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## **Referrals into a dedicated British penile cancer centre and sources of possible delay.**

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### **ABSTRACT**

**Objective:** To assess sources of delay in referral to a specialist Urology clinic for penile cancer.

**Methods:** Patients with penile cancer seen during the period December 2002 - December 2007 were identified from the unit's database. Information regarding presentation, diagnosis, and pattern of referral was retrieved from records. Delay was defined as the time between the patient first noticing a penile lesion and date of first seeking medical advice, or additional time before being seen by a Urologist resulting from referral to another speciality.

**Results:** Of 100 patients, with a median age 54yrs (range 2-81yrs), 19% were initially referred to other specialities (Genitourinary Medicine – 13%, Dermatology – 4%, Plastics 2%). Initial referrals to GUM and Dermatology resulted in mean delays of 6 and 3.5 months respectively, whereas mean duration for patients to present to any medical practitioner from onset of symptoms was 5.8 months. Overall, 47% presented with locally advanced disease

**Conclusion:** Approximately one fifth of patients with penile cancer are first referred to specialities other than Urology. This sometimes delays diagnosis, potentially affecting overall prognosis. The major source of delay, however, results from patient reluctance to seek medical advice. Thus, the greatest impact in this condition is likely to be achieved by increased public awareness and education.

### **INTRODUCTION:**

Penile cancer is rare, accounting for 0.4 to 0.6% of all malignancies in males in Europe and the United States, with an incidence of approximately 1-2 in 100,000 (1). Approximately 400 new cases and 100 deaths are reported annually in the United Kingdom (2). Delay in diagnosis and assessment for definitive treatment may

adversely influence survival, and also quality of life, by leading to more radical surgery, sometimes in association with adjuvant therapies (3). Despite the establishment of rapid referral pathways within the N.H.S. for suspected urological cancers, it was observed at our unit that a large proportion of men, with this initially superficial malignancy, continue to present with advanced disease. Furthermore, prior referral to other specialities seemed common, with some patients receiving inappropriate treatments for misdiagnoses. We, therefore, performed an audit of referrals to a regional specialist clinic for penile cancer, since the introduction of the twoweek urological cancer target in December 2002.

#### METHODS:

We carried out a retrospective study looking at all patients diagnosed with and treated for penile cancer at our regional specialist centre from December 2002 to December 2007. A list of these patients was generated from the unit's penile cancer database. The relevant medical records were obtained and information regarding presentation, initial diagnosis, staging and pattern of referral was retrieved. Further information was obtained, when necessary, from general practitioners and other specialists involved in the patient's care, and in some cases patients themselves.

#### RESULTS:

One hundred patients were diagnosed with and treated for penile cancer in the 5 year period at our regional specialist centre. Fifty-seven patients had early penile cancers (Tis/Ta/T1), while 43 had locally advanced disease (T2/T3/T4). Their age ranged from 21 to 81 yrs (mean 50.9yrs, median 53yrs) and the age band distribution is shown in Table 1.

Table 1. Ages of patients diagnosed with penile cancer

Patient Age (years)	Number of Patients
< 40	7
40-49	12
50-59	21
60-69	28
>70	32

Pathways of referral, inappropriate initial therapies and delay in referral to our clinic are shown in Table 2. Fifty-five per cent of patients were referred urgently to Urology as suspected cancers.

Table 2. Referral Pathways to Urology

	No. of Patients	Initial Therapy	Approximate mean delay due to referral (months)
Self-presented to GUM	6	Topical agents	3
GP to GUM	13 (3 with phimoses)	Topical agents Systemic antibiotics	6
GP to Plastic Surgery	2	Excision and grafting	2
GP to Dermatology	4	Topical agents	3.5
GP to Urology (benign phimosis)	4	None	-
GP to Urology (symptomatic phimosis)	11	None	-
GP to Urology (urinary symptoms)	3	None	-
GP to Urology (suspected cancer)	55	None	-
Incidental Finding upon catheterisation by other specialities	2	None	-

Topical agents = antifungals, steroids, podophyllin, salicylic acid

The second largest referral pathway was into Genito-urinary Medicine (GUM). Of those seen in GUM, 32% self-referred and 68% were referred by their GP. The median age of patients referred initially to GUM was 56yrs (range 21 to 81yrs), while the median age of the patients not referred to GUM was 51yrs (range 37-89yrs). The mean delay in seeking a urological opinion due to a preceding GUM referral was 6 months (range: 1-13 months). Of those who self presented to GUM, the mean delay to see a Urologist was 3 months. Of the patients who attended GUM clinics, up to six months was given to determine if the presenting lesion settled before being referred to Urology. Biopsies were carried out in GUM on 2 (10.5%) of the 19 patients seen. These were done after a period of 4 and 5 months respectively. The majority of the 19 cases (79%) were early penile cancer, Tis, Ta or T1. In comparison 50% referred directly to urologists were early penile cancers (Table 3). One patient was initially given prolonged treatment for balanitis by his GP before being referred to GUM, resulting in an overall delay of 13 months before being seen by a urologist.

Table 3. Histological staging

	Patients referred to GUM (n=19)	Patients referred to Dermatology (n=4)	Patients referred to Plastics (n=2)	Patients referred to Urology (n=75)
Tis	26%	0%	0%	3%
T1	53%	75%	100%	47%
T2	21%	25%	0%	41%
T3	0%	0%	0%	9%

Four patients (4%) aged 48-88yrs (median 57yrs) were initially referred to Dermatology by their GP. This resulted in a mean delay of 3.5 months (range: 1-6 months). Initial diagnoses at GUM and Dermatology clinics included fungal balanitis,

bacterial balanitis, plasma cell balanitis, lichen sclerosus, venereal warts and chancroid.

Two patients (2 %) aged 55 and 56 years were initially referred to Plastic Surgery, resulting in delays of 1 and 3 months. One of these was diagnosed with lichen sclerosus and proceeded to undergo excision and skin grafting, before histology demonstrated invasive cancer requiring more radical surgery.

The time between referral to our dedicated clinic and clinic appointment ranged from 1 to 35 days (mean 17 days). This included GP referrals, referrals from other urology units and other specialists. For 34 patients seen by their local urologist for penile lesions, the referral into our unit did not state that the referral was urgent, although all were treated as urgent referrals, so this did not act as a source of delay. Of these, 7 were initially seen by GUM, the rest having been referred by their GPs. Ten (29%) of these patients had already been biopsied at the time of referral. Of patients referred urgently, 66% were seen within 14 days, with the remainder seen at either 15 or 16 days.

Of the 100 patients, 18% had a phimosis and were unable to retract their foreskin. One of the patients had previously been circumcised but this was incomplete, as there was foreskin covering the glans penis on presentation. It was difficult to quantify the delay in presentation in these patients as it was impossible to identify when the lesion first appeared.

The average time taken for a patient to present (patients diagnosed due to incidental findings and patients with phimosis excluded) to any medical practitioner from onset of symptoms was between 2 days and 24 months (mean time 5.75 months). This information was obtained at patient interview and from case notes. Reasons for late presentation were not explored.

## DISCUSSION:

Carcinoma in situ normally presents of a red, velvety, well-marginated lesion of the

glans or, less frequently, the inner aspect of the foreskin. In contrast, invasive cancer usually begins with a small lesion, which may be papillary and exophytic, or flat and ulcerative. The presentation can range from relatively subtle induration to a small papule, warty growth or more exophytic lesion. It may appear as a shallow erosion or as a deeply excavated ulcer with elevated or rolled-in edges. Untreated, it may erode through the prepuce, causing a foul preputial odour and discharge, with or without bleeding. If penile cancer remains untreated it causes death in the majority of patients within 2 years (4). Tumours most commonly occur on the glans (48%) and prepuce (21%), but can also involve both the glans and prepuce (9%), the coronal sulcus (6%), or the shaft (<2%) (5). Pain is not usually associated with these lesions, and they are usually confined to the penis at presentation. The classification of penile cancer is shown in Table 4.

Table 4. Tumour Node Metastasis (TNM) classification of penile cancer (6).

T-Primary tumour

- TX Primary tumour cannot be assessed
- T0 No evidence of primary tumour
- Tis Carcinoma-in-situ
- Ta Non-invasive verrucous carcinoma
- T1 Tumour invades subepithelial connective tissue
- T2 Tumour invades corpus spongiosum or carvenosum
- T3 Tumour invades urethra or prostate
- T4 Tumour invades other adjacent structures

N –Regional lymph nodes

- NX Regional lymph nodes cannot be assessed
- N0 No evidence of regional lymph node metastasis
- N1 Metastasis in a single inguinal lymph node
- N2 Metastasis in multiple or bilateral superficial lymph nodes
- N3 Metastasis in deep inguinal or pelvic lymph nodes, unilateral or bilateral

M-Distant metastases

- MX Distant metastases cannot be assessed
- M0 No evidence of distant metastases
- M1 Distant metastases

Penile cancer is reported to be a disease of older men, with an abrupt increase in incidence in the sixth decade of life peaking around the age of 80 years (7). However, in our unit a large proportion of men with penile cancer are under the age of 50 at

diagnosis. This is important as many patients in this age group are thought to have a low risk of penile cancer and to be more at risk of sexually transmitted diseases, which may result in them being referred to GUM. Nevertheless, the mean age in our series for patients referred to GUM was similar to those referred along other pathways (51 vs. 53yrs). Perhaps surprisingly, a number of patients over the age of 70 were referred to GUM, despite sexually transmittable diseases being less likely in this age group (8).

The results also show that the majority of lesions referred to GUM are of early stage (79%). It seems likely that these tumours more frequently resemble other benign penile conditions, which are more common. Current UK guidelines on Balanoposthitis recommend penile biopsy in patients where the diagnosis is uncertain and the condition persists (9). However, biopsy was not done in the majority of our patients both in the GP and GUM clinic settings.

The incidence of penile cancer varies according to circumcision practice, hygiene, phimosis, number of sexual partners, Human Papilloma Virus infection, and exposure to tobacco products (10). In this study, patients with phimoses had a clear delay in initial presentation. This was difficult to quantify exactly, but is probably greater than we recorded. It is an important factor, as these patients may not notice any abnormality until the tumour has progressed significantly, with the cancer reaching an incurable stage in some. Greater education is needed to encourage men who have a phimosis to come forward urgently if they notice inflammation or discharge. Furthermore, GP's need to examine all patients with a phimosis carefully so as to exclude underlying induration. Current evidence does not support circumcision as a prophylactic measure for preventing penile cancer, as the risk is thought to outweigh the potential benefit, and the numbers needed to treat would be too high (11).

A major issue surrounding penile cancer and its prognosis is stage at presentation. It is a potentially curable disease once diagnosed in its early stages. Previous studies show decreased survival with longer delay in presentation (12). Furthermore, many early stage tumours can be treated with modern glans preserving surgical techniques. Apart from early referral, another important issue affecting this is the time taken for the patient to seek medical advice. In our study this contributed to by far the greatest



source of delay. There may be issues of denial in many of these cases but this has not been explored fully. A previous large series showed that patients with penile symptoms delayed medical care for more than a year (13). Explanations include embarrassment, guilt, fear, ignorance and personal neglect. The psychological issues surrounding penile cancer are complex and literature is lacking in this area. No significant relationship between age of patient and time taken to present to a medical practitioner was found.

As penile cancer is a somewhat rare disease, education can play a vital role in getting patients to present earlier. The late delay in presentation of this group of patients is a significant public health issue, which needs to be addressed. There is a tendency for men to delay presentation with other male urological cancers, when compared to female counterparts. This is an area which needs to be considered more fully across the male population. Greater awareness amongst GP's and other medical practitioners of the signs of this disease might also promote appropriate early referral to Urologists. Any patient presenting to a doctor with a penile lesion which does not respond promptly to medical therapy should be referred urgently to a Urologist for further assessment and biopsy.

## CONCLUSION:

Many patients with penile cancer experience delays in diagnosis. The majority do not have a phimosis and this superficial cancer should not present at an advanced stage. Approximately one fifth of patients with penile cancer are being referred to specialities other than Urology. This can result in a delay in diagnosis, potentially affecting overall prognosis. Nevertheless, the major source of delay results from patient reluctance to seek medical advice promptly. Thus, the greatest impact upon outcomes ought to be achieved by increased public awareness and education.

## KEY MESSAGES

- A significant number of patients with penile cancer are not initially referred to Urology

- Delay in diagnosis and assessment remains very common and may adversely influence both survival and the chances of penile preserving surgery
- Biopsy and referral to a Urologist should be considered in all penile lesions not responding to conservative treatment
- Patient reluctance to seek medical advice after noticing a penile lesion is a major cause of delay in the treatment of penile cancer
- A significant proportion of patients with penile cancer are young or middle aged; the condition should not be viewed as a disease of the elderly

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N. Parr – Data collection, patient interview and assistance in writing of paper.

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## LEGENDS

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