- MACKENZIE, A.F., WHITMORE, W.I. & MELAMED, M.R. (1968) Myosarcoma of the bladder and prostate. *Cancer*. New York, Philadelphia, etc., **22**, 833.
- REICH, C. (1936) A case of adenocarcinoma of the sigmoid colon with lymphatic leukemia blood picture. *American Journal of Cancer*, **26**, 781.
- POLAK, H. & NEMEC, J. (1959) Notes on the mechanism of leukocytosis. *Blood*, **14**, 931.
- POWERS, J.H., VAN ZANDT HAWN, C. & CARTER, R.D. (1956) Osteogenic sarcoma and traditional cell carcinoma occurring simultaneously in the urinary bladder. *Journal of Urology*, **76**, 263.
- TARA, H.H. & MENTUR, N.L. (1973) Leiomyosarcoma of the urinary bladder. *Urology*, **11**, 460.

Postgraduate Medical Journal (December 1977) **53**, 768-772.

Perianal Paget's disease

M. R. LOCK*
M.B., F.R.C.S.

SIR ALAN PARKS
M.Ch., F.R.C.S., F.R.C.P.

D. R. KATZ
M.B., Ch.B.

JAMES P. S. THOMSON
M.S., F.R.C.S.

St Mark's Hospital, London

Summary

Paget's disease involves the ducts of apocrine glands and the overlying epidermis and is considered to be locally neoplastic. It is capable of developing into invasive carcinoma and in this event the prognosis is poor.

The perianal skin may be affected by Paget's disease. This is a rare disorder and the four patients who have been seen with this disease at St Mark's Hospital since 1930 are described.

Introduction

In 1874 Sir James Paget described fifteen patients in whom the nipple and the surrounding skin of the breast was diseased and who, within 2 years, had developed a clinically recognizable ipsilateral breast carcinoma. The breast is an exocrine gland of the apocrine type and since that time an identical disease process has been found to affect apocrine glands at other sites. These include those situated in the skin of the axilla, the lower eyelid (Glands of Moll), the external genitalia and the perianal region (Glands of Gay).

During the last 50 years only four patients at St Mark's Hospital have been diagnosed as having Paget's disease of the perianal skin. The purpose of

this paper is to describe their clinical history and pathology, and to draw attention to this rare condition which should be considered in the differential diagnosis of perianal disorders.

Case reports

Case 1

Mr W.R. presented in 1959, aged 64, with a 5-month history of perianal soreness and irritation together with mucoid discharge. Examination showed a raw hyperaemic area 2 cm in diameter to the right of the anus. Rectal examination and sigmoidoscopy were otherwise normal and no inguinal lymph nodes were palpable. Biopsy showed the appearance of Paget's disease and local excision of the diseased skin was performed. In 1961 an adenoma was removed from the lower rectum and in 1963 his symptom of perianal soreness returned. Biopsy again showed that this was due to Paget's disease. No further treatment was undertaken at this time but he was kept under regular review. In 1967 two areas of induration were noted in the diseased skin which now extended into the lower anal canal for 1 cm and around the anus for 7.5 cm. Further biopsies were performed, these again showed the changes of Paget's disease but there was no evidence of invasive carcinoma. A wide excision of the diseased perianal skin was performed and the defect covered

*Reprint requests: Surgical Unit, Westminster Hospital, London.

by rotation skin flaps. One of the flaps underwent partial necrosis but total epithelialization was eventually achieved by the application of a split skin graft, although continence was impaired. In April 1969, he developed further Paget's disease in the perianal region and it was planned to excise the rectum and perianal skin and to construct a terminal colostomy. However he developed severe myocardial ischaemia and died from this in July 1969.

Case 2

Mrs A.F. first presented in August 1960, aged 55, with a 12-month history of perianal irritation and soreness. Examination showed raised and reddened desquamating areas to the left and right of the anus. Rectal examination and sigmoidoscopy to 24 cm were otherwise normal and no lymph nodes were palpable in either inguinal region. Biopsy of the diseased perianal skin showed the changes of Paget's disease. In October 1960 a local excision of the area to the left of the anus was performed. There was no invasive carcinoma but Paget's cells extended to the margin of excision. Further local excisions were performed in February and June 1962 and on each occasion the pathology showed that Paget cells were present to the limits of excision. Between 1963 and 1968, the disease persisted and the area of perianal skin involved slowly increased (Fig. 1). This resulted in her perianal soreness becoming very severe. In March 1968 a wide excision of the perineal skin was performed with a 2 cm margin of apparently normal skin except in the region of the posterior vulva and lower anal canal. The area was covered with a split skin graft and a loop colostomy constructed in the left iliac fossa. The pathology suggested that the excision was complete even in the parts where the margin was small and in the sections taken there were no signs of invasive carcinoma. The colostomy was closed after 4 months, by which time the perianal skin had completely re-epithelialized.

She remained well until at follow-up in July 1970 a palpable hard lymph node was found in each inguinal region. There was no hepatomegaly and there was no sign of recurrent disease in the perianal region. Biopsy of each lymph node showed invasion by metastatic squamous carcinoma. In September 1970, bilateral block dissections of the superficial and deep inguinal lymph nodes were performed. On the right no further lymph nodes were involved but on the left five out of six lymph nodes sectioned, including the highest, were invaded by carcinoma. In August 1971 she developed a pre-vascular hernia which was repaired. At the same time she was found to have a carcinoma of the vulva and also a fixed pelvic mass which was considered to be the same neoplastic process. She was referred for radiotherapy but, despite some palliation of her

FIG. 1. (A.F.) Desquamating perianal Paget's disease.

symptoms, she died of carcinomatosis in October 1973.

Case 3

Mr W.B. presented in November 1968, aged 76, with a 9-month history of perianal irritation and discomfort, pain on defaecation and increasing constipation. Examination showed two well demarcated areas of diseased perianal skin. The areas were soft and their surface varied in colour (Fig. 2). Rectal examination and sigmoidoscopy were otherwise normal and there were no palpable inguinal nodes. Biopsy showed the appearance of Paget's disease, and a barium enema showed extensive diverticular disease of the descending colon. At the time of presentation he was undergoing radiotherapy and oral cytotoxic treatment for a large squamous carcinoma of the nasopharynx with right cervical node metastases. Symptomatic treatment with hydrocortisone cream was therefore prescribed for the anal lesion. In June 1970 he was noted to have a small basal cell epithelioma of the right upper eyelid. He remained well until April 1971, when he complained of frequent loose bowel actions and the inability to pass urine. On examination he was found to have a fixed mass in the pelvis which encircled the rectum. At laparotomy the pelvic mass was found to

FIG. 2. (W.B.) Papilliferous perianal Paget's disease.

be firmly adherent to the bladder and rectum. This tumour, which biopsy subsequently showed to be a mucinous carcinoma, was inoperable and a palliative transverse colostomy was performed. The perianal Paget's disease remained unchanged and he subsequently died in August 1971.

Case 4

Mrs M.G. presented in September 1974, aged 85, with a 4-month history of perianal soreness together with a perianal lump which was increasing in size. Examination showed a raised red ulcerating area extending bilaterally from behind the anus to the urethra, measuring 11×5 cm. There was a thickened area in the posterior anal canal below the dentate line and an extension into the vagina. Sigmoidoscopy was normal and there were no palpable inguinal lymph nodes. Three biopsies of the area were performed and these showed the appearances of Paget's disease. In some areas there was underlying mucinous carcinoma.

A temporary transverse loop colostomy was performed and she subsequently underwent a course of neutron irradiation of 1440 rad in 12 fractions over 26 days to the involved area given by Dr Mary Catterall at the Hammersmith Hospital. There was considerable regression of the lesion and in April 1975 there was no evidence of recurrence. The colostomy was closed, in August 1976 she remains well.

Discussion

Paget's disease of the anogenital area was first described by Darier and Coullillaud in 1893 and is now a well recognized condition. The largest recorded series is that of Helwig and Graham (1963), who described 14 patients with perianal disease. As

in Paget's disease of the breast, the perianal condition affects the elderly. The four patients presented in this study were over 55 years of age. There is no predilection for either sex and there are no known causative factors. A familial case of Paget's disease of the scrotum in father and son has been recorded by Kuehn, Tennant and Brennehan (1973).

All the patients presented with a short history of common anal symptoms. The four patients had perianal soreness and pruritus. Other symptoms included anal pain, mucoid discharge and difficulty with defaecation. On examination the macroscopic perianal lesion appears as an elevated area which is usually erythematous but may be whitish-grey in colour. The surface may be crusted, scaly, ulcerated or papillary. On palpation the involved skin is usually soft and the presence of induration suggests malignant invasion. In all patients the inguinal nodes and abdomen should be examined to exclude secondary neoplastic disease. Digital rectal examination and sigmoidoscopy should also be done primarily to assess the intra-anal extent of the disease. This also allows the possibility of a concomitant adenocarcinoma of the rectum to be excluded as downward spread may be confused with Paget's disease.

If the condition is suspected clinically, a biopsy must be taken to confirm the diagnosis. It is interesting to note that in Helwig and Graham's series, only two patients were correctly diagnosed before biopsy. Conditions which may be confused with Paget's disease include leukoplakia, Bowen's disease, condylomata acuminata, squamous cell carcinoma, dermatitis, lichen planus and, as previously mentioned, downward spread of a rectal adenocarcinoma.

The diagnosis of Paget's disease was established by histology in all four patients. The specimens examined included both biopsies and wide local excision specimens as indicated in Table 1. Paget cells were an important feature in all the material examined. These are large, faintly basophilic or vacuolated cells situated at the dermo-epidermal junction (Fig. 3). The cytoplasm stains with Alcian blue and with the periodic acid Schiff (diastase resistant) reaction. The nuclei are vesicular and either central or compressed at the periphery. There is little mitotic activity. In association with Paget cells there are variable degrees of hyperkeratosis and acanthosis. The superficial dermis shows a chronic inflammatory infiltrate with vascular dilatation and engorgement.

While involved epidermis often extends in continuity to the ducts of the adnexal glands, involvement of the glands themselves with Paget cells is a late manifestation. This was the case in two of the patients (W.R., A.F.).

Three of the four patients developed carcinoma in association with extramammary Paget's disease.

TABLE 1

Patient Age (years)	Date	Operation	Microscopic features	
			Diagnosis	Comment
W. R. (64)	1959	Biopsy Local excision	Paget's disease Paget's disease	No adnexal gland involvement Margins of excision normal
	1963	Biopsy	Paget's disease	
	1967	Biopsy Local excision	Paget's disease Paget's disease	Adnexal glands infiltrated Margins of excision normal
A. F. (55)	1960	Biopsy Local excision	Paget's disease Paget's disease	No adnexal gland involvement Margins involved
	1962	Biopsy	Paget's disease	
	1963	Biopsy	Paget's disease	
	1968	Local excision	Paget's disease	Adnexal glands infiltrated Margins of excision normal
	1970	Bilateral inguinal lymph node biopsy	Carcinoma	Squamous type
W. B. (76)	1968	Biopsy	Paget's disease	No adnexal gland involvement
	1971	Biopsy of pelvic tumour	Carcinoma	Mucinous type
	1974	Biopsy	Paget's disease and carcinoma	Adnexal glands infiltrated Mucinous type

FIG. 3. Paget cells at the dermo-epidermal junction showing basophilic cytoplasm and large nuclei. Underlying inflammatory changes are also seen ($\times 28$).

In two of these patients, the carcinoma commenced in the perineal region; one, a squamous carcinoma of the vulva (A.F.) and the other a mucinous carcinoma of the perianal region (M.G.). The third patient (W.B.), developed a mucinous carcinoma in the pelvis which was not considered to have arisen in the extramammary Paget's tissue but from the sigmoid colon. This patient had previously had two other independent carcinomas (squamous cell carcinoma

of the nasopharynx and a basal cell carcinoma of the right upper eyelid).

Certain accepted features of mammary Paget's disease are relevant to the discussion of the perianal lesion. In the breast, atypical epithelial cells in the epidermis are regarded as neoplastic (Evans, 1966) rather than metaplastic; thus Paget's disease of the nipple is a malignant rather than a pre-malignant condition. The association of mammary Paget's

disease with an underlying breast carcinoma is regarded as virtually invariable.

If one then considers the striking microscopic similarity between the breast and the other apocrine glands, it is not surprising that Paget's disease has been described in both breast and other apocrine gland areas, such as the perianal region. Likewise, the relationship between perianal Paget's disease and carcinoma is striking. Helwig and Graham found this association in twelve of fourteen patients and Arminski and Pollard (1973) in twenty-five of thirty-two patients. Three of the four patients in the present study developed carcinoma, the fourth patient had several local recurrences of Paget's disease over an 8-year period.

The treatment of perianal Paget's disease is by wide local excision of the affected area with a margin of histologically normal skin (Linder and Myers, 1970). This may be curative, but careful follow-up is essential as further disease or a carcinoma may develop at any time. If this occurs then more radical treatment such as excision of the rectum may be necessary. Conventional radiotherapy, curettage and topical applications are of no curative value but may be employed as palliative measures where radical surgery is contraindicated owing to the patient's age or general condition. It is to be hoped that irradiation with neutrons may offer a better chance of cure without submitting patients to a permanent colostomy.

The prognosis must be guarded. Two of the four patients presented here have died from related malignancy. A third patient has been shown to have extensive carcinoma of the perineum but has had initial encouraging results with neutron therapy and 22 months after diagnosis, is clinically well. Of the

twelve cases which developed malignancy in the series of Helwig and Graham, nine had already died when the series was recorded. Potter (1967) found that once the disease had changed to a frank neoplasm, most patients were dead within 18 months. The reason for the large number of associated carcinoma with disease of the perianal area is unknown but it emphasizes the malignant nature of the condition and the necessity for its early treatment by radical excision.

Acknowledgments

We thank the surgeons of St Mark's Hospital for permission to study patients under their care. The illustrations are from the Department of Medical Illustration at St Mark's and the secretarial work was done by Mrs M. Green and Miss G. Baker. We are most grateful for their help.

References

- ARMINSKI, T.C. & POLLARD, R.J. (1973) Paget's disease of the anus secondary to a malignant papillary adenoma of the rectum. *Diseases of the Colon and Rectum*, **16**, 46.
- DARIER, J. & COULILLAUD, P. (1893) Sur un cas de maladie de Paget de la région périnéo-anale et scrotale. *Annales de dermatologie et syphiligraphie*, **4**, 33.
- EVANS, R.W. (1966) *Histological Appearances of Tumours*, 2nd edn, pp. 839–842. Livingstone, London.
- HELWIG, E.B. & GRAHAM, J.H. (1963) Anogenital (extramammary) Paget's disease: A clinicopathological study. *Cancer*, New York, Philadelphia, etc., **16**, 387.
- KUEHN, P.G., TENNANT, R. & BRENNEMAN, A.R. (1973) Familial occurrence of extramammary Paget's disease. *Cancer*, New York, Philadelphia, etc., **31**, 145.
- LINDER, J.H. & MYERS, R.T. (1970) Perianal Paget's disease. *American Journal of Surgery*, **36**, 342.
- PAGET, J. (1847) On disease of the mammary areola preceding cancer of the mammary gland. *St Bartholomew's Hospital Report*, **10**, 87.
- POTTER, B. (1967) Extramammary Paget's disease. *Acta dermato-venerologica* (Stockholm), **47**, 259.