Short reports

Urethral malignant melanoma closely mimicking urothelial carcinoma

J M Radhi

Abstract

Primary malignant melanoma of the urethra is very rare. In the male, the distal urethra is the most common site. The histopathology does not usually differ from that of melanoma at other body sites. This report describes a case of urethral malignant melanoma which closely resembled urethral carcinoma. It showed both papillary and solid growth, and the diagnosis only became apparent from special stains. Pathologists should be aware of this rare occurrence.

(*J Clin Pathol* 1997;50:250-252)

Keywords: urethra; malignant melanoma; transitional cell carcinoma.

Malignant melanoma is notorious for its great microscopic variability. The cell can be epithelioid, spindle shaped, or extremely bizarre. Melanin can be abundant, scanty, or absent. In addition, malignant melanoma may assume the histological guise of adenocarcinoma, small cell carcinoma, or sarcoma; it is therefore essential to use special studies to detect melanocytic differentiation.¹

Case report

An 88 year old male with a six month history of an enlarging lesion which protruded from the urethral meatus had symptoms of partial urinary obstruction and difficulty in voiding. He denied any history of dysuria, haematuria, or urethral discharge. On physical examination he was a healthy elderly man with a small polypoid growth protruding from the external urethral meatus. There was no evidence of inguinal lymphadenopathy. Rectal examination showed a moderately enlarged prostate, with no discrete nodule or induration. Urethroscopy revealed a reddish growth involving the left side of the fossa navicularis. Cystoscopy and intravenous pyelography showed no significant abnormality. Excisional biopsy was performed followed by partial amputation of the glans penis and distal urethra. The patient made an uneventful postoperative recovery and when discharged was voiding normally.

The tissue was fixed in 10% buffered formalin, embedded in paraffin, and stained with haematoxylin and eosin, periodic acid Schiff

Figure 1 (A) A low power view of urethral malignant melanoma showing striking resemblance to papillary urothelial carcinoma. (B) Higher magnification shows neoplastic cells with atypical nuclei and finely granular cytoplasm.

(PAS), Pearls, and Fontana-Masson. Immunohistochemical studies were performed on formalin fixed tissue using a routine avidin-biotin-peroxidase complex technique with appropriate positive and negative controls. The following antibodies were used: low molecular weight keratin (Becton-Dickinson); high molecular weight keratin, epithelial membrane antigen, carcinoembryonic antigen (Dako); S100 protein (HSC, Research Development Corporation, Toronto); and HMB45 (Enzo Diagnostic). Electron microscopy was performed on formalin fixed tissue after postfixation in 3.2% glutaraldehyde.

Histological examination of the urethral biopsy showed a papillary and a solid malignant neoplasm, with a striking resemblance to urothelial carcinoma. The papillary structures were covered by thickening urothelial-like epithelium, showing atypical nuclear features and mitotic activity. High power examination

Department of
Pathology, College of
Medicine, University
of Saskatchewan,
Saskatchewan, Canada
J M Radhi

Correspondence to:
Dr J M Radhi, Department
of Pathology, College of
Medicine, University of
Saskatchewan, B419 Health
Science Building, 107
Wiggins Road, Saskatoon,
Saskatchewan, S7N 5E5
Canada.

Accepted for publication
10 December 1996

Figure 2 Immunoperoxidase stain shows positivity for S100 protein marker.

Figure 3 Melanoma cells with aberrant melanosomes and premelanosomes (electron microscopy, $\times 18\,225$).

showed occasional cells with fine brown granules (fig 1, A and B). These granules were highlighted with melanin stain. Immunoperoxidase staining for S100 protein and HMB45 showed these to be strongly expressed by the neoplastic cells (fig 2). The tumour cells were negative for cytokeratin, EMA, and CEA. Electron microscopy showed polygonal tumour cells with irregular nuclei and variable expression of melanosomes and premelanosomes (fig 3). Individual cells did not have

junctions or basal lamina. The lesion extended to the glans penis and measured 3.7 mm in thickness. Based on these findings a diagnosis of malignant melanoma was made. The second excision contained a small focus of a residual malignant melanoma.

Discussion

Primary malignant melanoma of the genitourinary tract is a rare disease.² The most common areas of involvement are the penis and urethra. In the male the distal urethra (fossa navicularis and meatus) predominates over the pendulous, bulbous, and prostatic urethra as the sites of most frequent occurrence.²⁻⁴ The tumours may be multifocal and occur in any portion of the urethra.⁵ Ninety per cent of cases are patients in their sixth or seventh decade.

Presenting symptoms include palpable mass, haematoma, bloody urethral discharge, fistula, persistent dysuria, and obstructive symptoms. More specific for this disease is melanuria.⁵⁻⁷ Delays in diagnosis are common, with the interval from onset of symptoms to diagnosis averaging 24 months.⁷ The aetiology and pathogenesis is unknown, but origin from precursor naevus has been reported.³ Lesions in the urethra may also be secondary to melanomas of the glans penis or labia.⁸ The pathology does not differ from that at other body sites.

In our case pathological examination showed a papillary and solid lesion closely mimicking urothelial carcinoma. Its true nature became obvious only after high power examination and the finding of fine brown granules in some tumour cells. The diagnosis of melanoma was supported by immunohistochemical stains and electron microscopy. Melanin and haemosiderin pigments look identical in routine histological stains and require special stains for their identification. Without the application of immunohistochemical stains, this case would easily have been misdiagnosed as urothelial carcinoma. Moreover, if this was an amelanotic melanoma it would be very unlikely that it would receive further attention by special staining. Because the prognosis is different, it is important that pathologists and urologists are aware of this rare tumour. Though follow up information is limited on patients with urethral malignant melanoma, the risk of metastases and tumour related death within three years of diagnosis is high.^{2,9} The rarity of this lesion and the great variability of response to treatment make an assessment of the most beneficial type of treatment impossible.⁵

I thank Mrs Suniti Saini for typing this manuscript and Mrs Karen Slattery electron microscopic assistance.

- 1 Nakhleh RE, Wick MR, Rocamora A, Swanson PE, Dehner LP. Morphologic diversity in malignant melanomas. *Am J Clin Pathol* 1990;93:731-40.
- 2 Peterson RO. In: *Urologic pathology*, 2nd ed, chapter 5. Philadelphia: JB Lippincott, 1993:415-6.
- 3 Sanders TJ, Denable DD, Sanusi ID. Primary malignant melanoma of the urethra in a black man: a case report. *J Urol* 1986;135:1012-4.
- 4 Begun FP, Grossman HB, Diokno AC, Sogani PC. Malignant melanoma of the penis and male urethra. *J Urol* 1984;132:123-5.
- 5 Poore RE, McCullough DL. Urethral carcinoma. In: Gillenwater JY, Howards SS, Duckett JW, eds. *Adult and pediatric urology*, vol 2, 3rd ed, chapter 36. St Louis: CV Mosby, 1996:1845-6.

- 6 Oldbring J, Mikulowski P. Malignant melanoma of the penis and male urethra: report of nine cases and review of the literature. *Cancer* 1987;59:581-7.
- 7 Pow Sang JM, Klimbert IW, Hackett RL, Wajzman Z. Primary malignant melanoma of the male urethra. *J Urol* 1988;139:1304-6.
- 8 Katz JL, Grabstald H. Primary malignant melanoma of the female urethra. *J Urol* 1976;116:454-7.
- 9 Manivel JC, Fraley EE. Malignant melanoma of the penis and male urethra: 4 case reports and literature review. *J Urol* 1988;139:817-8.

Mucopolysaccharidosis type VII associated with hydrops fetalis: histopathological and ultrastructural features with genetic implications

A J Molyneux, E Blair, N Coleman, P Daish

Abstract

A case of mucopolysaccharidosis type VII (MPS VII, β glucuronidase deficiency) causing fatal hydrops fetalis in the third trimester is presented. The diagnosis was suspected on histopathological examination by the presence of foam cells in many of the viscera and foamy change in the placental Hofbauer cells. Electron microscopy showed empty cytoplasmic inclusion bodies within macrophages and in the Hofbauer cells. Enzyme assay of cultured fibroblasts showed markedly deficient β glucuronidase activity, thus confirming the diagnosis. A detailed and thorough histopathological examination of hydrops fetalis cases is important to detect subtle features of inherited metabolic disorders. Use of a structured necropsy protocol is recommended for cases of non-immune hydrops. Electron microscopy is a useful adjunct to light microscopy in cases where an inherited metabolic disorder is suspected. Precise necropsy diagnosis is important as there are implications for genetic counselling and possible prenatal diagnosis in subsequent pregnancies.

(*J Clin Pathol* 1997;50:252-254)

Keywords: mucopolysaccharidosis type VII; hydrops fetalis; electron microscopy.

Case report

This boy was the second child of healthy unrelated parents. Their first child, a girl aged three years, is well. The boy was delivered by caesarean section for fetal distress at 32 weeks' gestation. Birth weight was 3.06 kg (3.6 standard deviations above the mean). Gross hydrops was noted and there was no detectable heart beat. Attempts at resuscitation were unsuccessful. Initial investigations including direct Coombs test, haemoglobin electrophoresis, and parvovirus B19 IgM titres revealed no obvious cause for the hydrops.

PATHOLOGICAL FINDINGS

External examination confirmed a grossly hydropic male baby. Assessment of the facies was complicated by oedema but it was not obviously abnormal. Internal examination revealed a dilated heart and pulmonary hypoplasia (combined weight 10.6 g, expected 34±11 g; lung/body weight ratio 0.003). The liver was pale and slightly enlarged (82.4 g, expected 65±22 g) and there was splenomegaly (19.6 g, expected 4.1±2.1 g). There were blood stained pleural and peritoneal effusions and there was fresh haemorrhage into soft tissues in the neck and mesentery. Other gross features were unremarkable and there were no malformations.

The placenta was large (fixed weight 765 g) but otherwise appeared grossly normal.

Microscopic examination showed finely vacuolated interstitial foamy cells present in many organs, but most noticeably in the spleen, lung, myocardium, bowel mucosa, and bone marrow (fig 1). Similar vacuolation was seen in hepatocytes, proximal convoluted tubules, and cerebral cortex, probably in microglial cells. The placenta also showed a subtle vacuolation of villous Hofbauer cells and a normal appearance of the cytotrophoblast, features suggestive of MPS VII. Electron microscopy of lung tissue showed numerous mainly empty cytoplasmic vacuoles (fig 2). Although not specific, the ultrastructural findings also suggested the possibility of a metabolic storage disorder.

The diagnosis of MPS VII was confirmed by quantitation of enzyme activity in cultured fibroblasts. β Glucuronidase enzyme activity was negligible (0.27 nmol/h/mg protein, normal range 48-360 nmol/h/mg protein). Control enzymes (β galactosidase and α fucosidase) showed activity within their normal ranges.

Discussion

A wide variety of conditions may give rise to non-immune hydrops fetalis, and a structured approach to the perinatal necropsy is therefore

Department of Cellular Pathology, Northampton General Hospital NHS Trust, Northampton
A J Molyneux

Department of Clinical Genetics, Churchill Hospital, Oxford
E Blair

Department of Histopathology, Addenbrooke's Hospital, Hills Road, Cambridge
N Coleman

Department of Paediatrics, Northampton General Hospital NHS Trust, Billing Road, Northampton NN1 5BD
P Daish

Correspondence to: Dr A J Molyneux.

Accepted for publication 10 December 1996