Morphological development of the metanephric glomeruli in rat during peri-natal period

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Abstract:

Background
The metanephric glomeruli develop from the metanephric blastema and ureteric bud. The nephron anlage undergoes multiple differentiation stages, fusion and invagination that lead to the formation of nephron.

Objectives
To describe the morphological changes and transformations that lead to formation of metanephric permanent glomerulus during peri-natal period.

Method
The study was performed on albino rat as a model for mammalian embryonic development. Embryos of 20-22 days of gestation and neonatal litters were investigated for renal development. The specimens were double fixed, plastic embedded and semi-thin sections stained with methylene blue were examined

Results
It was shown that glomerular development continues during late pre-natal days and first week post-natally. Maturity was attended by the end of the 7th post-natal day. The developing glomerulus passes through the stages describes as vesicle, comma, S-shaped, double comma, elongation and ovale stage to become finally mature.

Conclusion
The metanephric glomerulus passes through sequential, multi-stage, pleomorphic development during peri-natal period. These features should be considered during evaluation of kidney during this period.

Key Words: Metanephros, Glomerulus, Development

Introduction

The renal system develops from the intermediate mesoderm which extends along the dorsal body wall of the embryo. This mesoderm gives rise to the nephrogenic ridge from which the renal systems develops (1). During the development of the urinary system, three nephric systems will develop, which overlap each other in position and time of development. These systems are the pronephros, mesonephros and metanephros (2).
Mammalian permanent kidney develops from two distinct elements, from the caudal part of the nephrogenic ridge which forms the meta-nephric blastema that gives rise to excretory system, and from the caudal part of the mesonephric duct which forms the ureteric bud that gives rise to the collecting system (3).The mesonephric reteric bud invades the metanephric blastema. This invading bud is directed to branch dichotomously to form a T-shaped structure. This branching mode is maintained sequentially to express the arborizing structure of the collecting ducts which establishes the general structure of the kidney (4).
The tips of the branching (collecting) buds induce the clustering of mesenchymal cells in the metanephric cap to convert into an epithelial phenotype. These cell aggregates represent a nephron anlage that undergoes many mitotic cycles and differentiation stages, fusion with the duct, invaginated by a tuft of capillary and subsequently generates the nephron (5).
The aim of this work is to describe the morphological changes and transformations that takes place during the period of the formation of the metanephric permanent glomerulus, with special emphasis on later stages of pre-natal life and during neonatal period.

Materials and Methods

This study was performed on albino rats (Rattus rattus norvegicus albinus), as a model for mammalian embryonic development. Mating was done by keeping female and male rats in combined cages. The presence of vaginal plug was considered as an indication of copulation. "Days post-coitum"(dpc) were subsequently designated and the pregnant rats were followed up till term.Near term females with 20-22 dpc were sacrificed and embryos retrieved. Each embryo was carefully dissected and the whole kidney was obtained. The total number of such full-term embryos included in this study was twenty.

Full-term pregnant female rats were allowed for normal vaginal delivery. The total number of such females was eleven. The litters were kept with their mother and the day of birth was labeled as post natal day one (P1). Subsequent days were accordingly labeled. On each post-natal day (up to the end of the first week), eight litters were sacrifices and the kidney was dissected out. Tissue was fixed in 2.5% glutaraldehyde then post fixed in 1% osmium tetra oxide. The specimens were dehydrated and cleared prior to embedding in araldite embedding resin. Plastic embedded blocks were sectioned by ultra cut (Reichert-Jung) ultra microtome into semi thin (0.5-1 µm) sections. The section was stained by heated 1% methylene blue aqueous solution and examined after drying.

Results

This study showed that pre-natal kidney is still in an immature state. It was observed that during the first four post-natal days, there were continuous formation of mature glomeruli. There was a co-existence of various stages of glomerular formation. By the 7th pos-natal day, the kidney appeared apparently identical with the mature kidney.

The stages of formation of mature metanephric glomerulus start with an ovoid nest of cells that separate from the metanephric cap. This cellular mass becomes surrounded by basal lamina and obtain a cavity that soon establish communication with the lumen of collecting tubule. This is the metanephric vesicle (Figure 1). In rat, the formation of renal vesicles continues to 4th post-natal day. The metanephric vesicle starts to elongate to form a comma (,) shaped body; with an outer layer of flattened cells and inner layer of cuboidal cells, this constitutes the comma-stage (Figure 2).

As elongation continues, the comma shaped body starts to attain the shape of (S), with two "clefts", upper and lower ones, and three "limbs", upper, middle and lower. This is the S-shaped body stage (Figure 3).

With progressive development and elongation of the developing glomerulus, a double-comma stage (Figure 4) is formed. This stage passes through a stage of elongation (Figure 5), during which the inner layer of cuboidal cells represent podocytes-precursor cells, and the outer layer of flattened cells become the parietal epithelium. The final stage of metanephric glomerular development is the ovale-stage (Figure 6). In this stage the metanephric glomerulus becomes oval or rounded in shape surrounded by parietal layer of Bomann's capsule and characterized by the presence of glomerular (urinary) space. The podocytes start to arrange themselves around developing blood capillaries. This ends the maturation of the glomerulus. These stages are diagrammatically represented in figure (7).

Discussion

The kidney is one of the organs that continues to develop post-natally. Embryonic development does not complete during intra-uterine life. In rat, the glomeruli and tubules continue to develop and mature during neonatal period confirming the findings of Neiss and Klehan (6).

This phenomenon of "peri-natal development" of the glomeruli makes the kidney liable to influences both internal and external during this period, and becomes vulnerable to injurious agents more than other organs. The glomeruli pass through well defined, standard and sequential morphological stages. This study puts forward the main stages of glomerular maturation as vesicle stage, comma stage, S-shaped body stage, double comma stage, elongation stage and ovale stage. Each glomerulus passes through these six stages during its development. We propose the inclusion of these stages in any account on neonatal nephrology.

The development of the glomeruli in the kidney is not uniformly paced. Not all the glomeruli pass through the same stage at a particular time. Some glomeruli are ahead of others in development, others are lagging behind. This results in the existence of various stages of glomerular development at the same time. However, by the end of the first week post-natally, almost all glomeruli reaches the ovale stage and are mature.

These outcomes of the current study confirm the early observations of Saxen and Sariola (7), whom tentatively touched upon the issue of morphological development of metanephric glomeruli more than 20 years ago. Recent studies were also in accordance with our conclusions. This reinforces the picture of multi-stage, pleomorphic development of glomeruli in perinatal period (4, 8). This picture should be taken in consideration during histological and histopathological evaluation of the kidney structure during neonatal period, as in the evaluation of renal biopsy material or performing autopsy for various causes. This should also be put in mind when trying to investigate the effects of drugs or other factors on the kidney.

In conclusion the neonatal kidney is morphologically distinct from that of adults and that described in standard textbooks of histology and similar accounts.

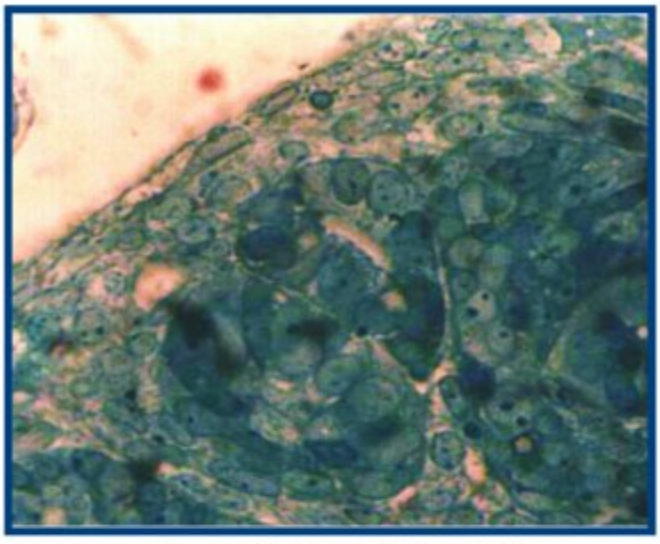
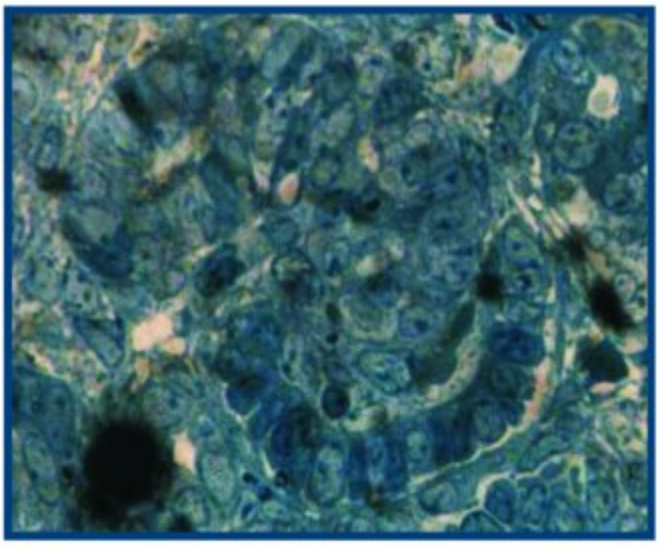


Figure (1): Metanephric vesicl



Figure(4): Double comma stage

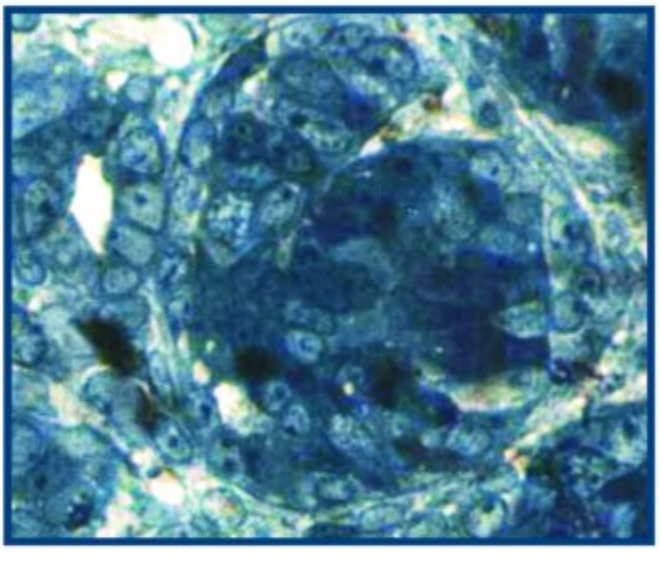


Figure (2): Comma-stage

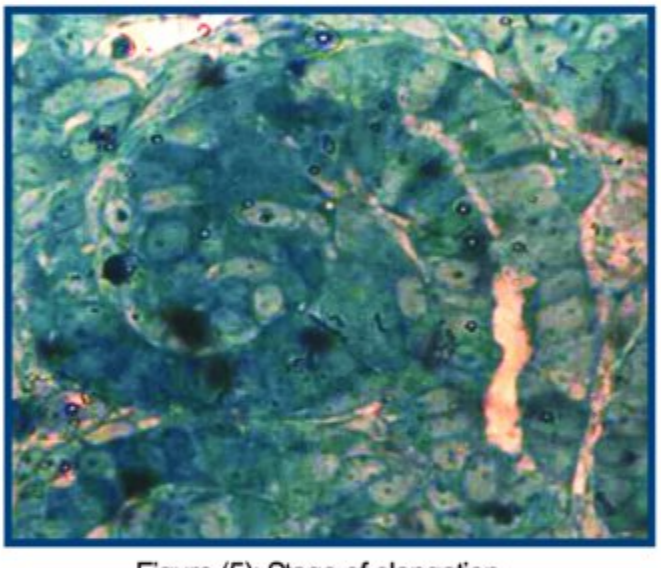


Figure (5): Stage of elongation

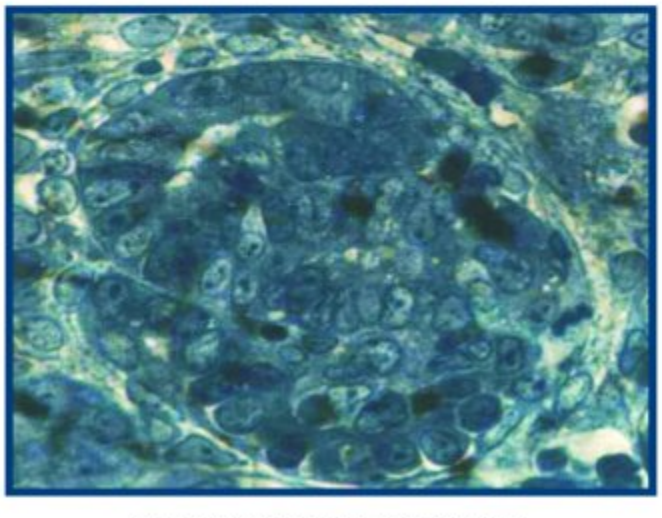


Figure (3): S-shaped body stage

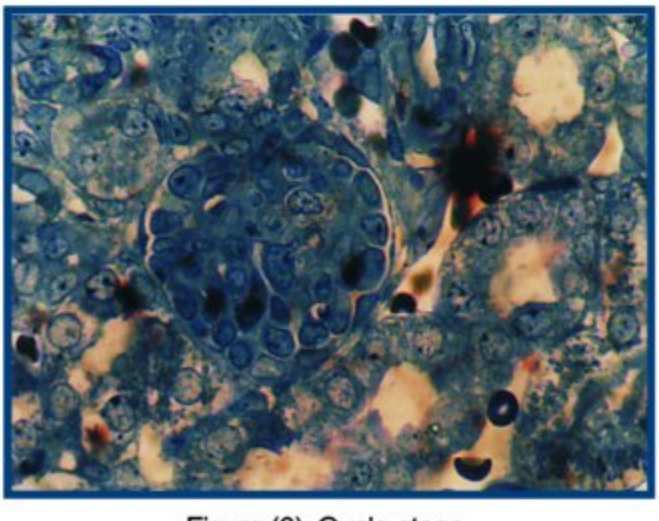


Figure (6): Ovale-stage

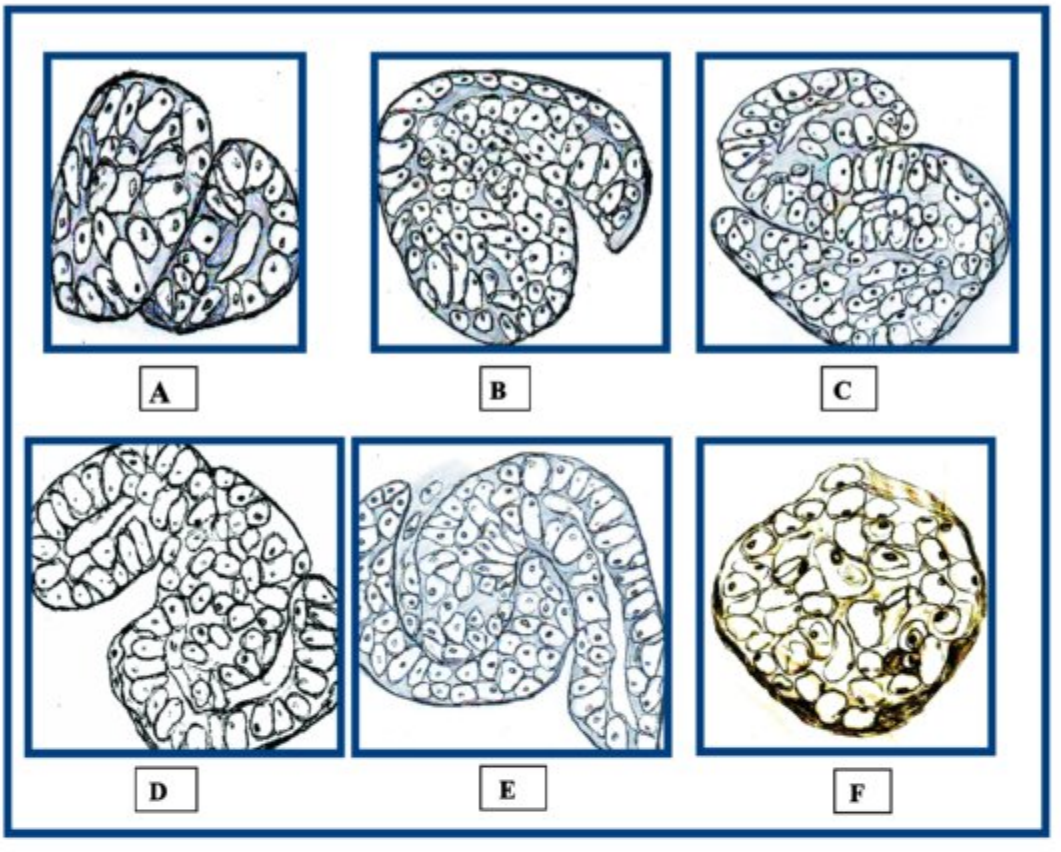


Figure (7): Schematic diagram of morphological stages of the development of the Metanephric glomerulus

A: The vesicle stage.
B: The comma stage.
C: The S- shape body stage
D: The double comma stage.
E: The elongation stage
F: The ovale stage

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