LETTERS TO THE EDITOR

Recurrent perianal warts and anal carcinoma

Anal carcinoma is a rare clinical entity, accounting for 2% of all ano-rectal cancers in the UK. However, recent reports have shown an increase in the incidence, mainly among women and homosexual men, especially those with a history of pre-existing warts and those known to harbour the human immunodeficiency virus (HIV). We report a case of anal carcinoma in a 38 year old heterosexual Caucasian male, which was preceded for many years by recurrent perianal warts.

This patient presented to the department of genitourinary medicine in April 1994 with a two year history of a lump in the perianal region, which was associated with a recent onset of perianal pain. He was treated for perianal warts in 1972 and subsequently in 1990. On the second occasion, he did not complete the treatment and defaulted from the clinic. On examination, he had an abscess in the left perianal region and a large mass 9.5 cm x 5.5 cm, on the right perianal region. There was no associated inguinal lymphadenopathy and no evidence of perianal warts. As malignancy was suspected, he was referred to the surgical unit for assessment.

At examination under anaesthesia, he was found to have a large shallow abscess with multiple openings and overlying necrotic tissue on the left perianal region. The cavity was deroofed and curettings from the base were sent for histology. On the right side, he had a large cauliflower lesion with areas of necrosis overlying the ischial tuberosity (fig). The mass extended upwards, involving the anal sphincter and ischiorectal fossa. Representative biopsy specimens were taken and it was felt that the tumour was too advanced for curative surgery. Histology showed carcinoma-in-situ on the sample obtained from the left perianal region and material from the right side showed a moderately differentiated squamous cell carcinoma. Hybrid capture DNA assay detected low risk human papillomavirus (HPV) types in the biopsy sample. He was then referred to the clinical oncologist who arranged for him to have a course of chemotherapy, to be followed by a course of radical radiotherapy. Treatment was initiated with two courses of the drugs mitomycin C, cisplatin and fluorouracil (the latter over five days), four weeks apart. Radiotherapy with 4500 rads in 20 fractions was commenced along with the second course of chemotherapy. He completed the above regime without significant adverse effects. A further five fraction electron boost was given four weeks later. He responded well to chemoradiation and is currently in complete remission, 12 months after treatment.

Various studies have reported the presence of HPV DNA in anal squamous carcinoma samples, the prevalence ranging from 0 to 100% depending on the sensitivity of assay used and the geographical origin of the population studied. The commonest type detected was HPV 16, although types 6, 11, 18, 31, 33, and 35 have also been detected. Enormous geographical variation has been reported with 43 to 47% of anal cancers in western Europe containing HPV type 16 compared with 11% from South Africa and only 3% from India. HPV types 6 and 11 appearing as free episomes have been detected in Bushke-Lowenstein tumours and HPV type 16 in the locally invasive variant, verrucous carcinoma. In a case controlled study, 16-9% of women with anal cancer gave a history of anal warts compared with 1% of women with colon cancer. More than half the patients reported an interval of more than 9 years between the diagnosis of warts and cancer. These studies suggest a causative role for HPV in the genesis of anal cancer. Although only the low risk HPV types were detected in this patient, it may be that the copy numbers of the high risk types may have been low in the small biopsy sample, which may have been detected by the highly sensitive polymerase chain reaction assays.

The conventional treatment for anal carcinoma has been abdominopерineal excision of the rectum. However, simultaneous chemoradiation is now the preferred method, which has an overall 5 year survival rate of 83%. Most reported chemoradiation regimens used mitomycin in a bolus dose with fluorouracil given over 4 days, the latter repeated after 4 weeks. The radiation dose varied from 3000...
to 5000 rads. Although the natural history of anal intraepithelial neoplasia is not yet clearly defined, it is possible that adequate treatment and follow-up in his case may have prevented the malignant transformation.

This case emphasises firstly, the need to ensure adequate treatment and follow-up in such cases to prevent this complication and secondly, to perform biopsies in those who have recalcitrant or atypical warts.

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### Photodynamic therapy for condylomata acuminata with local application of 5-aminolevulinic acid

In spite of the large therapeutic arsenal for the treatment of genital warts, results are still disappointing and relapse is common.

We performed a pilot study in which we investigated photodynamic therapy (PDT) with local application of 5-aminolevulinic acid (5-ALA). PDT is an experimental treatment modality for cancer in which tumour cells are killed as a result of photoactivation of a tumour-localising agent. 5-ALA is a precursor of protoporphyrin IX (PpIX) in the biosynthetic pathway of haem. Topically applied on some types of skin tumours it induces a temporarily increased PpIX level, without causing systemic photosensitisation. PDT with local application of 5-ALA has been used successfully by Kennedy et al1 for superficial non-melanoma skin cancer and actinic keratosis. We report the preliminary results of an open prospective pilot of seven patients with genital warts. The aim of this study was to determine the efficacy and adverse effects of PDT with local application of 5-ALA for the treatment of condylomata acuminata (CA). The treated group consisted of four males and three females aged 18 years and older with CA, localised perianal, penile, perivulvar and intravaginal. Diagnosis was made on clinical appearance. No therapy had been given for at least six weeks. The patients did not use other medication except for oral contraceptives, did not suffer from other diseases and were not pregnant or lactating. During the treatment period use of sunbeds was prohibited. Patients were informed of the investigational nature of PDT and other options were explained and offered. An informed consent form was signed. The protocol had been approved by the medical ethics committee of our hospital. Photographic documentation was done before application of 20% w/w 5-ALA in instillagel (gel containing lidocaine hydrochloride, chlorhexidine digluconate, methylhydroxybenzoate and propylhydroxybenzoate). The area was covered with a gauze, soaked in this gel, subsequently occluded under plastic and well fixed with tape. After 14 hours this was removed and an anaesthetic cream (with lidocaine and prilocaine) was applied. Two hours later the site was exposed to argon dye laserlight, wavelength 630 nm up to a total dose of 100 J/cm2. Light intensity was either 150 or 75 mW/cm2. After exposure patients received paracetamol 6 times daily 500 mg and naproxen twice daily 500 mg for one day. During illumination in vivo fluorescence was measured by means of a video camera with a filter for 690 nm. Photographic documentation was performed after 1, 2, 4, and 12 weeks. Efficacy was measured using the percentage of eradicated warts. The results are shown in the table.

### Table

<table>
<thead>
<tr>
<th>Patient</th>
<th>Gender</th>
<th>Localisation of CA</th>
<th>Applied light dose (J/cm2)</th>
<th>Percentage reduction</th>
<th>Follow up period</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Male</td>
<td>Perianal</td>
<td>100</td>
<td>100%</td>
<td>&gt; 3 months</td>
</tr>
<tr>
<td>2</td>
<td>Female</td>
<td>Perianal</td>
<td>50</td>
<td>Unknown</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Male</td>
<td>Perianal</td>
<td>100</td>
<td>75%</td>
<td>&gt; 3 months</td>
</tr>
<tr>
<td>4</td>
<td>Male</td>
<td>Penile</td>
<td>100</td>
<td>100%</td>
<td>&gt; 3 months</td>
</tr>
<tr>
<td>5</td>
<td>Male</td>
<td>Penile</td>
<td>100</td>
<td>Recurrence after 4 weeks</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Female</td>
<td>Perianal</td>
<td>100</td>
<td>100%</td>
<td>&gt; 3 months</td>
</tr>
<tr>
<td>7</td>
<td>Female</td>
<td>Vaginal</td>
<td>&lt; 10</td>
<td>100%</td>
<td>4 weeks</td>
</tr>
</tbody>
</table>

The 5-ALA was kindly provided by Janssen Clinica, Geel, Belgium.

These results, though in a very experimental stage, are promising. Pain is a major drawback. Up to now we did not use intraleional anaesthetics because of possible interference with PDT. A practical disadvantage is the relative long time that the 5-ALA has to be applied. Shorter application times will be investigated in the future.