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Case report

Glomerular changes in trisomy 18-related horseshoe kidney: report of a case and review of the literature

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Abstract

A case of horseshoe kidney is reported in a 11 week-old fetus affected by trisomy 18. Macroscopic examination did not show any other pathological change. The histological picture of the fused-kidney was characterized by architectural and glomerular changes. At x 100 magnification, large areas of metanephric mesenchyme, characterized by spindle cells surrounded by a loose oedematous stroma, were detected in the deep cortex and in the medulla. At higher power, multiple glomerular changes were observed. Maldeveloped glomeruli showed enlarged capsular spaces, adhesions between vascular tuft and capsular cells, podocytes in multiple layers, and large glomerular bodies formed by two vascular tufts. Our data confirm previous reports on glomerular changes in horseshoe kidney, and reinforce the hypothesis that horseshoe kidney should not be considered a simple fusion problem, but a complex developmental abnormality, possibly involving glomerular development.

Keywords

Horseshoe kidney, trisomy 18, glomerulus, clinical case, review.

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Introduction

The horseshoe kidney is a congenital disorder in kidney development: it is the most common renal fusion abnormality, affecting about 1 in 500 people [1]. It is the result of the fusion of the lower poles of both kidneys, to form a horseshoe-shape during intrauterine development, the fusion being called isthmus of the horseshoe kidney and consisting of connective tissue and renal parenchyma [2]. The fusion of the lower poles, that give rise to the horseshoe kidney, occurs before the rotation and the ascension of the kidneys: as a consequence, the renal pelvis is positioned ventrally and the caliceal system is positioned posteriorly. Horseshoe kidney is frequently associated with other malformations and, in particular, with additional urogenital anomalies, that are found in 5-10% of patient. The most frequent chromosomal anomaly associated with horseshoe kidney is trisomy 18 [3]. At histological study, the horseshoe kidney was reported to be characterized by a normal glomerular and tubular architecture, whereas nephron development was not affected by the fusion abnormality. As a consequence, horseshoe kidney is completely asymptomatic in the vast majority of subjects, eventhough carriers of this peculiar condition may experience kidney stones, hydronephrosis and urinary tract infections at greater frequency than those subjects with two distinct kidneys [2, 4, 5]. Since no microscopic changes are present in nephron structure in horseshoe kidney, it can be used for renal transplants [6]. The opportunity of observing the histological picture of a horseshoe kidney of a fetus carrying 18 trisomy, is the aim of this report.

Case report

Therapeutic abortion was performed in an 11-week pregnancy following the diagnosis of chromosome 18 trisomy. Macroscopic examination of the aborted fetus revealed the presence of a horseshoe kidney. No other significant pathological changes were observed; the cranial-sacral lengthness was 56 mm, whereas the foot length was 9 mm. Tissue samples from different organs were formalin-fixed and routinely processed. Kidney sections were stained with hematoxylin-eosin, PAS and Jones' silver stains. The histological picture of the fetal kidney was characterized, at x 100 magnification, by major architectural changes. The metanephric mesenchyme, characterized at histology by spindle-shaped cells immersed in an abundant loose and oedematous stroma, appeared much more diffuse than expected for gestational age, being detected in large areas both in the developing medulla and in the deep cortex (**Fig. 1A**). Moreover, roundish nodules of undifferentiated mesenchyme, surrounding renal vesicles were detected in the deep cortex, at the cortico-medullary junction (**Fig. 1B**). Small cysts were also observed in the cortex. At x 250 and x 400 magnification, while tubuli did not show major changes, the histological study of glomeruli revealed multiple pathological changes, detected in the majority of nephrons. The most relevant pathological glomerular changes were: 1) glomerular fusion, giving rise to large glomerular bodies formed by the confluence of two vascular tufts, and characterized by a large glomerular space (**Fig. 1C**); 2) hypertrophy and hyperplasia of developing podocytes, giving rise to glomeruli with podocyte precursors arranged in two-three layers (**Fig. 1D**); 3) mesangial nodules, occupying the core of enlarged atypical glomeruli (**Fig. 1E**); 4) atrophic glomeruli, characterized by a small retracted vascular tuft surrounded by an enlarged capsular space (**Fig. 1F**).

Discussion

Our case clearly shows that the horseshoe kidney may be associated with important architectural and glomerular changes, that are present in the early phase of renal development. The persistence, at 11 weeks of gestation, of large kidney areas occupied by metanephric mesenchyme, suggests the hypothesis that trisomy 18 might be associated with a delayed kidney development. In fact, the comparison with the histological picture of some kidneys from fetuses with the same gestational age evidenced the abundance of metanephric mesenchymal cells in the horseshoe kidney, as compared with normal kidneys. Moreover the detection of severe structural anomalies in the vast majority of glomeruli, lay stress on the hypothesis of a abnormality in nephrogenesis in the horseshoe kidney, with possible important consequences on kidney function. A previous study on renal function in a large series of adult subjects with horseshoe kidney showed that all had at least one abnormality, including hypovolemia, hypercalcuria and hypocitraturia with an average

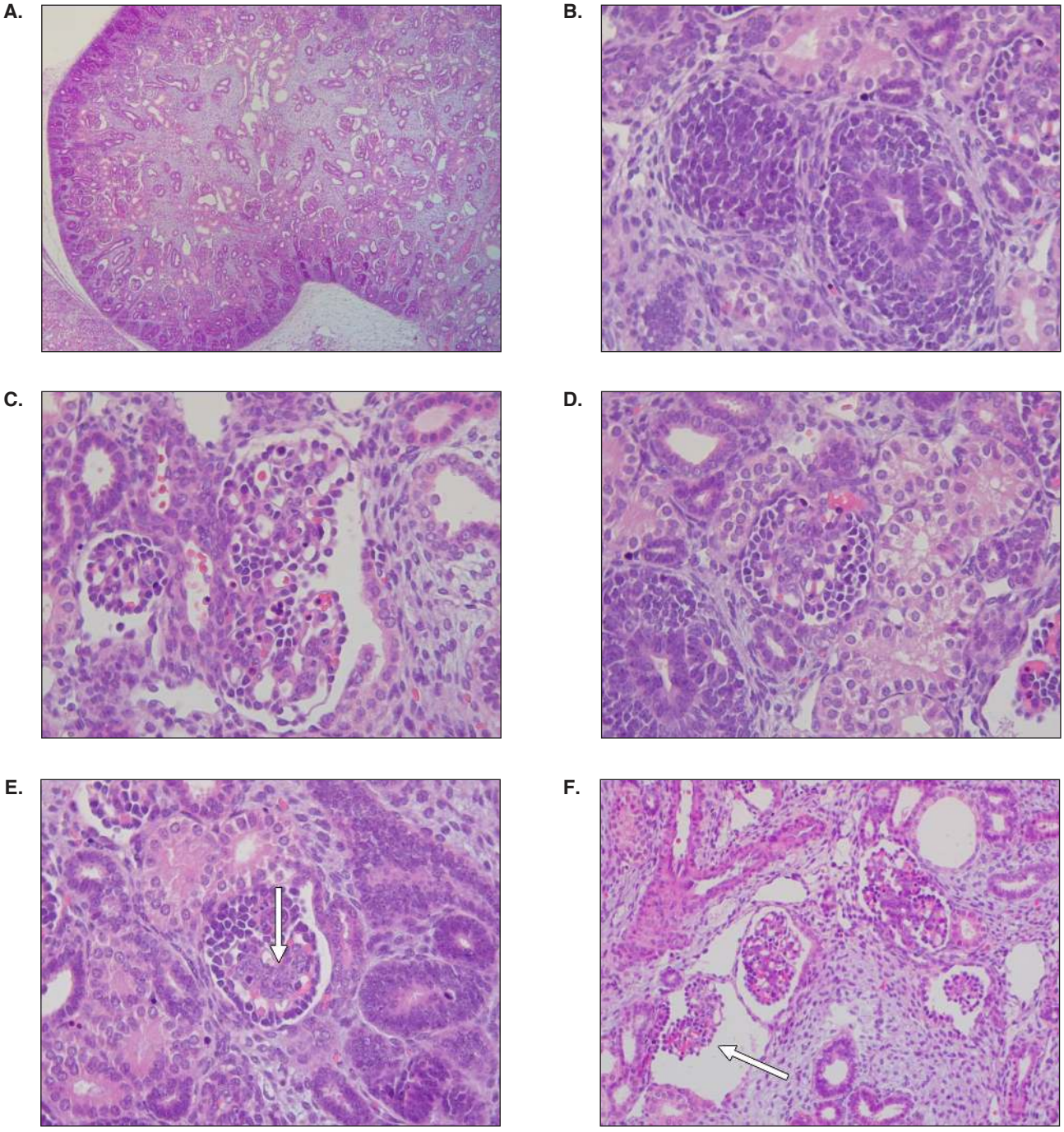

Figure 1. Architectural and glomerular changes in horseshoe kidney.

A. Original magnification x 100. The metanephric mesenchyme, characterized at histology by spindle-shaped cells immersed in an abundant loose and oedematous stroma, is much more diffuse than expected for gestational age, being detected in large areas both in the developing medulla and in the deep cortex.

B. Original magnification x 400. Roundish nodules of undifferentiated mesenchyme, surrounding renal vesicles, is detected in the deep cortex, at the cortico-medullary junction.

C. Original magnification x 400. The glomerular fusion gives rise to a large glomerular body formed by the confluence of two vascular tufts, and characterized by a large glomerular space.

D. Original magnification x 400. The hypertrophy and hyperplasia of developing podocytes gives rise to glomeruli with podocyte precursors arranged in two-three layers.

E. Original magnification x 400. Mesangial nodules (arrow) occupying the core of enlarged atypical glomeruli.

F. Original magnification x 250. The atrophic glomeruli (arrow) are characterized by a small retracted vascular tuft surrounded by an enlarged capsular space.

of 2.68 abnormalities per 24-hour urine collection (range 1-4). Low urine output was noted in eight out of 37 patients [4].

Regarding the histological glomerular changes hereby described, a previous study evidenced the occurrence in a case of horseshoe kidney of a decrease in the number of glomeruli, associated with a compensatory enlargement of the glomeruli. In the same fused-kidney, other glomeruli appeared atrophied and filled with eosinophilic material [1]. Glomerular changes were also described in the early 90's in a horseshoe kidney. In that study, glomerulocystic kidney disease (GCD) was described in a 3 months old child affected by trisomy 18 [7] and in another 6 months old child. In the second case, GCD was restricted to one side of a horseshoe kidney.

Our data evidence the possibility that the horseshoe kidney should not be solely considered a "fusion" problem, but it should be seen as a complex abnormality of kidney development, and confirm previous isolated case-reports on the occurrence of glomerular changes associated with this disease [1, 7]. In our case, glomeruli appeared to be the mainly altered nephron segment, in the absence of severe pathological changes in proximal and distal tubules. These findings suggest the hypotesis that the horseshoe kidney might represent a spectrum of histological pictures: at one extreme, normal kidney development, in the absence of any pathological change; at the other extreme of the spectrum, we could hypothesize a horseshoe kidney with important glomerular modifications, possibly leading to major functional impairment in the kidney. Our finding of major glomerular change in a case of horseshoe kidney associated with trisomy 18, together with the previous finding of glomerularcystic kidney disease associated with trisomy 18, might induce to hypothesize that this trisomy could be associated with structural and glomerular changes. Further studies are needed on the histological picture of large series of horseshoe kidneys, in order to better understand if our report should be considered as an occasional finding, or if developmental and histological changes could be present in some cases of horseshoe kidneys. Immunohistochemical analyses are also needed, in order to determine if the expression of protein products typically found during kidney development [8, 9] are modified in horseshoe kidneys.

Declaration of interest

No conflicts of interest exist.

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