Urinary tract infection: The role of canine transmissible venereal tumour

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ABSTRACT

The role of transmissible venereal tumours in the pathogenesis of urinary tract infection in dogs was investigated in 86 dogs. Fifty-five had transmissible venereal tumours, and the remaining 31 animals were used as controls. A thorough clinical examination of the external genitalia was carried out in each case. In the dogs with transmissible venereal tumours, the sites of attachment were recorded. Urine samples were taken by cystocentesis and the external genitalia swabbed; the samples were cultured for bacteria using standard methods. Tumours were found on the prepuce and other parts of the penis in male dogs; in bitches they were found in the vagina, vestibule or the vestibulovaginal junction. Dogs with transmissible venereal tumours were found to be at a high risk of having bacteriuria (odds ratio \([OR] = 7.04\)). Obliteration of the urethral orifice by the tumour, possibly leading to urine retention, was thought to be the main reason for the high incidence of urinary tract infection among dogs with transmissible venereal tumours. Long-standing cases of transmissible venereal neoplasia had a higher chance of becoming bacteriurioc compared with recent cases \((OR=29-60)\). This study indicates that transmissible venereal tumour may be a predisposing factor for the development of urinary tract infection.

INTRODUCTION

Urinary tract infection (UTI) is defined as the invasion of the normally sterile areas of the urinary tract by pathogenic bacteria, with subsequent clinical signs (Brown and Barsanti 1989). The most commonly isolated causes of UTI in dogs are Escherichia coli, Staphylococcus species, Proteus species, Klebsiella species and Streptococcus species (Bush 1984). E. coli is the bacteria most commonly isolated.

UTI is said to develop when normal host defences are compromised, thus allowing entrance and proliferation of opportunistic microbes (Lees and Osborne 1979). The most important host defence mechanism is the frequent and complete voiding of urine, which helps mechanically to remove the bacteria from the urinary tract (Senior 1985). Thus urine retention caused by obstruction, calculi or neoplasia of the urethra is a frequent cause of UTI (Bush 1984).

Transmissible venereal tumour (TVT) in bitches has the vestibulovaginal junction as its predilection site (Boscos 1988, Batamuzi and others 1990). The vestibulovaginal junction is the anatomical site of the urethral opening (Ellenport 1975) and, therefore, TVT in bitches can cause urethral obstruction resulting in dysuria and dribbling of urine. Phimosis, a condition that interferes with voiding of urine, has been reported to occur in male dogs with TVT (Ndiritu 1979). The prepuce forms a complete sheath around the cranial part of the penis (Ellenport 1975). Thus fully established preputial TVT is very likely to lead to obstruction of urine outflow.

In view of the threat that TVT poses in the development of UTI and the paucity of information available, the objective of the present study was to investigate the role of TVT in the development of UTI.

MATERIALS AND METHODS

Animals

Dogs with and without TVT were used in the study, selected from the Veterinary Clinic of the Sokoine University of Agriculture and from the dog dipping centre in Morogoro, Tanzania. The dogs belonged to different owners in Morogoro and its surroundings, and were either pets, guard dogs or hunting types. They were of different age groups and of both sexes, but only entire animals were used. For both the study and the control groups, systematic random sampling was done. In the case of the TVT group, every other dog
The role of TVT in urinary tract infection

with TVT attending the veterinary clinic was selected. For the control group, every fifth dog entering the dipping premises was selected. To ensure dogs selected for the control group did not have TVT, they were subjected to exfoliative cytology in a manner similar to that of Batamuzi and Kessy (1993).

Physical examination

All the dogs were subjected to a thorough physical examination of the genital system to establish the presence or absence of TVT and to assess the influence of the sites of attachment of TVT on the development of UTI. The stage of TVT, whether recent or long-standing and the extent of involvement of the external genitalia were also investigated. For the purposes of this study, recent cases were defined as those with small, solitary and easily accessible tumours. Long-standing cases were those with large, multilobulated and multifocal tumours.

Samples

Ten millilitres of urine was collected from each dog by cystocentesis using a sterile syringe and needle. The vestibulovaginal junction and the preputial cavity in females and males, respectively, were swabbed using a sterile swab. Urine and swabs were cultured within 30 minutes of collection on blood and MacConkey's agars, then incubated at 37°C for 24 hours. Qualitative urine culturing including isolation and identification of bacteria was undertaken (Osborne 1995). Where necessary, subculturing and biochemical tests to identify bacterial species were also carried out (Cowan 1974). For the purposes of this study, bacteriuria was defined as the bacterial invasion of the urinary tract (upper urinary tract and, or, urinary bladder) whereby infection is restricted to the urine (Osborne 1995).

Urine sediment examination

Some of the urine collected was used for preparation of the urine sediment and its microscopic examination as described elsewhere (Batamuzi and Kristensen 1995).

Statistical analysis

Frequencies of UTI for different independent variables were compared using a χ² analysis. The degree of association between the independent variables and UTI was measured by an odds ratio (OR) as described by Thrusfield (1986). In all calculations to measure the degree of association, it was assumed that there were no confounding factors other than sex. Thus the latter was the only variable for which the Mantel Haenszel technique – an analytical procedure for controlling the effect of extraneous factors – was employed to remove its effect. Using this technique, data were collected about potential predisposing factors and UTI, and on the presence or absence of potential confounding variables. These data were then stratified and displayed in a series of 2 × 2 tables, one table for each level of confounding variable. Additionally a summary of the tables was made to display a summary measure of association between the predisposing factors considered and UTI.

RESULTS

Of the 86 dogs examined, 55 (33 males and 22 females) had TVT while 31 (16 males and 15 females) had no TVT.

Sites of attachment

Of the 37 bitches examined, 22 had TVT. The tumour was found in the vagina in six bitches, the vestibule in six cases, the vestibulovaginal junction in eight cases, and there was diffuse involvement of the genital tract in two cases. Of the 49 males, 33 had TVT. The tumour was found on the caudal parts of the penis in 15 cases, middle parts of the penile shaft in three cases, prepuce 9 cases, penile tip in one case and there was diffuse involvement of external genitalia in five cases.

Bacteria from the external genitalia

Table 1 presents the bacterial species isolated and their frequency in male and female dogs. Bacteria isolated from the external genitalia were, in order of decreasing frequency, S aureus, Pasteurella species, E coli, Streptococcus species, Proteus species and Bacillus subtilis.

Bacteriuria

Of the 86 animals examined, 22 had bacteriuria. E coli, S aureus and Streptococcus species were isolated from these dogs (Table 2). E coli

<p>| Table 1. Bacteria isolated from the genital mucosa |</p>
<table>
<thead>
<tr>
<th>Species</th>
<th>Number of isolations</th>
<th>Control Male</th>
<th>Control Female</th>
<th>TVT cases Male</th>
<th>TVT cases Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aureus</td>
<td></td>
<td>4</td>
<td>3</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>Pasteurella multocida</td>
<td></td>
<td>4</td>
<td>2</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td></td>
<td>2</td>
<td>2</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>β-haemolytic streptococcus</td>
<td></td>
<td>1</td>
<td>3</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Bacillus subtilis</td>
<td></td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Proteus species</td>
<td></td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Pasteurella haemolytica</td>
<td></td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>α-haemolytic Streptococcus</td>
<td></td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>
was the most frequently isolated. Of the 22 cases of bacteriuria, 19 were from animals with TVT; controls accounted for three cases. E. coli was isolated from all three controls with bacteriuria.

There was a strong association between genital TVT and the development of bacteriuria (OR=7-05, χ²=6-27 and P<0-05). Even after using the Mantel Haenszel technique to remove the effect of sex, there remained a strong association between TVT and bacteriuria (OR=7-4, χ²=6-06 and P<0-05). Eighteen of the bacteriuric cases were from dogs and bitches in which TVT was found attached to areas surrounding the urethral opening. These sites were the prepuce, penile tip and diffuse involvement of external genitalia in males, and the vestibulovaginal junction and diffuse involvement of the external genitalia in bitches. Of the 55 TVT cases, 26 were long-standing and 29 were recent. Sixteen long-standing cases were bacteriuric compared with only two recent cases. Long-standing cases had a higher chance of becoming bacteriuric compared with recent cases (OR=29-60, χ² = 22-05 and P<0-05).

Of the 22 cases of bacteriuria, seven (30 per cent) had signs of cystitis based on urinary sediment findings (Kruger and Osborne 1993, Osborne 1995). These cases had bacteria and many white blood cells as well as red blood cells in the urinary sediment.

**DISCUSSION**

The entire urinary tract is at risk of microbial invasion once any of its normally sterile parts become colonised with bacteria (Brown and Barsanti 1989). The main source of infection is the skin and rectal bacteria (Bush 1984). In this study, a number of bacteria which are important in UTI were isolated from the external genitalia of dogs with TVT. This could mean that the external genitalia may be another important source of bacteria causing UTI. Studies of human patients indicate that colonisation of the vaginal and urethral mucosae precedes the occurrence of bacteriuria (Bollgren and Winberg 1976). The same mechanisms may be involved in the development of UTI in dogs. It is known that TVTs easily become traumatised, ulcerate and are frequently secondarily invaded by bacteria (Boscos 1988). Under these circumstances, the environment is ideal for invasion, colonisation and subsequent infection of the urinary tract by such bacterial pathogens.

The same bacteria were isolated from the urinary bladder as from the vagina; however, not all the species were involved.

Qualitative urine culture is considered an ideal technique when urine samples are obtained by cystocentesis (Stamey and Kindrachuk 1985). However, the possibility of false positive results as a consequence of contamination does exist (Osborne 1995). In view of this, it may be advantageous to perform quantitative urine culture, which aids in differentiating between pathogens and contaminants (Kruger and Osborne 1993).

In the majority of cases, E. coli was isolated from the urinary bladder. According to Schaeffer (1992), E. coli is endowed with fimbriae, an important facet for adherence on mucosal surfaces. Also some strains of E. coli do produce K antigens (Schaeffer 1992). Fimbriae and K antigens could be important in determining the pathogenicity of E. coli and could explain why it was a frequent isolate from the urinary bladder compared with other bacteria that had an equal chance of reaching it. About 25 per cent of all the dogs examined had bacteriuria and most of these were from cases of TVT. There was also a strong association between TVT and bacteriuria as indicated by a high OR of 7-4, even after eliminating the confounding effect emanating from the sex of the patient. There is therefore a strong indication that dogs with TVT are at a higher risk of contracting UTI compared to those without TVT.

If the location of TVT is taken into account, however, it becomes clear that dogs are at an even higher risk when the tumour is located in areas surrounding the urethral opening. Thus male dogs with TVT on the penile tip and prepuce and bitches with the tumour on the vestibulovaginal junction were more likely to have bacteriuria compared to those with the tumour in areas detached from the urethral orifice. The vestibulovaginal junction, the natural opening of the urethra, has been reported to be a predilection site for TVT in bitches and this has been found to cause dysuria in affected dogs (Boscos 1988). For male dogs, the caudal parts of the penis, mainly the area behind the bulbus glandis, is the site preferred by TVT (Boscos 1988, Batamuzi and others 1990). However, preputial TVT, especially in long-standing cases, is not uncommon (Batamuzi and others 1990). In these cases, phimosis and dysuria have been reported (Ndiritu 1979). Thus the location of TVT in these areas could explain the relationship between TVT and bacteriuria.

Long-standing cases of TVT were at a very high

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**Table 2. Bacteria isolated from urine of dogs with and without TVT**

<table>
<thead>
<tr>
<th>Species</th>
<th>Number of isolations</th>
<th>Control Male</th>
<th>Control Female</th>
<th>TVT Male</th>
<th>TVT Female</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Escherichia coli</em></td>
<td>1</td>
<td>2</td>
<td>9</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td><em>β-haemolytic Streptococcus</em></td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

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risk of becoming bacteriuric as indicated by the very high OR (29-60) that was obtained. Long-standing cases tend to lead to extensive involvement of the external genitalia in both sexes (Boscos 1988). Under these circumstances, obliteration of the urethral opening, especially in bitches, is likely to occur. Urine retention, a putative causal factor in the pathogenesis of UTI, becomes more likely (Lees and Osborne 1979).

Of the 22 cases with bacteriuria, seven (30 per cent) had signs of cystitis. This appears to suggest that a good proportion of bacteriuric cases have a chance of developing into clinical UTI. Certain factors may be required before clinical disease develops from the bacteriuric cases (Kruger and Osborne 1993, Osborne 1995). It was not the purpose of this study to identify those factors.

**CONCLUSION**

This study indicates that TVT may be a risk factor for the development of UTI. However, other factors may be required for initiating clinical UTI from bacteriuric cases of TVT. More studies are therefore necessary to establish the role of other factors in UTI causation.

**REFERENCES**


LEGRANGE, S. N., BREITSCHEIDER, E. E., GRINDEM, C. B. (1995) Erythrocyte fragility and chronic intermittent pigmenturia of one year’s duration. A TWO-year-old Shetland sheepdog had chronic intermittent pigmenturia of one year’s duration. The bitch was healthy between episodes. Multiple urinalysis had revealed haemoglobin and protein, but no erythrocytes. Survey and contrast radiography of the kidneys were negative. Results of physical examination were within normal limits. A complete blood count was normal except for mildly hypochromic erythrocytes. Erythrocytes from the bitch and two healthy control dogs were tested for alkaline and osmotic fragility. Both were markedly abnormal in the bitch, suggesting an increase in erythrocyte fragility. This was consistent with an erythrocyte enzyme abnormality that induced intravascular haemolysis and haemoglobinuria, and probably precipitated by stressful events such as exercise. The owners were advised to restrict exercise because the pigmenturia usually appeared after exercise. Although the commonest cause of erythrocyte fragility in dogs is a lack of enzymes, such as phosphofructokinase, three attempts to find a deficiency in this animal failed. Erythrocyte fragility was found to occur at a blood pH induced by hyperventilation, which is abnormal. Moderate exercise was consistently found to lower blood pH values to 7-5, a pH at which extensive lysis was found to take place in vitro.


**ABSTRACT**

Erythrocyte fragility and chronic intermittent pigmenturia in a dog

A TWO-year-old Shetland sheepdog had chronic intermittent pigmenturia of one year’s duration. The bitch was healthy between episodes. Multiple urinalysis had revealed haemoglobin and protein, but no erythrocytes. Survey and contrast radiography of the kidneys were negative. Results of physical examination were within normal limits. A complete blood count was normal except for mildly hypochromic erythrocytes. Erythrocytes from the bitch and two healthy control dogs were tested for alkaline and osmotic fragility. Both were markedly abnormal in the bitch, suggesting an increase in erythrocyte fragility. This was consistent with an erythrocyte enzyme abnormality that induced intravascular haemolysis and haemoglobinuria, and probably precipitated by stressful events such as exercise. The owners were advised to restrict exercise because the pigmenturia usually appeared after exercise. Although the commonest cause of erythrocyte fragility in dogs is a lack of enzymes, such as phosphofructokinase, three attempts to find a deficiency in this animal failed. Erythrocyte fragility was found to occur at a blood pH induced by hyperventilation, which is abnormal. Moderate exercise was consistently found to lower blood pH values to 7-5, a pH at which extensive lysis was found to take place in vitro.