous ducts where the growth, together with a collar of chronic inflammatory exudate, sloughs off through the dilated duct, and the whole area heals. In other instances this may not occur and squamous carcinoma persists.

As can be seen from Table I, only in a proportion of cases could histological diagnosis of molluscum sebaceum be certainly made. Even considering the clinical features there was a substantial number of suspected cases where the diagnosis remained in doubt. This would obviously lead one to recommend excision of the lesion and not slicing off the top as recommended by Bear.¹⁰

It is interesting to note that since this investigation was completed, another case was seen very recently of a man of 38 with a typical molluscum sebaceum on his upper lip for 3-4 weeks. Biopsy showed a lesion which was molluscum sebaceum in many respects, but squamous epithelium was undoubtedly present between bundles of striated muscle. There was therefore no option but to regard this case as a squamous carcinoma, because although it might have resolved in a month or two, if it was in fact a squamous carcinoma growing so fast, by that time it would be in regional lymph nodes. (Similar features were noted in Case 2 where squamous

epithelium was seen between bundles of collagen in subcutaneous region.)

DISCUSSION

1. In this series the average age incidence of 50 and the peak incidence in the 5th decade is lower than in the series of

TABLE II. INFLUENCE OF SUNLIGHT IN CAUSATION*

	Number of cases	%
(1) Male	17	77
Female	5	23
Total	22	100
(2) Basophilic degeneration of dermal collagen present	21	95
Not present	1	5
Total	22	100
(3) Type of male patient:		
Railwayman	13	76
Private	3	17
Hospital	1	7
Total	17	100
(4) Site of lesion exposed to sunlight?		
Yes	21	100
No	0	0
Total	21	100

*As seen in (1) Sex distribution, (2) basophilic degeneration of dermal collagen, (3) probable outdoor occupation of male patients (in this connection it is worthy of note that the number of private surgical pathological specimens received during the period of this investigation was between 2 and 3 times as many as railway surgical pathology specimens. Yet the number of railway patients with this condition is 4 times as many—which is a probable difference in incidence of approximately tenfold. Amongst railway workers there is obviously a large number of outdoor workers), and (4) site of lesion exposed to sunlight?

McCormack and Scarff³ where all cases were over 60. Beare¹⁰ had an average age incidence of 55. This feature may be due to the influence of sunlight in South Africa as compared with the two British series.

2. The lesions in this series were not confined to the face, but, as seen in Table I, occurred also on ear, neck and dorsum of hand—sites also exposed to sunlight.

3. It seems that there is considerable evidence, on the basis of this investigation, that molluscum sebaceum can be caused or precipitated by sunlight, namely:

(i) Basophilic degeneration of the upper dermal collagen was present in every case.

(ii) The condition occurs in men more than women (Table II). This finding differs from that of McCormack and Scarff³ who found an equal distribution between the sexes in Britain.

(iii) The lesion occurs approximately 10 times as frequently in white railwaymen as in white private patients. Railwaymen generally are outdoor workers, and private patients are usually employed indoors.

(iv) All the lesions in this investigation occurred in sites exposed to sunlight (Tables I and II).

(v) All cases were of the white or non-pigmented racial group.

4. It is speculatively suggested that some cases of molluscum sebaceum may arise as slowly growing, well-differentiated squamous carcinomata of sebaceous ducts, that the duct dilates, and that finally the carcinoma, together possibly with a collar of chronic inflammatory exudate, is sloughed off and the area heals. Where this sloughing fails to occur or is incomplete, squamous carcinoma persists.

5. Molluscum sebaceum must be clearly distinguished from familial, multiple, 'self-healing', squamous carcinoma as described by Smith,^{1,2} Somerville and Milne,⁴ and Charteris:⁵

(a) Family history is entirely absent in the present series.

(b) None of the lesions was multiple. Where more than one had occurred they were not concurrent (3 cases, Table I).

(c) Molluscum sebaceum is a common condition, particularly in South Africa where, in my own experience, it occurs more frequently than was found in Scotland. Multiple, 'self-healing', squamous carcinoma on the other hand is a rare disease. 'Self-healing' in reference to this latter condition is

something of a misnomer, since it appears that some of the lesions are self-healing and some progressively destructive.² In this connection support must be given to Beare¹⁰ who maintains that molluscum sebaceum is distinct from multiple, 'self-healing', squamous carcinoma, in contradistinction to Fouracres and Whittick¹¹ who fail to make this distinction.

The case of Grzybowski⁵ is of obscure nature and is possibly neither a molluscum sebaceum nor a typical multiple squamous carcinoma.

6. The difficulty of certain histological diagnosis, even in conjunction with clinical information, must be emphasized. Beare¹⁰ correctly maintains that clinical diagnosis of the condition is more reliable than histological diagnosis.

In my 22 patients certain histological diagnosis was made in only 8. In a further 2 clinical information confirmed the diagnosis by reason of young age or very short history. It is clear, however, that despite considerable study of this condition, the diagnosis cannot be made with sufficient assurance in enough cases to justify treatment other than by complete excision. Willis, Muir, Shaw-Dunn and Lever have all diagnosed this type of lesion as well-differentiated squamous carcinoma. Beare's advice to cut the lesion off flush with the skin is regarded as unsound. These lesions should always be completely excised.

My thanks are due to the many general practitioners, dermatologists and surgeons of the Cape Province and Cape Town who so helpfully assisted this work by allowing their cases to be quoted and by providing clinical advice.

The microphotographs were taken in the Department of Surgery, University of Cape Town by the courtesy of Prof. J. H. Louw.

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