Acta Med. Nagasaki 61: 9 − 15

Case Report

A case of nephronophthisis discovered due to pregnancy with review of literatures

Satoru Oka[1, 2, 3], Yoko Obata[1, 2, 4], Atsushi Mori[1, 3], Masayuki Nakazawa[3], Naoya Morisada[5], Kazumoto Iijima[5], Hiroshi Mukae[2] and Tomoya Nishino[1, 2]

(1) Department of Nephrology, Nagasaki University Hospital, 1-7-1 Sakamoto, Nagasaki-city, Nagasaki, 852-8501, Japan
(2) Department of Respiratory Medicine, Nagasaki University Graduate School of Biomedical Sciences, 1-7-1 Sakamoto, Nagasaki-city, Nagasaki, 852-8501, Japan
(3) Department of Nephrology, Sasebo City General Hospital, 9-3 Hirase-cho, Sasebo-city, Nagasaki, 857-8511, Japan
(4) Medical Educational Development Center, Nagasaki University Hospital, 1-7-1 Sakamoto, Nagasaki-city, Nagasaki, 852-8501, Japan
(5) Department of Pediatrics, Kobe University Graduate School of Medicine, 7-5-1, Kusunoki-cho, Chuo-ku, Kobe-city, Hyogo, 650-0017, Japan

A 20-year-old woman presented to the Department of Obstetrics and Gynecology of our hospital for a prenatal checkup at 33 weeks' gestation. No abnormalities had been ever found in routine urine testing at school health checkups. Blood tests revealed renal impairment, with a creatinine level of 1.77 mg/dL, and she was referred to our department. Hematuria and proteinuria were not found; therefore, she was allowed to continue the pregnancy while being followed for renal function. Renal biopsy was performed after delivery. Pathological examination revealed irregular renal tubular dilatation and atrophy associated with thickening, thinning, and disruption of the tubular basement membrane and diffuse fibrosis and cell infiltration in the interstitium. Based on these findings, nephronophthisis was suspected. Genetic analysis revealed complete homozygous deletion of *NPHP1*, and nephronophthisis was definitively diagnosed. Currently, the only curative treatment available for nephronophthisis is renal transplantation, and thus, symptomatic treatment for chronic kidney disease eventually becomes necessary. Because nephronophthisis lacks clear clinical symptoms, early diagnosis is difficult. Thus, if young patients present with renal impairment, a detailed examination is necessary to consider nephronophthisis in the differential diagnosis.

ACTA MEDICA NAGASAKIENSIA 61: 9−15, 2017

Key words: nephronophthisis, cystic kidney disease, polyuria, hyposthenuria, gestation, pregnancy

Introduction

Nephronophthisis is an autosomal-recessive cystic kidney disorder that frequently causes end-stage kidney disease in pediatric and adolescent patients [1]. Because urinary abnormalities such as hematuria and proteinuria are usually uncommon in nephronophthisis, the disease is difficult to detect using simple urine tests such as those used in schools. This often delays the diagnosis of nephronophthisis, and when it is found, renal impairment is often at an advanced stage. Although recent advances in genetic analysis have identified the genetic mutations responsible for nephronophthisis, responsible genes have been identified in only < 30% of cases of clinically diagnosed nephronophthisis [2]. Here, we report a case in which renal impairment was found during pregnancy and nephronophthisis due to complete homozygous deletion of *NPHP1* was diagnosed using genetic analysis.

Address correspondence: Yoko Obata, M.D., Ph.D., Department of Nephrology, Nagasaki University Hospital, 1-7-1 Sakamoto, Nagasaki-city, Nagasaki, 852-8501, Japan,
e-mail: yobata@nagasaki-u.ac.jp, TEL +81-95-819-7273, FAX +81-95-849-7285

Received February 6, 2016; Accepted May 2, 2016

Case report

The patient was a 20-year-old woman in whom urinary abnormalities had not been identified during school health checkups. She was followed up for a prenatal checkup in the Department of Obstetrics and Gynecology at our hospital. She presented with intermittent fever and lower back pain beginning at 32 weeks' gestation. At 33 weeks' gestation, a prenatal checkup, conducted in the Department of Obstetrics and Gynecology at our hospital, revealed elevated inflammatory responses and renal impairment and was referred to our department. There was no family history of renal impairment. The findings at the initial visit were as follows: consciousness, awake and alert; height, 151.8 cm; body weight, 41.5kg; body temperature, 36.7ºC; blood pressure, 92/48 mmHg; pulse, 68 beats per minute (regular); and urine volume, 3300mL/day. No anemia or jaundice was observed in the palpebral conjunctive, and the heart and respiratory sounds were normal. Percussion tenderness was observed in the left costovertebral angle. No edema was found in any of the four limbs, and no significant findings were observed in the skin.

Laboratory findings at the initial visit were as follows: increased white blood cell count (10,960/μL) and elevated inflammatory response (C-reactive protein, 7.98 mg/dL), anemia (hemoglobin, 8.8 g/dL), renal impairment (blood urea nitrogen, 27.7 mg/dL; creatinine (Cr), 1.77 mg/dL), mild hyponatremia and hypokalemia (Na, 136 mEq/L; K, 3.4 mEq/L), metabolic acidosis (HCO_3^-, 17.8 mmol/L), and hyposthenuria (urine osmolality, 182 mOsm/kg). Neither proteinuria nor hematuria was observed (Table 1).

Because left lower back pain and pyuria were observed and *Escherichia coli* was detected in the urine culture, pyelonephritis was diagnosed. Moreover, since we suspected the involvement of pyelonephritis as the cause of renal impairment, an antibacterial agent (flomoxef sodium 500 mg × 2 for 5 days) was administered. As a result, clinical symptoms and inflammatory responses improved, but renal impairment was still present (Cr, 1.57 mg/dL). Pregnancy was continued while following the course of renal function. She delivered a baby by induced labor at 36 weeks' gestation. No exacerbation of renal impairment was observed during the perinatal period. No clear postpartum renal atrophy, border irregularity, or cysts were observed on abdominal computed tomography. To closely investigate the cause of renal impairment, renal biopsy was performed 1 month after delivery. Light microscopy of the biopsy samples revealed diffuse fibrosis, cell infiltration, and irregular tubular dilatation in the interstitium by Masson trichrome staining (Figure 1a). Periodic acid-Schiff staining (Figure 1b-c) showed that more than half (8/14) of the glomeruli were sclerotized; however, me-

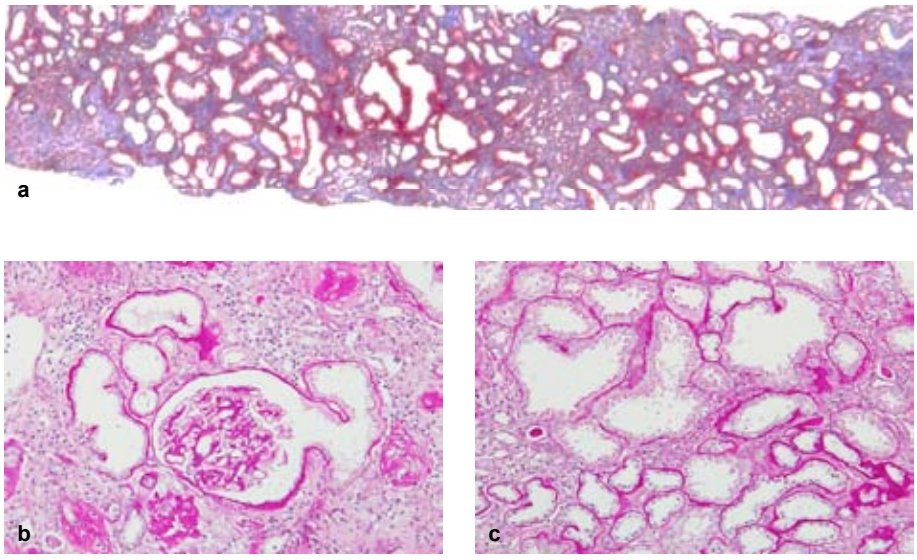

Fig. 1 Renal biopsy (light microscopy) findings
a: Diffuse fibrosis, cell infiltration, and irregular dilatation of the tubules are observed in the interstitium (Masson trichrome staining × 40).
b: More than half (8/14) of the glomeruli are sclerotized; however, mesangial proliferation, thickening of base membrane, or crescent bodies were not found (Periodic acid-Schiff [PAS] staining × 200).
c: In the interstitium, irregular tubular dilatation and irregular hourglass-shaped atrophy are seen, particularly in the proximal tubules. The tubular basement membrane is thickened but locally thinned and disrupted (PAS staining × 200).

sangial proliferation, thickening of the base membrane, or crescent bodies was not observed. In the interstitium, irregular, hourglass-shaped tubular dilatation and atrophy were observed, particularly in the proximal tubules. The tubular basement membrane was thickened but locally thinned and disrupted. Results of immunofluorescence staining were all negative. The findings of electron microscopy revealed no dense deposits in the glomeruli but local serpiginous thickening of the glomerular basement membrane. Based on the renal biopsy findings, nephronophthisis or medullary cystic kidney disease were considered in the differential diagnosis. To make a definitive diagnosis, genetic analysis was performed after obtaining consent from the patient and her family. With regard to *NPHP1* analysis (20 exons), the bands of exon 1, 9, and 19 were not detected by polymerase chain reaction, and complete homozygous deletion of *NPHP1* was observed by multiplex ligation-dependent probe amplification (Figure 2). Based on the above observations, nephronophthisis was definitively diagnosed due to complete homozygous deletion of *NPHP1*. Because nephronophthisis is an autosomal-recessive disease, close examination of her siblings was performed, but neither renal impairment nor urinary abnormalities were observed. Currently, we are treating the patient symptomatically while observing the course of her condition, keeping in mind the possibility of future renal transplantation.

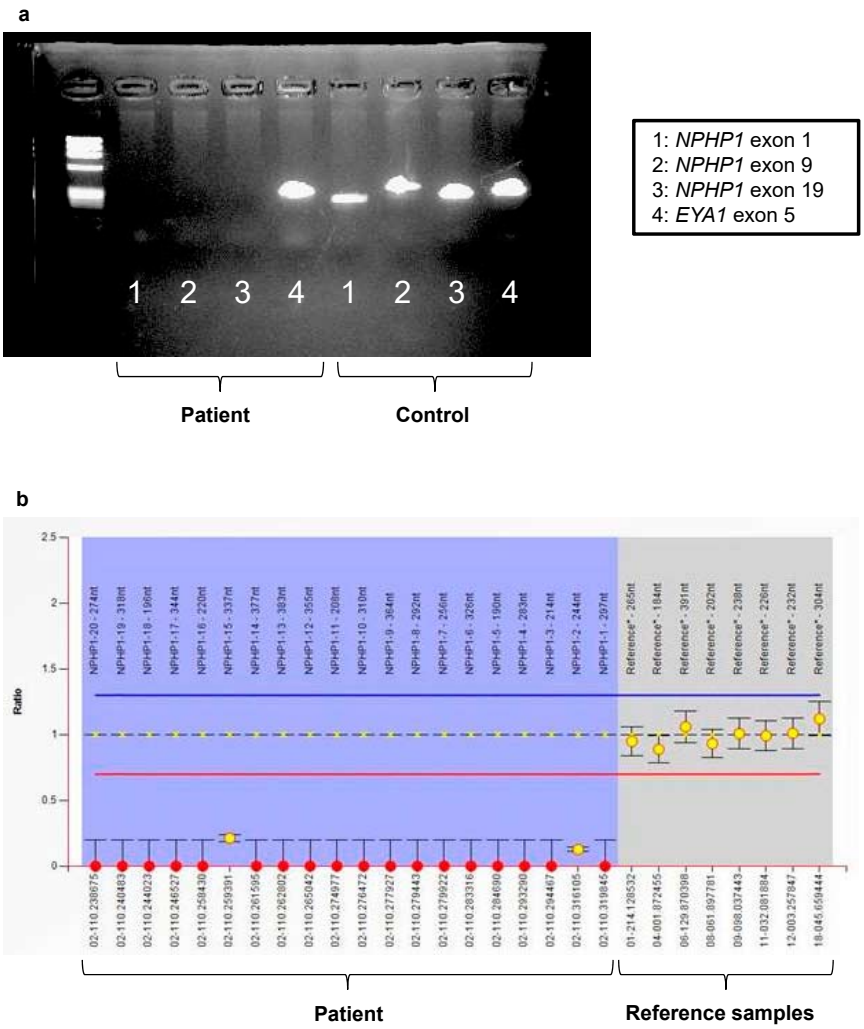

Fig. 2 Genetic analysis findings
a: Polymerase chain reaction (PCR)
In *NPHP1* analysis of (20 exons), *NPHP1* bands were detected in the control samples tested simultaneously by PCR (right); however, the bands of exon 1, 9, and 19 were not detected in this patient's samples (left).
b: Multiplex ligation-dependent probe amplification (MLPA).
Complete homozygous deletion is observed by MLPA. Slight reactions are seen for exons 2 and 15; however, the bands for these exons were not detected in PCR.

Table 1 Laboratory data on the first visit at 33 weeks' gestation

Complete blood count			Blood chemistry			Serological test		
WBC	10960	/μL	Na	136	mEq/L	RF	10	IU/mL
RBC	280 × 10^4	/μL	K	3.4	mEq/L	ANA	< 40	
Hb	8.8	g/dL	Cl	107	mEq/L	CH50	60	U/mL
Hct	24.8	%	Adjusted Ca	10.3	mg/dL	C3	153	mg/dL
PLT	24.3 × 10^4	/μL	IP	2.9	mg/dL	C4	42	mg/dL
			BUN	27.7	mg/dL	IgA	160	mg/dL
Urinalysis and urine chemistry			Cr	1.77	mg/dL	IgG	871	mg/dL
U-specific gravity	1.006		eGFR(Cr)	32.5	ml/min/1.73m^2	IgM	274	mg/dL
U-pH	5.5		CysC	1.93	mg/L	IgE	1150	IU/mL
U-protein	(-)		eGFR(CysC)	37.6	ml/min/1.73m^2	Anti-GBM Ab	0.5	U/mL
U-occult blood	(-)		UA	9.1	mg/dL	MPO-ANCA	0.5	IU/mL
RBC	<1	/HPF	TP	6.3	g/dL	PR3-ANCA	0.5	IU/mL
WBC	30 ～ 49	/HPF	Alb	2.6	g/dL			
Cast	(-)		T-Bil	0.2	mg/dL	Arterial blood gas		
TP/Cr	0.27	g/g・Cr	AST	19	U/L	pH	7.414	
NAG/Cr	11.29		ALT	14	U/L	PCO_2	28.4	mmHg
β_2-MG/Cr	414		γ-GTP	21	U/L	PO_2	128.7	mmHg
U-osmotic pressure	182	mOsm/kg H_2O	ALP	406	U/L	HCO_3-	17.8	mmol/L
			LDH	387	U/L			
			CK	107	U/L			
			TC	284	mg/dL			
			TG	286	mg/dL			
			LDL-C	182	mg/dL			
			CRP	7.98	mg/dL			
			Fe	149	μg/dL			
			Fer	1148	ng/mL			
			S-osmotic pressure	283	mOsm/ kg H_2O			

WBC; white blood cells, RBC: red blood cells, Hb; hemoglobin, Hct; hematocrit, PLT; platelets, U; urine, TP; total protein, Cr; creatinine, NAG; N-acetylglucosaminidase, β_2-MG; β_2-microglobulin, BUN; blood urea nitrogen, eGFR; estimated glomerular filtration rate, CysC; cystatin C, UA; uric acid, Alb; albumin, T-Bil; total bilirubin, CK; creatine kinase, TC; total cholesterol, TG; triglyceride, LDL-C; low density lipoproteinn cholesterol, CRP; C-reactive protein, Fer; ferritin, S; serum, RF; rheumatoid factor, ANA; antinuclear antibody, Anti-GBM Ab; anti-glomerular basement membrane antibody, MPO-ANCA; myeloperoxidase-specific antineutrophil cytoplasmic antibodies, PR3-ANCA; proteinase-3 antineutrophil cytoplasmic antibodies

Table 2 Previous reports that nephronophthisis caused by homozygous deletion of *NPHP1* was diagnosed in adults of the age of 20 years and older

	Age (years) / sex	Motive of discovery	Renal function	Polyuria / polydipsia	Proteinuria (g/day)	hematuria	Kidney Cysts	Extra-renal symptoms	Family history of renal disease
Bollee [15]	22 / F	Asthenia	sCr: 2.5 mg/dL	-	0.2	-	+	-	-
	22 / F	Asthenia	sCr: 5.0 mg/dL	-	0.4	-	+	-	NPHP (elder brother)
	25 / M	Sibling with NPHP	sCr: 4.7 mg/dL	+	1.6	-	-	Retinal dystrophy, neurologic bladder	NPHP (younger sister)
Caridi [16]	21 / M	Sibling with NPHP	sCr: 1.3 mg/dL	+	ND	ND	ND	-	NPHP (two younger brothers)
Hoefele [17]	43 / M	Edema, breathlessness	sCr: 10.0 mg/dL	+	ND	ND	+	-	NPHP (daughter and two younger sisters)
	27 / F	Dizziness, nausea	sCr: 10.0 mg/dL	ND	ND	ND	ND	-	NPHP (elder brother, younger sisters, and niece)
	31 / F	Weight loss	sCr: 10.0 mg/dL	ND	ND	ND	ND	-	NPHP (elder brother, elder sisters, and niece)
Haghighi [18]	24 / M	Hematuria	sCr: 4.0 mg/dL	+	< 0.15	+	+	-	NPHP (elder brother and elder sisters)
	31 / F	Sibling with NPHP	sCr: 6.0 mg/dL	+	0.3 – 0.5	-	+	-	NPHP (two younger brothers)
	26 / M	Sibling with NPHP	sCr: 7.0 mg/dL	+	0.3 – 0.5	-	-	-	NPHP (elder sister and younger brother)
Present case	20 / F	Prenatal checkup	sCr: 1.77 mg/dL	+	0.27 g/g・Cr	-	-	-	-

M; male, F; female, sCr; serum creatinine, ND; no data available, NPHP; nephronophthisis, + ; present, − ; absent

Discussion

Nephronophthisis was first reported by Smith and Graham in 1945 and was termed familial juvenile nephronophthisis by Fanconi et al. in 1951 [3, 4]. Nephronophthisis is an autosomal-recessive cystic kidney disease and is one of the most frequently occurring genetic conditions causing end-stage renal disease (ESRD) in pediatric and adolescent patients [1]. The reported incidence of nephronophthisis varies and has been reported as 1 in 50,000 in Canada, 9 in 8,300,000 in the United States, and 1 in 61,800 in Finland [2, 5, 6]. With regard to the prevalence of nephronophthisis in Japan, there are studies reporting that nephronophthisis accounts for 4.2% of the primary diseases among pediatric patients with stage 3 to 5 chronic kidney disease and 3.3% of the primary diseases among pediatric kidney transplant patients [7, 8].

The symptoms of nephronophthisis are unspecific and include polydipsia, polyuria, growth retardation, and anemia, and they start to appear around the age of 4 to 6 years [9]. Polydipsia and polyuria are caused by decreased urinary concentrating capacity in the renal tubules and collecting duct as well as the loss of sodium [10, 11]. Therefore, hyponatremia may be observed. Because symptoms such as edema, hematuria, and proteinuria are not usually observed during the early phase, it is often difficult to detect this disease using urinary testing conducted in schools, and diagnosis is often delayed. In addition, patients with nephronophthisis may often show extra-renal symptoms, such as retinal degeneration (Senior–Loken syndrome), cerebellar vermis hypoplasia (Joubert syndrome), hepatic fibrosis, ocular motor apraxia (Cogan syndrome), or conical epiphyses [2]. In our present case, neither symptoms such as polydipsia and polyuria nor abnormalities in urinary tests in schools were found, although renal impairment associated with polyuria, hyposthenuria, hyponatremia, and anemia was identified by close examination during the patient's pregnancy. Extra-renal symptoms have not been observed to date.

Nephronophthisis has differences in the onset of ESRD and symptoms by the causative genes and have been distinguished three clinical forms; Infantile, juvenile, and adolescent nephronophthisis. In infantile nephronophthisis, it is reported that patients develop ESRD by the age of 3 years and the causative gene is *NPHP2* [12-14]. In juvenile nephronophthisis, it is reported that patients develop ESRD at the median age of 13 years, but some rare cases develop in adulthood [15-18]. The most causative gene is *NPHP1*, however, mutations in all *NPHP* except *NPHP2* have been associated with juvenile nephronophthisis [10]. In adolescent nephronophthisis, it is reported that patients develop ESRD at the median age of 19 years and the causative gene is *NPHP3* [19, 20]. However, there is no clear correlation between the age at ESRD and the genotype, as some patients with *NPHP3* mutations develop ESRD before the age of 10 years, while some patients with *NPHP1* deletions develop ESRD in adulthood [10]. Table 2 shows a summary of the previous reports that nephronophthisis caused by homozygous deletion of *NPHP1* was diagnosed in adults of the age of 20 years and older. It seems that they have the less frequency of extra-renal symptoms and show the older age for onset of ESRD compared with those of nephronophthisis caused by homozygous deletion of *NPHP1* under the age of 20 years [21, 22]. In addition, it is reported that the course of chronic renal failure in nephronophthisis might be influenced by unidentified modifier genes or environmental factors [15]. These findings may be involved in the delayed diagnosis of nephronophthisis in the patients of the age of 20 years and older.

Pathological findings of nephronophthisis include renal tubular atrophy associated with thickening and thinning of the renal tubular basement membrane, cysts in the corticomedullary junction, and interstitial fibrosis [23, 24]. However, these findings are not necessarily characteristic of nephronophthisis, as they are also observed in patients with medullary cystic kidney disease. Examination of the renal biopsy specimen showed irregular tubular dilatation and atrophy associated with thickening, thinning, and disruption of the tubular basement membrane, as well as diffuse fibrosis and cell infiltration in the interstitium; therefore, nephronophthisis or medullary cystic kidney disease were considered in the differential diagnosis.

The gene most often responsible for nephronophthisis is *NPHP1*, with mutations in *NPHP1* accounting for 21% of cases with nephronophthisis, and approximately 90% of *NPHP1* variants are reported to represent complete homozygous deletion [2, 25]. Other genetic mutations causing nephronophthisis have been identified in only 3% of patients with this disease, and the responsible genes in approximately 70% of such patients remain unknown [2]. Therefore, even if nephronophthisis is suspected and genetic analysis is performed, it is often necessary to arrive at a diagnosis in an integrated manner using the patient's past history, laboratory findings, imaging findings, and pathological findings. In our present case, based on the results of genetic analysis, we made a diagnosis of nephronophthisis due to complete homozygous deletion of *NPHP1*. Although detailed information regarding her parents' medical history was not available, we closely examined her siblings because nephronophthisis

is an autosomal-recessive disease, and as a result, neither renal impairment nor urinary abnormalities were found.

NPHP1 is located on chromosome 2q12-13 and codes nephrocystin-1. Nephrocystin-1 is expressed in the primary villus, which plays an important role in the transduction of signals from the outside to the inside of tubular epithelial cells, and in the adherence junction and desmosome, which play important roles in cell signal transduction, cell adhesion, and cytoskeleton maintenance [26]. Therefore, when nephrocystin-1 abnormalities are present, the above functions may be disrupted, and thus, structural and functional disorders may result due to tubular epithelial cell dysfunction.

Currently, because renal transplantation is the only curative treatment for nephronophthisis, symptomatic treatment for chronic kidney disease is recommended. Recurrence after renal transplantation in patients with nephronophthisis has not been reported [27]. In our present case, we are treating the patient symptomatically while observing the disease course, considering the possibility of future renal transplantation.

We encountered a woman in whom renal impairment was found during pregnancy. Nephronophthisis was diagnosed due to complete homozygous deletion of *NPHP1* by genetic analysis. Fortunately, renal impairment was not exacerbated during pregnancy, and she was able to deliver the baby. Nephronophthisis lacks clear clinical symptoms and is difficult to diagnose in the early phase; therefore, it is important to closely examine younger patients presenting with polydipsia, polyuria, anemia, or renal impairment, suspecting nephronophthisis as a possible cause.

Conflict of interests

The authors have declared that no conflict of interest exists.

References

1. Hildebrandt F, Otto E. Cilia and centrosomes: a unifying pathogenic concept for cystic kidney disease? Nat Rev Genet 6:928–940, 2005
2. Hildebrandt F, Attanasio M, Otto E. Nephronophthisis: disease mechanisms of a ciliopathy. J Am Soc Nephrol 20:23–35, 2009
3. Smith CH, Graham JB. Congenital medullary cysts of the kidneys with severe refractory anemia. Am J Dis Child 69:369–377, 1945
4. Fanconi G, Hanhart E, von Albertini A, et al. Familial, juvenile nephronophthisis (idiopathic parenchymal contracted kidney). Helv Paediatr Acta 6:1–49, 1951
5. Potter DE, Holliday MA, Piel CF, et al. Treatment of end-stage renal disease in children: A 15-year experience. Kidney Int 18:103–109, 1980
6. Ala-Mello S, Koskimies O, Rapola J, et al. Nephronophthisis in Finland: epidemiology and comparison of genetically classified subgroups. Eur J Hum Genet 7:205–211, 1999
7. Ishikura K, Uemura O, Ito S, et al. Pre-dialysis chronic kidney disease in children: results of a nationwide survey in Japan. Nephrol Dial Transplant 28:2345–2355, 2013
8. Hattori M, Mieno M, Aikawa A, et al. Etiology of pediatric kidney transplant patients in Japan (in japanese). Jpn J Transplant 44:69–78, 2009
9. Ala-Mello S, Sankila EM, Koskimies O, et al. Molecular studies in Finnish patients with familial juvenile nephronophthisis exclude a founder effect and support a common mutation causing mechanism. J Med Genet 35:279–283, 1998
10. Salomon R, Saunier S, Niaudet P: Nephronophthisis. Pediatr Nephrol 24:2333–2344, 2009
11. Krishnan R, Eley L, Sayer JA. Urinary concentration defects and mechanisms underlying nephronophthisis. Kidney Blood Press Res 31:152–162, 2008
12. Gagnadoux MF, Bacri JL, Broyer M, et al. Infantile chronic tubulointerstitial nephritis with cortical microcysts: variant of nephronophthisis or new disease entity? Pediatr Nephrol 3:50–55, 1989
13. Haider NB, Carmi R, Shalev H, et al. A Bedouin kindred with infantile nephronophthisis demonstrates linkage to chromosome 9 by homozygosity mapping. Am J Hum Genet 63:1404–1410, 1998
14. Otto EA, Schermer B, Obara T, et al. Mutations in INVS encoding inversin cause nephronophthisis type 2, linking renal cystic disease to the function of primary cilia and left-right axis determination. Nat Genet 34:413–420, 2003
15. Bollee G, Fakhouri F, Karras A, et al. Nephronophthisis related to homozygous NPHP1 gene deletion as a cause of chronic renal failure in adults. Nephrol Dial Transplant 21:2660–2663, 2006
16. Caridi G, Dagnino M, Rossi A, et al. Nephronophthisis type 1 deletion syndrome with neurological symptoms: prevalence and significance of the association.. Kidney Int 70:1342–1347, 2006
17. Hoefele J, Nayir A, Chaki M, et al. Pseudodominant inheritance of nephronophthisis caused by a homozygous NPHP1 deletion. Pediatr Nephrol 26:967–971, 2011
18. Haghighi A, Savaj S, Haghighi-Kakhki H, et al. Identification of an NPHP1 deletion causing adult form of nephronophthisis. Ir J Med Sci 2015; doi: 10.1007/s11845-015-1312-7
19. Omran H, Fernandez C, Jung M, et al. Identification of a new gene locus for adolescent nephronophthisis, on chromosome 3q22 in a large Venezuelan pedigree. Am J Hum Genet 66:118–127, 2000
20. Olbrich H, Fliegauf M, Hoefele J, et al. Mutations in a novel gene, NPHP3, cause adolescent nephronophthisis, tapeto-retinal degeneration and hepatic fibrosis. Nat Genet 34:455–459, 2003
21. Halbritter J, Porath JD, Diaz KA, et al. Identification of 99 novel mutations in a worldwide cohort of 1,056 patients with a nephronophthisis-related ciliopathy. Hum Genet 132:865–884, 2013
22. Sugimoto K, Miyazawa T, Enya T, et al. Clinical and genetic characteristics of Japanese nephronophthisis patients. Clin Exp Nephrol 2015; doi: 10.1007/s10157-015-1180-5
23. Waldherr R, Lennert T, Weber HP, et al. The nephronophthisis complex a clinicopathologic study in children. Virchows Arch A Pathol Anat Histol 394:235–254, 1982
24. Zollinger HU, Mihatsch MJ, Edefonti A, et al. Nephronophthisis (medullary cystic disease of the kidney). A study using electron microscopy, immunofluorescence, and a review of the morphological findings. Helv Paediatr Acta 35:509–530, 1980
25. Chaki M, Hoefele J, Allen SJ, et.al. Genotype-phenotype correlation in 440 patients with NPHP-related ciliopathies. Kidney Int 80:1239–1245, 2011
26. Donaldson JC, Dise RS, Ritchie MD, et al. Nephrocystin-conserved domains involved in targeting to epithelial cell-cell junctions, interaction with filamins, and establishing cell polarity. J Biol Chem 277:29028–29035, 2002
27. Steel BT, Lirenman DS, Battie CW. Nephronophthisis. Am J Med 68:531–538, 1980