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"NEPHRONOPHTHISIS" EMBRYOLOGICAL BASIS AND ITS CLINICAL IMPORTANCE

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ABSTRACT

Nephronophthisis (NPH) is an autosomal recessive disease characterized by chronic tubulointerstitial nephritis that progress to terminal renal failure during the second decade (juvenile form) or before the age of 5 years (infantile form). In the juvenile form, a urine concentration defect starts during the first decade, and a progressive deterioration of renal function is observed in the following years. Kidney size may be normal, but loss of cortico-medullary differentiation is often observed, and cysts occur usually after patients have progressed to end-stage renal failure.

Introduction

Nephronophthisis is an autosomal recessive cystic kidney disease. The most frequent genetic cause present at the end-stage renal disease which is up to the third decade of life[1]. These are caused mainly by mutations in 11 different types of genes, and are denoted as nephrocystins (NPHP1-11, NPHP1L)[2]. The increasing numbers of these genes are identified. Recent studies have described that the ciliary expression of the nephrocystins together with the other cystoproteins, such as the polycystins 1 and 2 and the fibrocystin[3]. These findings have shifted our focus to a pathomechanism that involves the defects in the ciliary function the and planar cell polarity[4]. In addition to it many findings regarding the new nephrocystin genes have shown that the disease spectrum of the NPHP is much broader than the previously anticipated one. There are different forms of mutations within the same NPHP gene that can cause various different disease severities [5]. The clinical spectrum has now become even more complex with the possibility of the oligogenicity in the NPHP.

Nephronophthisis is literally means the 'disappearance of nephrons'. Typical ultrasound features are including in the normal or in the reduced renal size, the loss of [6]corticomedullary differentiation and the corticomedullary cysts. The Renal biopsy findings include the tubular atrophy, the interstitial fibrosis and the tubular basement membrane defects, including the [7]abrupt transition between the thickening and attenuation or disintegration.

Incidence

This is a rare congenital renal anomaly in which medical council recorded that approximately about 10 to15% of Nephronophthisis patients have extra renal symptoms are found and which[8] includes the retinal degeneration of cerebellar vermis aplasia, liver fibrosis, oculomotor apraxia and also cone-shaped[9].

Ontogenesis of the normal development of the Kidney

The normal embryological development of the kidney is mentioned below with further embryological aspects.[10] There are mainly three kidney systems which are formed in a cranial-to-caudal sequence [11]during the intrauterine life in humans; they are (i) Pronephros (ii) Mesonephros and (iii) Metanephros respectively.

The first of these systems is mainly rudimentary and nonfunctional,[12] but in the second may function for a short time during the early fetal period, and the third forms the permanent kidney.

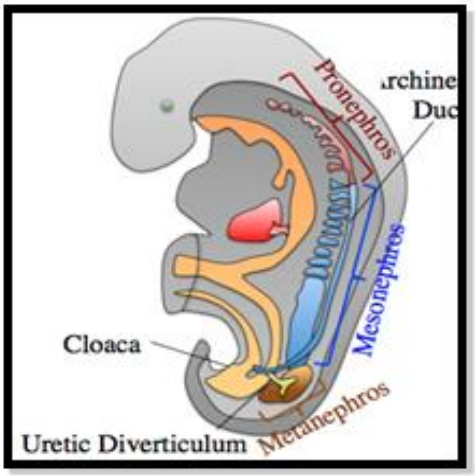

Fig 1. Normal development of kidney.

Pronephros

At the[13] beginning of this pronephros the fourth week, the pronephros is represented by 7 to 10 solid cell groups in

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the cervical region. [14]These groups form the vestigial excretory units, nephrotomes that regress before it more caudal ones are formed[15]. By the end of this fourth week, the pronephric system will disappears[16].

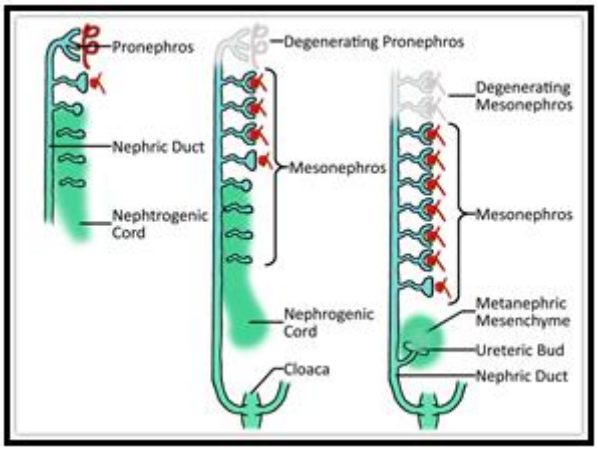

Fig 2. Development of pronephros.

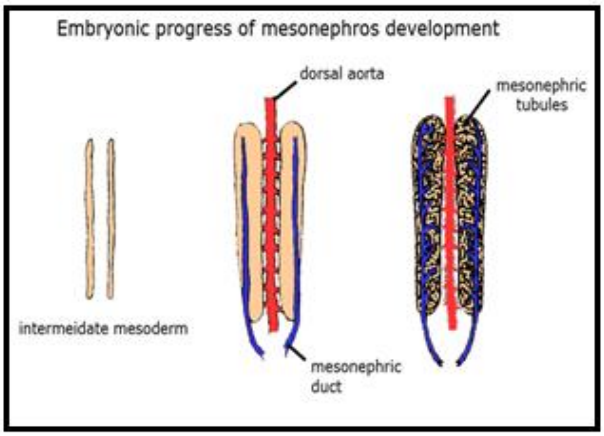

Fig 3. Embryonic development of mesonephros.

Mesonephros

The Mesonephros and [17] the mesonephric ducts are derived from the intermediate mesoderm from the upper thoracic to the upper lumbar (L3) segments [18]. In the early 4th week of the development, the first excretory tubules of the mesonephros appear[19]. They lengthen rapidly, and forms an S-shaped loop,[20] and which acquire a tuft of the capillaries that will form a glomerulus at[21] their medial extremity. Around the glomerulus, the tubules form Bowman's capsule,[22] and together these structures constitute into a renal corpuscle.

Laterally, [23] this tubule enters into the longitudinal collecting duct known as the mesonephric or Wolffian duct. [24]While the caudal tubules are still differentiating, the cranial tubules and the glomeruli show the degenerative changes, and by the end of this [25] 2nd month the majority will be disappeared.[26] In the male a few of the[27] caudal tubules and the mesonephric duct persist and participate in formation[28] of the genital system,[29] but they disappear in the female.

Metanephros

The third urinary organ[30], the metanephros or permanent kidney appears in the 5th week. [31]The excretory units develop from metanephric mesoderm (blastema) in the same manner as in the mesonephric system. [32]The development of the duct system usually differs from that of the other kidney systems[33].

Ontogenesis for the Nephronophthisis:

The abnormal condition [34] is due to the disappearance of the [35] nephrons during the embryonic period [36]. Nephronophthisis that affects the development of the microscopic tubules deep within the kidneys in which that concentrate the [37] urine and which reabsorb the sodium [38]. As a result the excessive amounts of sodium they are excreted in the urine and resulting in too little sodium in the blood and in the body[39]. Excessive amounts of acids may also leads to accumulate in the blood.[40]The damaged tubules become inflamed and scarred,[41] eventually these causing leads to the chronic kidney disease severe enough to[42] result in end-stage renal disease.

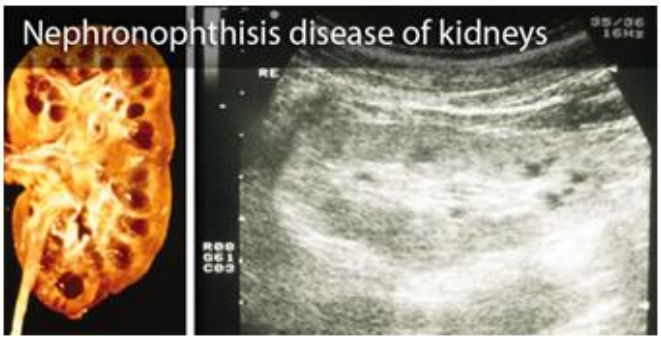

Fig 4. Diseased condition of the kidneys

Discussion

Nephronophthisis is literally means the 'disappearance of nephrons'[43]. Typical ultrasound features are including in the normal or in the reduced renal size, the loss of cortico medullary differentiation and the cortico medullary cysts. [44]The Renal biopsy findings include [45] the tubular atrophy, the interstitial fibrosis and the tubular basement membrane defects, including the abrupt transition between the [46] thickening and attenuation or disintegration. [47]There are different forms of mutations within the same NPHP gene [48] that can cause various different disease severities. The clinical spectrum has[49] now become even more complex with the possibility of the oligogenicity in the[50] NPHP. There are various types of Nephronophthisis like [51] Juvenile Nephronophthisis, Adolescent Nephronophthisis and Infantile Nephronophthisis [52].

Chronic kidney disease[53] which causes many problems throughout the body: When the loss of kidney function is mild or moderately severe, the kidneys cannot absorb the water from [54]the urine to reduce the volume of the urine and concentrate it. The[55] kidneys have less ability to excrete the acids normally and is produced by the body and the[56] blood becomes more acidic, and this condition is called acidosis. The production of the red blood cells [57]decreases and leads to anemia.[58] High level of the metabolic waste products in the blood can damage the[59] nerve cells in the brain, trunk, arms, and the legs. The Uric acid levels may increase but sometimes causing gout. This diseased kidneys produce hormones that increase the blood pressure. [60]In addition to it the diseased kidneys cannot excrete excess of salt and water. This salt and water retention can contribute to high blood pressure and a chance of heart failure. [61]Through Blood tests, urine tests, Ultrasonography& Sometimes biopsy also we can diagnose the defect.

In normal development [62]There are mainly three kidney systems which are formed in a cranial-to-caudal sequence[63] during the intrauterine life in humans. The first of these systems is mainly rudimentary and nonfunctional,[64] but in the second may function for a short time during the early fetal

period[65], and the third forms [66]the permanent kidney. Certain treatment measures are[67] the restricting protein, controlling acidosis,[68],[69] lowering triglyceride levels, restricting sodium and potassium and controlling the phosphorus levels[70].

Conclusion

Nephronophthisis is an autosomal recessive cystic kidney disease. From the practical point of view the diagnosis of the NPH should be considered if a child presents with polyuria, urinary sodium loss, growth failure, renal insufficiency without hematuria or proteinuria the normal blood pressure, and the normal-sized kidneys without the dilatation of the urinary tract. These patients should be administrated for screening for homozygous or heterozygous NPHP1 deletion, which are found in 20 to 40% of this type cases. In the absence of heterozygous NPHP1 deletion, the renal biopsy may be proposed to confirm the diagnostic process. At present the screening for mutation in all the other NPHP genes is not performed well due to the low frequency in the detected mutations and the high cost of the procedure.

References

[1] Ganesh Elumalai, Sushma Chodisetty. Anomalous "Mutilated Common Trunk" Aortic Arch Embryological Basis and its Clinical Significance. Texila International Journal of Basic Medical Science. 2016; 1(1): 1-9.

[2] Ganesh Elumalai, Emad Abdulrahim Ezzeddin. "The sudden soul reaper" - hypertrophic cardiomyopathy – its embryological basis. Elixir Embryology. 2016; 99: 43284-43288.

[3] Ganesh Elumalai, Muziwandile Bayede Mdletshe. "Arteria lusoria"- aberrant right subclavian artery embryological basis and its clinical significance. Elixir Embryology. 2016; 99: 43289-43292.

[4] Ganesh Elumalai, Sushma Chodisetty, Pavan Kumar D.2016. Ganesh Elumalai et al Classification of Type - I and Type - II "Branching Patterns of the Left Arch Aorta". Imperial Journal of Interdisciplinary Research. 2(9): 161-181.

[5] Ganesh E, Sushma C. The deer horn aortic arches" embryological basis and surgical implications. Anatomy Journal of Africa.2016; 5(2): 746 – 759.

[6] Ganesh Elumalai, Sushma Chodisetty. Teratological Effects of High Dose Progesterone on Neural Tube Development in Chick Embryos. Elixir Gynaecology. 2016; 97: 42085-42089.

[7] Ganesh Elumalai, Sushma Chodisetty. "The True Silent Killers" - Bovine and Truncus Bicaroticus Aortic Arches its Embryological Basis and Surgical Implications. Elixir Physio. & Anatomy. 2016; 97: 42246-42252.

[8] Ganesh Elumalai, Sushma Chodisetty, Bridget Omo Usen and Rozminabanu Daud Patel. "Patent Ductus Caroticus" - Embryological Basis and its Clinical significance. Elixir Physio. & Anatomy. 2016; 98: 42439-42442.

[9] Ganesh Elumalai, Sushma Chodisetty, Eliza Arineta Oudith and Rozminabanu Daud Patel. Common anomalies origin of left vertebral artery and its embryological basis. Elixir Embryology. 2016; 99: 43225-43229.

[10] Ganesh Elumalai, Sushma Chodisetty, Sanjoy Sanyal. Common Nasal Anomalies and Its Implications on Intubation in Head and Neck Surgeries. Journal of Surgery. 2016; 4 (4): 81-84.

[11] Ganesh Elumalai, Malarvani Thangamani, Sanjoy Sanyal, Palani Kanagarajan. Deficient sacral hiatus cause mechanical low back pain: a radiological study. Int J Anat Res. 2016; 4(1):1758-64.

[12] Ganesh Elumalai, Amal Satheesh Sujitha. "Anomalies origin of left coronary artery" its embryological basis and clinical significance. Elixir Embryology. 2016; 100: 43446-43449.

[13] Ganesh Elumalai, Anto Sicily Norbert. "APVC - Anomalies Pulmonary Venous Connections" embryological basis and its clinical significance. Elixir Embryology. 2016; 100: 43450-43453.

[14] Ganesh Elumalai, Nnolika Millington. "Coarctation of Aorta" embryological basis and its clinical significance. Elixir Embryology. 2016; 100: 43425-43428.

[15] Ganesh Elumalai, Logeshwaran Anbazhagan. "Laryngomalacia" embryological basis and its clinical significance. Elixir Embryology. 2016; 100: 43420-43424.

[16] Ganesh Elumalai, Amodini Dharmalingam. "Left superior vena cava" embryological basis and its clinical significance. Elixir Embryology. 2016; 100: 43429-43432.

[17] Ganesh Elumalai, Thelma U. Ebami. "Patent Ductus Arteriosus" embryological basis and its clinical significance. Elixir Embryology. 2016; 100: 43433-43438.

[18] Ganesh Elumalai, Mouna Arumugam. "Persistent Left superior vena cava" embryological basis and its clinical significance. Elixir Embryology. 2016; 100: 43454-43457.

[19] Ganesh Elumalai, Moganelwa Sharline Mampa. "Pulmonary Agenesis" embryological basis and its clinical significance. Elixir Embryology. 2016; 100: 43439-43441.

[20] Ganesh Elumalai, Shubham Jain. "Subglottic stenosis" embryological basis and its clinical significance. Elixir Embryology. 2016; 100: 43458-43461.

[21] Ganesh Elumalai, Hariharan Arjet. "Tracheoesophageal fistula" embryological basis and its clinical significance. Elixir Embryology. 2016; 100: 43414-43419.

[22] Ganesh Elumalai, Jenefa Princess. "Transposition of Great Vessels" embryological basis and its clinical significance. Elixir Embryology. 2016; 100: 43442-43444.

[23] Ganesh Elumalai, Manoj P Rajarajan. "Type-I vascular rings" Embryological basis and its clinical importance Elixir Embryology. 2016; 100: 43700-43705.

[24] Ganesh Elumalai, Ebenezer Asare Sakyi. "Right sided aortic arch" Embryological basis and its clinical importance Elixir Embryology. 2016; 100: 43706-43709.

[25] Ganesh Elumalai, Enian Senguttuvan. "Double aortic arch" Embryological basis and its clinical importance Elixir Embryology. 2016; 100: 43710-43713.

[26] Ganesh Elumalai, Danesha Sanicharan. "Abnormal origin of the right subclavian artery from the right pulmonary artery" Embryological basis and its clinical importance Elixir Embryology. 2016; 100: 43714-43718.

[27] Ganesh Elumalai, Siva Brinda Jeyapaul. "Choanal Atresia" Embryological basis and its clinical importance Elixir Embryology. 2016; 100: 43719-43722.

[28] Ganesh Elumalai, Kelly Deosaran. "Congenital diaphragmatic hernia" Embryological basis and its clinical importance Elixir Embryology. 2016; 100: 43723-43728.

[29] Ganesh Elumalai, Basim Arif. "Subclavian Steal Syndrome" Embryological basis and its clinical importance Elixir Embryology. 2016; 100: 4372943733.

[30] Columbia university department of obstetrics and gynecol ogy. Uterine anomaly. www. columbiaobgyn. org/condition_treatments/ uterine- anomaly

[31] Congenital uterine anomalies. Medfem. www. medfem. co.za/ congenital – Uterine - anomalies

[32] Grimbizis F. Grigoris. Clinical implications of uterine mal formations and hysteroscopic treatment results. PubMed. 2001 ; vol. 7(1): pg. 161-173.
[33] Keith L. Moore, Atthur F. Dalley, Anne M.R. Agur. Moore clinically oriented anatomy. Lippincott Williams & Wilkins. 2014; 7th ed.: 324.
[34] Lawrence S. Amesse. Mullerian duct anomalies. WebMD. 2016. emedicine.medscape.com/article/273534-overview
[35] Marıa Luisa Martınez Frıas. Congenital anomalies in the offspring of mothers with a bicornuate uterus. Aappublication. 1998; vol. 101(4): pg. 1-3.
[36] Ronald W. Dudek. BRS Embryology. Lippincott Williams & Wilkins.2016; 6th ed: 171, 175.
[37] Sadler, T. &Langman, J. Langman's Medical Embryology. Lippincott Williams & Wilkins. 2012; 12th ed: 248-250.
[38] Schoenwolf Gary C. Larsen's Human Embryology. Churchill Livingstone Elsevier. 2008; 4thed: 518-520.
[39] Fanconi G, Hanhart E, von Albertini A, Uhlinger E, Dolivo G, Prader A (1951) Familial, juvenile nephronophthisis (idiopathic parenchymal contracted kidney). Helv Paediatr Acta
[40] Smith C, Graham J (1945) Congenital medullary cysts with severe refractory anemia. Am J Dis Child
[41] Saunier S, Salomon R, Antignac C (2005) Nephronophthisis. Curr Opin Genet Dev
[42] Caridi G, Dagnino M, Gusmano R, Ginevri F, Murer L, Ghio L, Piaggio G, Ciardi MR, Perfumo F, Ghiggeri GM (2000) Clinical and molecular heterogeneity of juvenile nephronophthisis in Italy: insights from molecular screening. Am J Kidney Dis
[43] Hildebrandt F, Waldherr R, Kutt R, Brandis M (1992) The nephronophthisis complex: clinical and genetic aspects. Clin Investig
[44] Waldherr R, Lennert T, Weber HP, Fodisch HJ, Scharer K (1982) The nephronophthisis complex. A clinicopathologic study in children. Virchows Arch A Pathol Anat Histol
[45] 7. Stavrou C, Koptides M, Tombazos C, Psara E, Patsias C, Zouvani I, Kyriacou K, Hildebrandt F, Christofides T, Pierides A, Deltas CC (2002) Autosomal-dominant medullary cystic kidney disease type 1: clinical and molecular findings in six large Cypriot families. Kidney Int
[46] Hildebrandt F, Zhou W (2007) Nephronophthisis-associated ciliopathies. J Am Soc Nephrol
[47] Pistor K, Olbing H, Scharer K (1985) Children with chronic renal failure in the Federal Republic of Germany: I. Epidemiology, modes of treatment, survival. Arbeitsgemeinschaft fur Pädiatrische Nephrologie. Clin Nephrol
[48] Potter DE, Holliday MA, Piel CF, Feduska NJ, Belzer FO, Salvatierra O Jr (1980) Treatment of end-stage renal disease in children: a 15-year experience. Kidney Int
[49] 1. Fanconi G, Hanhart E, von Albertini A, Uhlinger E, Dolivo G, Prader A (1951) Familial, juvenile nephronophthisis (idiopathic parenchymal contracted kidney). HelvPaediatrActa
[50] 2. Smith C, Graham J (1945) Congenital medullary cysts with severe refractory anemia. Am J Dis Child
[51] 3. Saunier S, Salomon R, Antignac C (2005) Nephronophthisis. CurrOpin Genet Dev
[52] 4. Caridi G, Dagnino M, Gusmano R, Ginevri F, Murer L, Ghio L, Piaggio G, Ciardi MR, Perfumo F, Ghiggeri GM (2000) Clinical and molecular heterogeneity of juvenile nephronophthisis in Italy: insights from molecular screening. Am J Kidney Dis
[53] 5. Hildebrandt F, Waldherr R, Kutt R, Brandis M (1992) The nephronophthisis complex: clinical and genetic aspects. ClinInvestig
[54] 6. Waldherr R, Lennert T, Weber HP, Fodisch HJ, Scharer K (1982) The nephronophthisis complex. A clinicopathologic study in children. Virchows Arch A PatholAnatHistol
[55] 7. Stavrou C, Koptides M, Tombazos C, Psara E, Patsias C, Zouvani I, Kyriacou K, Hildebrandt F, Christofides T, Pierides A, Deltas CC (2002) Autosomal-dominant medullary cystic kidney disease type 1: clinical and molecular findings in six large Cypriot families. Kidney Int
[56] 8. Hildebrandt F, Zhou W (2007) Nephronophthisis-associated ciliopathies. J Am SocNephrol [PubMed]
[57] 9. Pistor K, Olbing H, Scharer K (1985) Children with chronic renal failure in the Federal Republic of Germany: I. Epidemiology, modes of treatment, survival. Arbeitsgemeinschaft fur PädiatrischeNephrologie. ClinNephrol
[58] 10. Potter DE, Holliday MA, Piel CF, Feduska NJ, Belzer FO, Salvatierra O Jr (1980) Treatment of end-stage renal disease in children: a 15-year experience. Kidney Int
[59] "Nephronophthisis". Genetics Home Reference. Retrieved 2015-08-08.
[60] Hurd TW, Hildebrandt F (2011). "Mechanisms of nephronophthisis and related ciliopathies". Nephron Exp. Nephrol..
[61] Chapter 35, in: Avner, Ellis D.; Harmon, William; Niaudet, Patrick; Yoshikawa, Norishige. Pediatric Nephrology (Avner, Pediatric Nephrology). Springer.. (stating the incidence in the United States as 9 per 8.3 million people.
[62] Hildebrandt, Friedhelm; Zhou, Weibin (2007). "Nephronophthisis-Associated Ciliopathies". Journal of the American Society of Nephrology.
[63] Kanwal, Kher (2007). Clinical Pediatric Nephrology, Second Edition (2nd ed.). McGraw-Hill. p. 205.
[64] Medullary Cystic Disease~clinical at eMedicine
[65] Salomon, Rémi; Saunier, Sophie; Niaudet, Patrick (2009). "Nephronophthisis". Pediatric Nephrology. 24 (12): 2333–44.
[66] Hildebrandt, Friedhelm; Attanasio, Massimo; Otto, Edgar (2009). "Nephronophthisis: Disease Mechanisms of a Ciliopathy". Journal of the American Society of Nephrology. 20 (1): 23–35.
[67] McCormack, Francis X.; Panos, Ralph J.; Trapnell, Bruce C. (2010-03-10). Molecular Basis of Pulmonary Disease: Insights from Rare Lung Disorders. Springer Science & Business Media.
[68] Badano, Jose L.; Mitsuma, Norimasa; Beales, Phil L.; Katsanis, Nicholas (2006). "The Ciliopathies: An Emerging Class of Human Genetic Disorders". Annual Review of Genomics and Human Genetics. 7: 125–48.
[69] Stokman, Marijn; Lilien, Marc; Knoers, Nine (1 January 1993). "Nephronophthisis". GeneReviews(®). University of Washington, Seattle. Retrieved 1 August 2016.update 2016
[70] Hildebrandt, Friedhelm (2009). "Nephronophthisis". In Lifton, Richard P.; Somlo, Stefan; Giebisch, Gerhard H.; et al. Genetic Diseases of the Kidney. Academic Press. pp. 425–46.