WARTY DYSKERATOMA
A review of clinicopathological features, nature, morphogenesis, classification & nomenclature

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Summary

Warty dyskeratoma is an interesting cutaneous tumour due to its striking histopathology with an uncharacteristic clinical feature. Though a few large series of cases are reported in Western literature, the tumour is probably very rare in India. Its exact nature and morphogenesis has not been clarified and the tumour has not been classified properly. The present paper is a review of the up-to-date knowledge regarding the tumour and an attempt to suggest its origin, nature, morphogenesis, a plausible classification and a more explicit nomenclature.

Introduction

Warty dyskeratoma[1] was defined as a rare cutaneous tumour of unknown etiology arising from a solitary pilosebaceous follicle, located usually in the head of an elderly patient, the clinical character of which was not distinctive but the histopathology characteristic and diagnostic and comparable to hypertrophic lesions of Darier's disease.

Darier's type of dyskeratosis in a solitary isolated lesion, without any stigmata of the disease in the patient or in the family, was documented by earlier observers[2,3], but Szymanski[1] called it a separate entity for the first time and coined the new term Warty dyskeratoma. Graham and Helwig[4] in their excellent review and study of 50 cases, claimed an earlier report by Helwig[5] and contradicted Szymanski's view regarding the neoplastic nature of the lesion and preferred the nomenclature 'Isolated Dyskeratosis Follicularis'. This was supported by Nikolowski[6]. Jablonska and Chorzelski[7,8] in their papers on neoplasms characterized by acantholysis of Darier's type, recognized two types of dyskeratotic tumours, benign dyskeratoma and malignant epithelioma dyskeratoticum segregans. Tanay and Mehregan[9] in a review of 80 cases from the literature and 32 of their own, presented the clinical and histopathological features of the tumour and affirmed it as a distinct entity. Besides these reports, other published data[10,11,12] are only a few. Panja[13] reported an unusual case, which has probably been the only one reported from India, as evidenced from the literature.

Clinical Features

It is interesting to note that the disease, though not uncommon in the Western countries, is probably extremely rare in India[13]. It is, however, possible that small asymptomatic solitary keratotic lesions in the aged are missed by clinicians.

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As most of the lesions so far reported were of very small size, no detailed clinical description of the disease was available. The findings from large reports[1,4,9] are summarised in Table I.

TABLE 1

Clinical Features of Warty Dyskeratoma	
Look :	elevated papule or nodule with an umbilicated porelike crusty keratotic centre.
Site :	skin of head and neck.
Size :	3-8 mm in diameter 2-3 mm elevated from the surface.
Colour :	variable - commonly flesh.
Border :	raised & rolled, sometimes heavily pigmented.
Base :	slightly indurated.
Symptoms :	practically asymptomatic.
Duration :	a month to several years.
Rate of growth :	slow.
Age group :	5th decade (22-60)
Sex :	males more commonly.
Family history of Darier's disease :	nil.

Some patients may present with atypical features. The size of the lesion may be up to 1 cm[9] or rarely very large upto 3 cm[13]. Occasional sites may be chest[1], inguinal region[9] or even dorsum of a toe[13], indicating that warty dyskeratoma, though commonly a tumour of the skin of head, may arise from anywhere except palms and soles[13] unless it affected an ectopic pilosebaceous follicle[14].

Pain and tenderness had been reported by some of the previously reported cases and were ascribed to the presence of small nerves in relation to the connective tissue sheath[4].

One strikingly interesting point was that though a host of clinical diagnoses was offered for the lesions[1,4] (Table 2), none of the cases except two (pimple, folliculitis) were diagnosed clinically as 'follicular'. While dealing with a solitary keratotic tumour, unless one thinks of warty dyskeratoma, it is most likely to be misdiagnosed as one of the more common keratotic, inflammatory neoplastic or nevoid lesions.

TABLE 2

Warty Dyskeratoma Clinical Differential Diagnosis		
Wart	...	Senile Keratosis
Seborrhoeic Keratosis	...	Senile keratosis with malignant change
Sebaceous cyst	...	Basal cell carcinoma
Senile sebaceous adenoma	...	Epithelioma
Pimple	...	Squamous cell carcinoma
Folliculitis	...	Mole

Histopathology

The three fundamental histopathologic changes of warty dyskeratoma are its follicular origin and a striking combination of a 'lytic' and a 'hyperplastic' process, namely, benign acantholytic dyskeratosis and hyperplasia of the follicular epithelium respectively[13]. (Fig. 1 Page No. 7).

The follicular origin is demonstrable by the linkage with sebaceous gland[4] in smaller lesions. In large lesions evidences of normal pilosebaceous elements disappear[9,13] though, presence of glycogen in the tumour epithelia[4,13] confirms the site of morbid change.

Various gradations of suprabasal separation with formation of chords of basal cells and acantholytic dyskeratosis of overlying epithelium is the primary change[13] as seen even in the smallest of tumours[1,4,9]. Consequent proliferative process of the rete ridges results in the formation of lacunae and villi, making the histopathology distinctive and fascinating (Fig. 2 Page No. 7).

Epithelial hyperplasia depends on the size of the tumour. While in smaller tumours 'lytic' reaction was prominent resulting in cystic change[4], in older and larger tumours the hyperplasia may even be pseudoepitheliomatous[9,13]. In some rete pegs the intercellular bridges are maintained while in others there are variable degrees of acantholysis and dyskeratosis (Fig. 3 Page No. 8). The dyskeratotic process continues and becomes more prominent with differentiation of the cells and as a result the superficial keratinising cells assume the form of corps ronds sometimes in very large numbers[13] (Fig. 3 Page No. 8). The hyperplasia of the malpighian layer is undoubtedly tumourous but consistently benign though Jablonska & Chorzelski[8] found gradations of benign and malignant dyskeratosis and suggested a passable transition.

The dermis shows a mild to moderate chronic nonspecific inflammatory infiltrate[1,4,9] with some degree of proliferation of capillaries[13].

Histochemistry

The reticulin fibres at the dermo-epidermal junction show irregular condensation at the papillary dermal prolongations inside the tumour with more or less maintenance of the brush border pattern[4,13]. The elastica at the dermal epidermal junction was fragmented and occasionally some torn fibrils would be seen in the connective tissue core of the substance of the tumour[13] comparable to that in keratoacanthoma[16]. The elastica of deeper dermis might also show collection of fragmented fibrils as in Pseudoxanthoma[13].

Diastase-labile PAS reaction of the tumour cells (Fig. 4 Page No. 8) showed presence of glycogen[4,13], while intense diastase resistant reaction of the basement zone[13] corroborated by positive alcian blue (pH 2) staining suggested presence of mucopolysaccharides. PAS reaction was mild or absent in cystic lesions with predominant 'lytic' reaction but was very prominant in hyperplastic lesions[13]. Amyloid was absent[4,13].

Marked intracytoplasmic pyroninophilia indicated the possibility of viral particles[1,4] or the presence of immature dyskeratin[13]. Similarly intranuclear Fuelgen positive bodies suggested presence of virus[1], or just nuclear fragments in the dyskeratotic cells[13].

Differential Diagnosis

Keeping in mind the probability of Warty Dyskeratoma for any solitary keratotic tumour and a close and careful look at the characteristic histopathological changes will give a correct clinico-pathological diagnosis.

The features of gross acanthosis, occasional pseudohorn-pearl formation, dyskeratosis, acantholysis, suprabasal separation and villi formation would be the points of similarity and/or differentiation from diseases listed under differential diagnosis (Table III), which was brilliantly discussed in detail by Szymanski (1957) and Graham & Helwig (1958). Errors in histopathologic diagnosis (Table III) can be avoided by close and careful look at the characteristic histopathological changes in the light of clinical features.

Nature of Warty Dyskeratoma

The different theories in literature regarding the nature of warty dyskeratoma are critically reviewed.

Though histologically indistinguishable, the strictly follicular, isolated and organized nature of the lesion without any genetic background and stigmata like punctate keratosis and nail changes, should negate its linkage with *Darier's disease*, contrary to the suggestion of some authors[1,5,6,22].

TABLE 3

Warty Dyskeratoma

Histological differential diagnosis	Errors in histological diagnosis
Keratosis Follicularis	Basal cell carcinoma
Isolated Darier's Disease	Trichoepithelioma
Senile keratosis	Adnexal carcinoma
Syringocystadenoma papilliferum	Hidradenoma papilliferum
Familial benign chronic pemphigus	Epidermoid cyst
Keratoacanthoma	Spiradenoma
Adenoacanthoma	Apocrine gland adenoma
Squamous cell carcinoma	Unclassified carcinoma
	Nevus
	Folliculitis
	Chronic dermatitis
	Molluscum contagiosum

That the morbid change might be initiated by a folliculotrophic virus, as suggested by histological findings[4], might be antagonized by lack of cultural evidence in any of the reported cases and spontaneous regression.

The hypothesis that the lesion could be *secondary to some underlying dermal pathology*, as suggested by the finding of papular or nodular lesions showing focal keratosis follicularis overlying a variety of dermal pathological conditions[18], would not be substantiated because of the insignificant dermal changes in comparison to the profound pathology in the affected hair follicle in warty dyskeratoma.

The contention that this condition is a form of *deep seated solar keratosis*[7,10] on the evidences of its location on exposed sites, suprabasal separation, dyskeratosis and certain histological similarities to senile keratosis[16] might be contradicted by the limitation of lesion to hair follicles[4], absence of malignant change[1,4,6,9] and occasional involvement of nonexposed sites[1,12]. In senile keratosis, the hair follicles remain unaffected[17] and the dyskeratosis is of a potentially malignant nature. Tanay & Mehregan[9] also held the view that warty dyskeratoma was unrelated to solar keratosis.

Lever (1967)[21] classified the lesion as a *precancerous tumour of the surface epidermis*. While the tumour arises undoubtedly from the hair follicle[4] it has never been reported to undergo malignant transformation[1,9] and therefore such classification would face criticism.

The points are strongly in favour of the lesion being a *benign tumour*[1,8,9] *of the hair follicle*, as suggested by its follicular origin[4], solitary organoid character[1,13], recurrence after incomplete removal[1], absence of spontaneous resolution[1,4,9] and histological features of hyperplasia and acantholytic dyskeratosis without any acquired or genetic cause[13].

Histologically the smaller lesions are almost indistinguishable from Darier's disease or sometimes familial benign chronic pemphigus but a clinical correlation helps to differentiate them. The larger lesions on the other hand, had many points of similarities with keratoacanthoma[13] (Table IV). However, the two could be distinguished by acantholytic dyskeratosis in warty dyskeratoma and pseudomalignant non-acantholytic dyskeratosis as well as the unique behaviour of autoimmune spontaneous resolution[24] in kertoacanthoma.

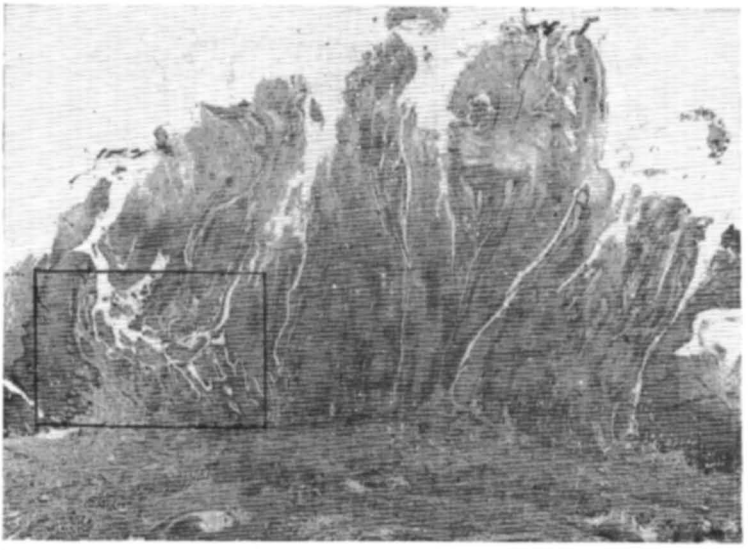

Fig. 1 Low power scanner view along the whole breadth of the tumour and surrounding skin showing pseudoepitheliomatous hyperplasia resembling keratoacanthoma with the added feature of suprabasal separation and villi and lacunae formation (Box) (H & E × 6)

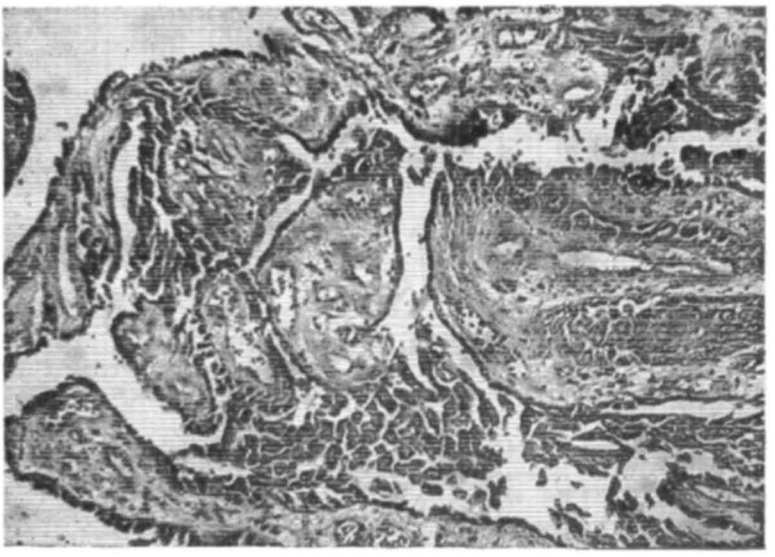

Fig. 2 Acantholytic cells among villi lined by single layer of basal cells (H & E × 240)

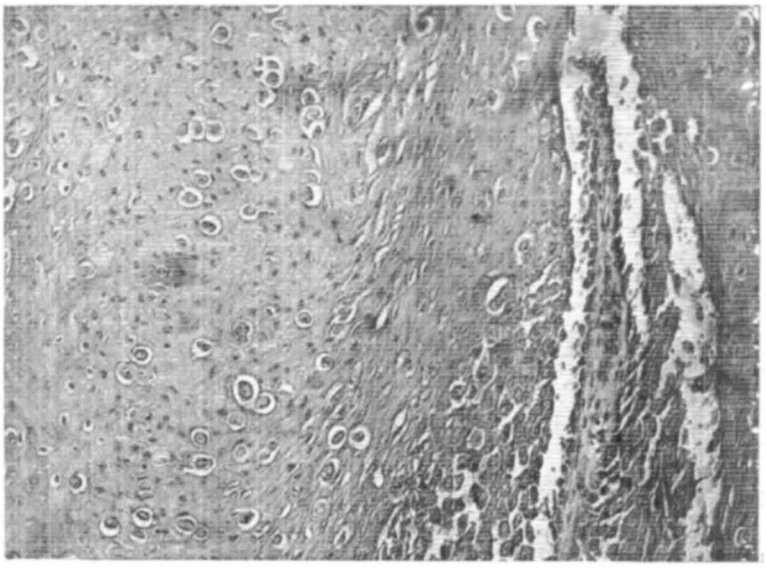

Fig. 3 Massive benign dyskeratosis resembling corps ronds in an acanthotic column separated from a chord of basal cells by some acantholytic cells. (H & E × 240).

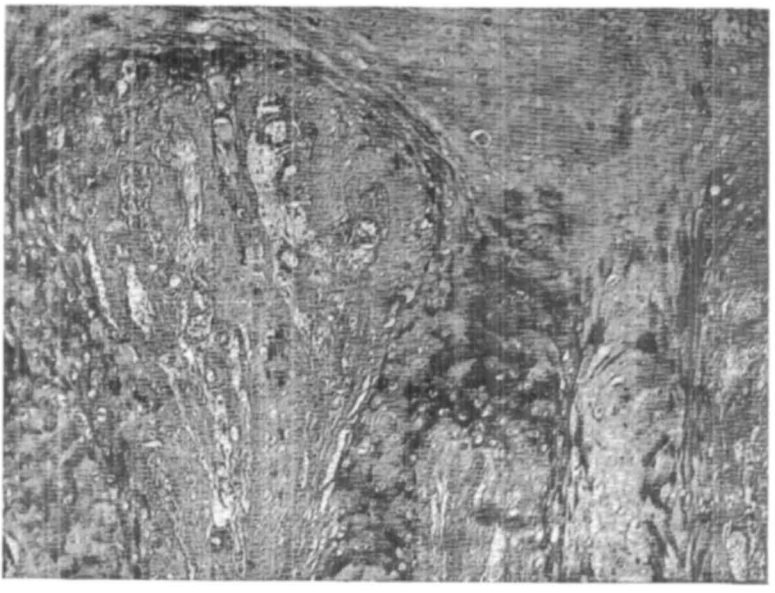

Fig. 4 PAS positive cells of the tumour. The reaction was diastase-labile indicating presence of glycogen and follicular origin (MacManus Lillie × 240)

TABLE 4

Solitary Keratoacanthoma and Warty Dyskeratoma

SIMILARITIES

A. CLINICAL :

1. Elderly Age
2. Common Site Head
3. Solitary Lesion
4. Keratotic Centre
5. No Genetic Factor
6. No Malignant Change

B. HISTOLOGY :

1. Follicular Origin (4,13,20)
2. Tumourous Nature (1,8,9,13,20)
3. Pseudoepitheliomatous Hyperplasia (9,13,21)
4. Pseudohorn-Pearl Formation (13,20)
5. Exocytosis (13,22)
6. Tendency to Lipping at the Margin (13,19,21)
7. Maintenance of Basement Zone Reticulin (4,13,19)
8. Fragments of Elastica within the Tumour (13,15)
9. Presence of Glycogen in the Tumour Cells (4,13,23)
10. Absence of Evidence of Malignant Transformation (1,4,9,13,19)

DIFFERENCES

	Keratoacanthoma	A Warty Dyskeratoma
A. CLINICAL :		
1. Usual Size	Large	Small
2. Spontaneous Resolution	Yes	No
B. HISTOLOGY :		
1. Suprabasal Separation	No	Yes
2. Villi, Lacunae	No	Yes
3. Acantholysis	No	Yes
4. Dyskeratosis	Pseudomalignant	Benign
5. Basal Infiltrate	Moderate	Mild

Classification

There is no accepted and proper classification of warty dyskeratoma among tumours of the skin. Graham and Helwig (1958)[4] was opposed to its inclusion as a tumour as it did not fit into any of the accepted classification. Considering the localised and organized malformed keratinisation and hyperplasia involving a hair follicle in **both** keratoacanthoma and warty dyskeratoma, it is suggested by the author that they should be classified together in a special category of Dyskeratotic Benign Tumours of the Hair Follicle — the former of pseudomalignant non-acantholytic type and the latter - benign acantholytic type.

Morphogenesis

It would not be irrational to postulate that the basic abnormality in warty dyskeratoma lies in a clone of keratinocytes in the outer root sheath of the affected hair follicle which was destined to develop benign hyperplasia and defective keratinisation without any evident genetic or infective cause. The clone supported by the connective tissue stroma of the basement zone and the papillary dermis would gradually give rise to a slow but perpetuating proliferative reaction resulting in hyperplasia of the entire follicle. The keratinisation process being defective, suprabasal separation and benign acantholytic dyskeratosis would ensue.

The cells though acantholytic, remains viable, allowing the keratinisation process to continue within individual cells that are ultimately shed as corps ronds within the lumen of the follicle. A concommitant proliferation of the rete ridges adjoining suprabasal separation would be manifested as villi. Downward invasion of the tumour is prevented by intact basement membrane and the collagenous follicular sheath. The resultant reaction is comparable to keratoacanthoma on one hand and Darier's disease on the other. The onset of the lesion in the older age group can be expressed as a form of abiotrophy.

Nomenclature

The interesting nature of the tumour and its idiopathic origin justifies its acceptance as a separate entity[9,21]. The term 'Isolated Dyskeratosis follicularis' (Graham & Helwig, 1958; Nikolowski, 1959) no doubt points towards its location and basic pathologic change, but appear too modest to clarify the organised tumourous hyperplasia. The term 'Warty Dyskeratoma' is more appropriate though it does not indicate the origin of the tumour from the hair follicle. For a more specific nomenclature, therefore, the name "Follicular Dyskeratoma" is suggested.

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TRUE or FALSE?

Antibodies to epidermal cytoplasmic antigens are universally present in normal individuals and their presence therefore is of no significance.

(Answer Page No. 45)