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Hypospadias and the embryogenesis of the penile urethra

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Summary—The findings of a histological study of a rare specimen of a human hypospadias penis are presented. These findings suggest that distal pits are due to arrested development of the glandar urethra. The present findings also indicate that accessory urethrae and possibly the ventral position of the urethral meatus are the result of an intrinsic abnormality of the urethral plate.

Specimens of the human hypospadias penis rarely become available for anatomical study with the result that published histological studies of a complete hypospadias penis are uncommon (Marshall *et al.*, 1978).

Recently, the present authors were fortunate enough to acquire an intact specimen of a human penis with a hypospadias deformity. The aim of the present study was to undertake a histological study of this specimen, and to relate the urethral abnormalities found to the normal embryological development of the penile urethra.

The normal penile urethra develops in two phases. Before the 9th week of gestation the external genitalia of both sexes are represented by a genital tubercle and an urethral plate. The mesenchyme on either side of the urethral plate proliferates to form the urethral folds, which in turn enclose the urethral groove. The urethral folds do not reach the tip of the genital tubercle (Fig. 1).

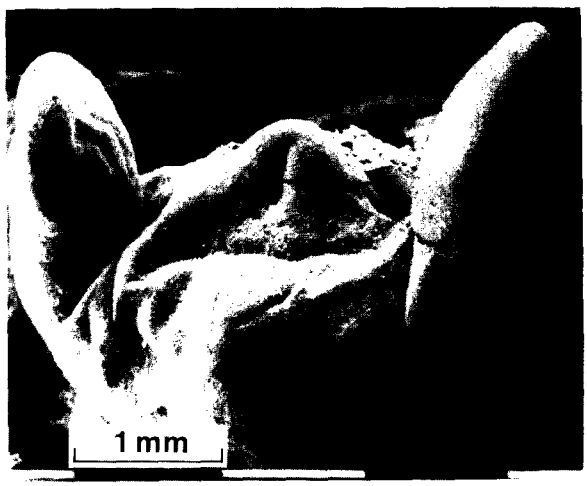

Fig. 1

Figure 1—Scanning electron micrograph of the genital tubercle of a 7 week human embryo. The urethral folds, which are on either side of the urethral groove (arrow), do not reach the tip of the genital tubercle.

From the 9th week of gestation onwards the external genitalia develop a male configuration under the influence of hormones secreted by the developing testes, and the genital tubercle elongates to form the phallus. This elongation of the genital tubercle is accompanied by the appearance of the coronal sulcus which delineates the glans from the shaft of the developing penis.

On the ventral surface of the shaft the urethral folds become increasingly more pronounced, and at the end of the 12th week these folds begin to fuse in the mid-line to form the urethra (Fig. 2).

There is general agreement that fusion of the urethral folds from proximal to distal results in the formation of the penile urethra as far distal as the coronal sulcus (Moore, 1982). However, there is no such agreement about the formation of the urethra distal to the coronal sulcus.

Hart in 1908 and Jones in 1910 concluded from their respective studies, that the whole of the glandar urethra is formed by the in-growth, and subsequent canalisation, of a cord of epithelial cells from the tip of the glans.

An alternative theory was proposed by Hunter in 1935 when he reported that the whole of the glandar urethra is formed by the fusion of the urethral folds. Hunter's concept of the formation of the glandar urethra has been recently supported by Devine (1980).

A third view of the formation of the glandar

Fig. 2

Figure 2—Scanning electron micrograph of the phallus of a 12 week male human foetus. The coronal sulcus (arrow) separates the glans from the shaft of the penis, and the urethral folds have met in the midline on the ventral surface of the shaft.

urethra was proposed by Glenister in 1954, following his study of 37 human embryos. Although Glenister confirmed that the distal part of the glandar urethra is formed by a lamellar in-growth of epithelial cells from a terminal tag at the tip of the glans (Fig. 3), he concluded that the proximal part of the glandar urethra is formed by fusion of the urethral folds.

Method

The hypospadias penis included in the present study was obtained from a 9-week-old infant who had died with severe cardiac defects comprising double outlet right ventricle and interrupted aortic arch. The left kidney was small with marked hydronephrosis and moderate dilatation of the ureter. The penis had a ventral meatus just proximal to the coronal sulcus, the prepuce was deficient ventrally and there was some degree of chordee (Fig. 4). There was a distal pit visible at the tip of

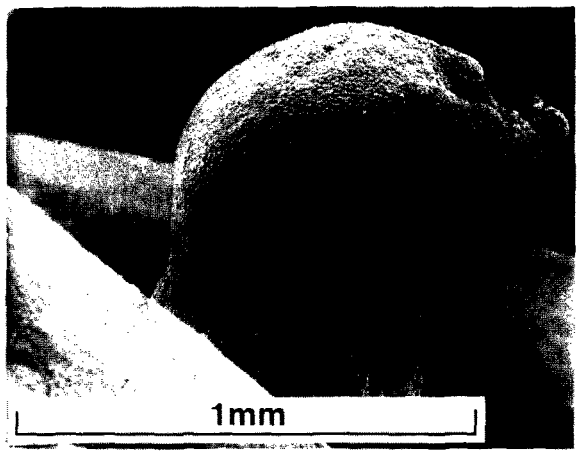

Fig. 3

Figure 3—Scanning electron micrograph of the glans of a male human foetus demonstrating the terminal epithelial tag.

the glans and some of the skin on the ventral surface of the shaft was missing (Fig. 5).

The penis was fixed in formol saline, and serial transverse histological sections were made from distal to proximal. Each section was stained with haematoxylin and eosin.

Results

Figure 6 is a photomicrograph of a transverse section through the distal third of the glans, and in the centre of the section there is an epithelial lined tube which corresponds to the distal pit. In the centre of the transverse section taken through the middle third of the glans, there is a vertical lamella of epithelial cells (Fig. 7).

In the section through the proximal part of the glans just distal to the ventral meatus, there are no epithelial cells within the substance of the glans (Fig. 8A). On the ventral surface of the glans at this level there is a remnant of the urethral plate (Fig. 8B).

A transverse section of the penile shaft proximal to the ventral meatus (Fig. 9A) shows the presence of the corpora cavernosa, the spongy urethra and an accessory urethra. The accessory urethra is more obvious at higher power (Fig. 9B).

Discussion

The three urethral abnormalities seen in the hypospadias penis examined in the present study

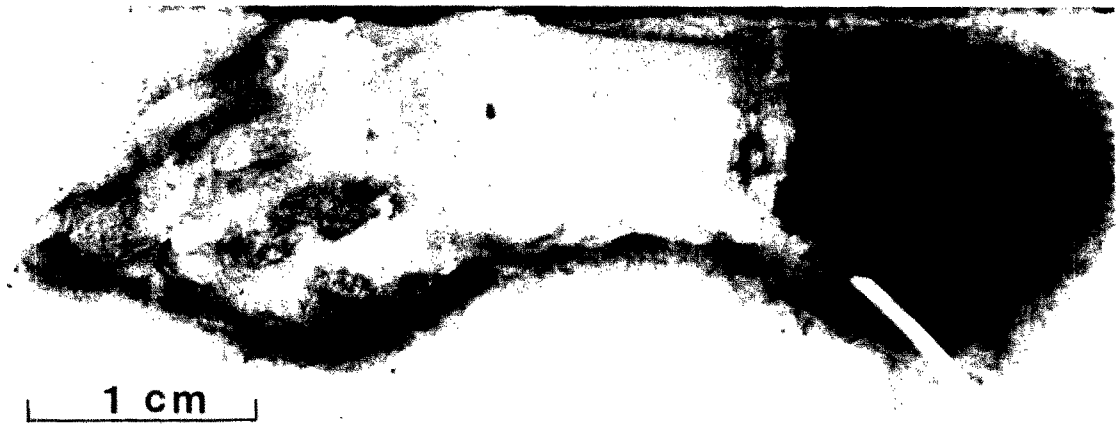

Fig. 4

Figure 4—Macroscopic view of the hypospadias penis showing the ventrally deficient prepuce and the ventral curvature. A piece of clinifeed tube has been placed in the urethral meatus.

Fig. 5

Figure 5—Macroscopic view of the hypospadias penis with the distal pit indicated by the arrow. Much of the skin is missing from the ventral surface of the shaft.

were: the ventral meatus, the distal epithelial lined pit and the accessory urethra. In this discussion an attempt will be made to explain these urethral abnormalities in terms of the embryological development of the penile urethra.

The presence of the epithelial lamella in the middle third of the glans (Fig. 7), which is in continuity with the distal epithelial lined pit (Fig. 6), endorses the view that the distal glandar urethra is formed by the canalisation of a cord of epithelial cells which have grown in from the tip of the glans (Hart, 1908; Jones, 1910; Glenister, 1954). The urethral plate remnant found on the ventral surface of the proximal glans (Fig. 8B) is in keeping with Glenister's conclusion that the proximal glandar urethra is formed by the fusion of the urethral folds. Therefore, Glenister's concept of the embryogenesis of the whole of the glandar urethra is supported by the findings in this specimen.

In terms of the pathogenesis of the hypospadias

Fig. 6

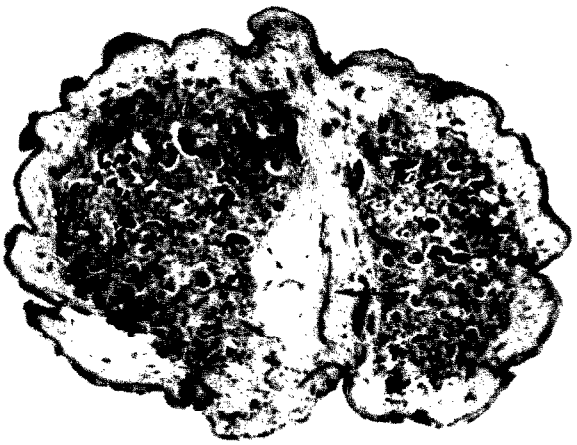

Fig: 7

Figure 6—Photomicrograph of a transverse section through the distal third of the glans. In the centre of the section the epithelial lined tube is indicated by the arrow. Figure 7—Photomicrograph of a transverse section through the middle third of the glans. The vertical lamella of epithelial cells is indicated by the arrow.

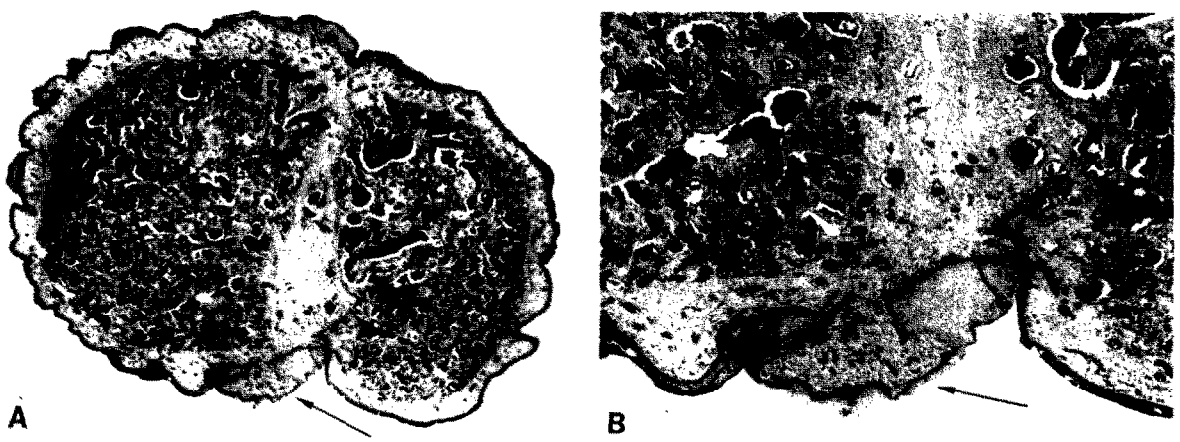

Fig. 8

Figure 8—(A) Photomicrograph of a transverse section through the proximal third of the glans. On the ventral surface is the urethral plate remnant (arrow); no epithelial cells are seen within the substance of the glans. (B) A high power view of the same section showing the urethral plate remnant (arrow) more clearly.

deformity, the presence of a distal pit, a lamella of epithelial cells and an urethral plate remnant in the glans can be explained by an arrest of normal development of the glandar urethra.

In our specimen it was not possible to demonstrate any continuity between the epithelial lamella seen in the glans and the accessory urethra present in the distal shaft (Fig. 8A). This lack of continuity indicates that the accessory urethra, which is a common feature of the hypospadias deformity (Townsend, 1978), is not the canalised proximal remnant of an in-growing cord of epithelial cells, but occurs as the result of a primary urethral plate abnormality.

The ventral urethral meatus, which is an integral part of the hypospadias deformity, is due to a failure

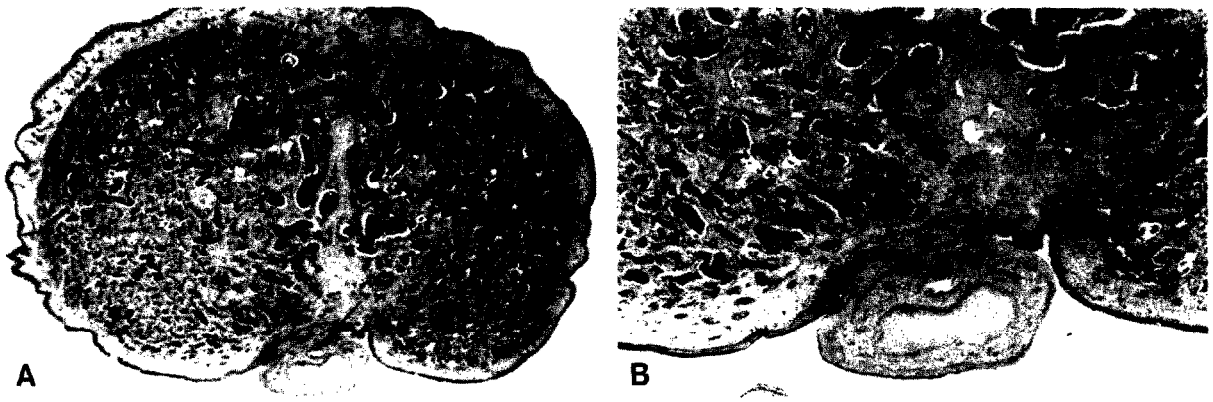

Fig. 9

Figure 9—(A) Photomicrograph of a transverse section through the shaft proximal to the ventral meatus. An accessory urethra is visible (arrow) just dorsal to the spongy urethra. (B) A high powered view of the same section shows the accessory urethra (arrow) more clearly.

of fusion of the urethral folds. Some controversy exists as to whether this failure of fusion is due either to an arrest of normal development or to testicular hypogonadism (Vaughan and Middleton, 1975). Alternatively, failure of fusion of the urethral folds could be the result of the intrinsic urethral plate abnormality. Irrespective of the cause of the failure of fusion it can be concluded, from our present knowledge of the embryological development of the spongy urethra, that the earlier in gestation that the fusion of the urethral folds fails, the more proximal will be the ventral meatus.

Although there have been many studies of "chordee tissue" (Paul and Kanagasuntheram, 1956; Avellan and Knutsson, 1980; Page, 1981), there is some evidence that ventral curvature of the penis is a feature of the normal embryological development of the penis (Glenister, 1954; Jirasek, 1971; Kaplan and Lamm, 1975). The absence of a definite band of chordee tissue in the present specimen is in agreement with the findings of Kaplan and Lamm (1975) who found that 41 of the 46 normal male foetuses in their study had a ventral curvature of the penis. Kaplan and Lamm also reported that the ventral curvature involved all penile layers and that no cord or band was seen in any specimen.

However, it is not possible to draw any firm conclusion about the apparent absence of chordee tissue in our specimen because of the very distal position of the meatus.

Conclusion

The findings of the present study indicate that in the hypospadias penis the presence of a distal pit can be explained in terms of an arrest of normal development of the glandar urethra. Our findings also indicate that presence of accessory urethrae, and possibly the failure of fusion of the urethral folds, occur because of an intrinsic abnormality of the urethral plate.

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References

Avellan, L. and Knutsson, F. (1980). Microscopic studies of curvature-causing structures in hypospadias. *Scandinavian Journal of Plastic and Reconstructive Surgery*, **14**, 249.

Devine, C. J. (1980). Embryology of the male external genitalia. *Clinics in Plastic Surgery*, **7**, 141.

Glenister, T. W. (1954). Origin and fate of urethral plate in man. *Journal of Anatomy*, **88**, 413.

Hart, D. Berry (1908). On the role of the developing epidermis in forming sheaths and lumina to organs, illustrated specially in the development of the prepuce and urethra. *Journal of Anatomy*, **42**, 50.

Hunter, R. H. (1935). Notes on development of prepuce. *Journal of Anatomy*, **70**, 68.

Jirasek, J. E. (1971). *Development of the genital system and male pseudohermaphroditism*. Cohen, M. M. (Ed.). Baltimore and London: The Johns Hopkins Press.

Jones, F. W. (1910). The development and malformations of the glans and prepuce. *British Medical Journal*, **1**, 137.

Kaplan, G. W. and Lamm, D. L. (1975). Embryogenesis of chordee. *Journal of Urology*, **114**, 769.

Marshall, M., Beh, W. P., Johnson, S. H., Price, S. E. and Barnhouse, D. H. (1978). Etiologic considerations in penoscrotal hypospadias repair. *Journal of Urology*, **120**, 229.

Moore, K. L. (1982). *The developing human: Clinically orientated embryology*. 3rd. Ed. Philadelphia: W. B. Saunders and Co.

Page, R. E. (1981). Hypospadias revisited. *British Journal of Plastic Surgery*, **34**, 149.

Paul, M. and Kanagasuntheram, R. (1956). The congenital anomalies of the lower urinary tract. *British Journal of Urology*, **28**, 118.

Townsend, P. L. G. (1978). Accessory urethras in hypospadias. *British Journal of Plastic Surgery*, **31**, 309.

Vaughan, E. D. Jr. and Middleton, G. W. (1975). Pertinent genitourinary embryology: Review for Practising Urologist. *Urology*, **6**, 139.

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