Bowenoid papulosis: clinical and histological study of eight cases

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SUMMARY Eight cases of bowenoid papulosis are reported. The clinical diagnoses were confirmed by histology. In one case an immunoperoxidase method showed the presence of papillomavirus antigen in the nucleus of the most superficial epidermal cells.

We consider bowenoid papulosis to be a condition with specific features that distinguish it clinically and histologically from carcinoma in situ and condylomata acuminata.

Introduction

In 1977 Kopf and Bart used the term bowenoid papulosis to describe a clinical condition characterised by the appearance of papules in the genital region.¹ These papules were either discrete or coalesced into plaques, and mainly affected men. The histology was similar to that of carcinoma in situ.

The disease had first been described in 1970 by Lloyd, who called it "multicentric pigmented Bowen's disease".² Various synonyms have been proposed in referring to the clinical characteristics, histology, and probable aetiology of the disease. Friederich called it "reversible vulvar atypia",³ whereas Kimura *et al* described it as "pigmented viral papulosis of the genitals".⁴

The most important histological changes described in bowenoid papulosis (loss of cellular polarity, presence of atypical mitoses, and multinucleated atypical keratinocytes with dyskeratosis) were attributed to changes secondary to irritative treatment carried out on benign lesions.⁵ Since the studies by Wade *et al* in 1978,⁶ however, increased evidence points to the role of human papillomavirus (HPV) in the aetiology of the disease.

As HPV has been considered as being potentially

oncogenic,⁷ careful treatment and observation has been recommended for these patients. Different authors have recommended various treatments, including simple removal with direct suture, electrocoagulation,⁸ topical cytostatic agents, cryotherapy,⁹ and oral administration of aromatic retinoids.¹⁰ Spontaneous regression has also been reported.¹¹

Patients and methods

During the four years 1982-85 we diagnosed bowenoid papulosis in eight men, aged between 22 and 50, who attended the section of sexually transmitted diseases (STD) of this hospital. Epidemiological characteristics of age, sexual orientation, history of STD, and numbers of sexual partners were studied. Paraffin sections of biopsy samples were stained with haematoxylin and eosin, and HPV antigen was looked for with an immunoperoxidase method (PAP Kit K521-025/2; Dakopatts, USA). The sexual contacts of the patients were asked to attend for clinical and, when indicated, histopathological study; the sexual partner of one patient underwent colposcopy.

According to the size or location of the lesion or the patient's preference, treatment consisted of applying liquid nitrogen or 25% podophyllin resin in alcohol, electrocoagulation, surgical removal, or oral administration of 13-cis-retinoic acid. One patient refused any treatment. All patients were followed up for one to two years.

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TABLE 1 *Epidemiological findings for eight heterosexual men with bowenoid papulosis*

Case No	Age	History of sexually transmitted diseases	No of sexual partners/year
1	34	Non-gonococcal urethritis	11-20
2	26	None	1
3	50	None	5-10
4	22	Syphilis	3-5
5	43	Gonorrhoea, syphilis	3-5
6	28	Gonorrhoea, syphilis	6-10
7	30	None	1
8	24	Gonorrhoea	2

Results

All eight patients were heterosexual men aged 22 to 50 (mean age 32). Five had been treated previously for STD (table 1). The clinical lesions, each of several months' duration, consisted of multiple erythematous or hyperpigmented papules, some discrete, located on the shaft of the penis, prepuce, glans, or fraenum, or coalescing to form plaques (figs 1 and 2). None of the patients had local pain or irritation.

FIG 1 *Isolated erythematous papules on shaft of penis.* FIG 2 *Coalescent verrucous papules into plaques on shaft of penis.*

Histological study showed epidermal psoriasiform hyperplasia (fig 3), hyperkeratosis with focal parakeratosis, prominent granulomatous foci, loss of cellular polarity, atypical mitoses, and multinucleated, necrotic, atypical keratinocytes with dyskeratosis (fig 4). At the papillary dermis level, oedema with dilated tortuous capillaries surrounded by a chronic inflammatory infiltrate was observed.

Of the eight biopsy specimens, four presented all the histological characteristics described above; in two of them the stratum granulosum was normal. In one case no multinucleated keratinocytes were found. In the second case the dermal capillaries were not dilated and the dermal inflammatory infiltrate was discrete.

In one case the immunoperoxidase method showed the presence of papillomavirus antigen in the nuclei of the most superficial epidermal cells (fig 5).

Treatment was carried out with 13-cis-retinoic acid in one case, liquid nitrogen in three cases, and simple surgical removal in another. No relapses were observed in these patients during one to two years. In the patient who refused treatment, the lesions regressed spontaneously, reappeared, and disappeared again. In another case, after several relapses after treatment

FIG 3 Epidermal psoriasiform hyperplasia. (Haematoxylin and eosin.)

with liquid nitrogen, podophyllin resin was applied without success. The lesions were finally eliminated by electrocoagulation (table II).

The sexual contact of only one of the eight patients attended the clinic. Colposcopy showed plane cervical lesions of HPV. This was confirmed by the histological study of a biopsy specimen of the lesion.

Discussion

Several different theories on the aetiology of bowenoid papulosis have been advanced; all refer to the action of different irritating factors on primary lesions that in principle are benign.^{5,7} One of our patients had been treated with podophyllin before being referred to us.

The aetiological role of HPV has been shown by electron microscopy,^{5,12} though viral particles were only identified in one quarter of cases, possibly because incomplete forms of the virus are not detectable by electron microscopy.⁶ Immunoperoxidase methods have shown the presence of papillomavirus antigen in the nucleus in a small percentage of cases.¹³ In our study this antigen was detected in only one patient, an incidence (12.5%) comparable with that reported by Braun *et al.*¹³ Molecular hybridisation

FIG 4 Loss of cellular polarity, atypical mitoses, and multinucleated, necrotic, atypical keratinocytes with dyskeratosis. (Haematoxylin and eosin).

methods have identified HPV in most cases.¹⁴⁻¹⁶ Bowenoid papulosis may be the result of infection with HPV 6, HPV 11, or HPV 16.¹⁵

Several studies have shown that about 20 to 30% of patients with carcinoma in situ of the penis or cervix

TABLE II Treatment and follow up of eight men with bowenoid papulosis

Case No	Treatment	Relapse	Period of follow up (months)
1	13-cis-retinoic acid	No	24
2	Liquid nitrogen	No	23
3	None	Spontaneous remission	
		Relapse	
		Spontaneous remission	24
4	Liquid nitrogen	No	14
5	Surgical removal	No	22
6	Refused	No follow up	None
7	Liquid nitrogen	No	12
8	Liquid nitrogen		
	Podophyllin resin		
	Electrocoagulation	Several	11

FIG 5 *Papillomavirus* antigen in nuclei of superficial epidermal cells. (Immunoperoxidase method, PAP kit K521-025/2; Dakopatts, USA.)

had previously been treated for condylomata acuminata.^{17 18} The recent finding of DNA sequences specific for HPV 16 in cervical dysplasias of women with sexual partners who presented with bowenoid papulosis with HPV 16 sequences shows the impor-

tance of epidemiological studies aimed at assessing sexual transmission. It is therefore necessary to examine all sexual partners of patients with bowenoid papulosis.¹⁹ As we were only able to study one sexual partner of one of our patients, we could draw no appreciable conclusions.

Table III shows that the clinical and histological differential diagnosis of bowenoid papulosis includes Bowen's disease, condylomata acuminata, and condylomata acuminata treated with podophyllin resin.^{5 21 22} Clinically, bowenoid papulosis appears at an earlier age than Bowen's disease and presents as multiple small papule that have a tendency to coalesce into verrucous plaques;²⁰ these may recede spontaneously. Our patients presented with these clinical characteristics and one case of spontaneous regression.

Four of our patients satisfied all the histological criteria for bowenoid papulosis. Though in one case no multinucleated keratinocytes were observed, there was clear focal parakeratosis with loss of cellular polarity and a large number of atypical keratinocytes with dyskeratosis, as in the four other patients. In another two patients the stratum granulosum was normal, but the complete bowenoid papulosis pattern was present, with a large number of dilated tortuous capillaries, a pattern that is not observed in Bowen's disease. In another case, though the dermal capillaries were normal, the epidermal alterations were not as pronounced as in Bowen's disease; moreover, the patient presented with focal hypergranulosis.

There seems to be a relation between bowenoid papulosis and sexual promiscuity. In our group five patients had a history of episodes of STD and considerable sexual activity (table I).

We consider bowenoid papulosis to be a condition with specific characteristics that distinguish it clinically and histologically from carcinoma in situ and condylomata acuminata.

TABLE III *Histological differential diagnosis of bowenoid papulosis*

	<i>Bowenoid papulosis</i>	<i>Bowen's disease</i>	<i>Condyloma acuminatum</i>	<i>Podophyllin treated condyloma acuminatum</i>
Pattern	Papulous			
• Stratum corneum	Focal parakeratosis	Focal parakeratosis	Condylomatous	Condylomatous
Stratum granulosum	Focal acanthosis	Normal	Orthokeratosis	Haemorrhage
Cellular polarity	Lost	Lost	Focal acanthosis	
Keratinocytes:			Maintained	Maintained
Atypical	++	+++	-	+
Dyskeratotic	++	+++	-	-
Multinucleated	+	++	-	-
Necrotic	++	+++	-	++++
Exocytosis	-	-	-	++
Spongiosis	-	-	-	++
Dermal capillaries	Dilated & tortuous	Normal	Dilated & tortuous	Endothelial proliferation
Dermal infiltrate	Lymphohistiocytic	Lymphohistiocytic	Lymphohistiocytic	Neutrophils & nuclear dust

- = none, + = few, ++ = moderate, +++ = abundant, ++++ = very numerous.

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