Aegean Pathology Journal **2**, 71–76, 2005
Available on line at www.epd.org.tr/apj.php

A regional panorama of non-tumoral nephrectomy reasons in childhood

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Accepted for publication on 24 May 2005

Aims and background: Evaluation of the reasons of nephrectomy in children with severe renal disfunction without neoplastic disease may be useful in the management of pediatric end-stage renal disease. We aimed to evaluate the childhood nephrectomy reasons and to determine the frequency of xanthogranulomatous pyelonephritis (XGP).

Materials and methods: We, retrospectively, reviewed 74 pediatric patients who underwent nephrectomy between 1991 and 2003. Reasons of nephrectomy, weight of kidneys, findings in radiological and scintigraphic investigations, presence of urinary infection at operation time, age and sex of patients and the relationship of these parameters were assessed.

Results: This series consisted of 45 boys (60.8%) and 29 girls (39.2%) with a mean age of 6.01 years (1 month-15 years). All patients present loss of renal function more than 90- 95 percent detected by the radiological and scintigraphic evaluation. The etiology of renal failure led to surgery was infection in 44 cases (59.5%); trauma in 4 cases (5.4%); renal calculi in 5 cases (6.7%) and congenital malformations in the other 21 cases (28.4%). XGP was found in 8 cases (10.8%). While kidney size was found as normal or small in 62.2% of all, it was large in 75% of XGP cases. Urinary infection was determined in 31 cases (41.9%). Hypertrophy of kidney was associated with both the presence of urinary infection at operation time (p=0.040) and XGP (p=0.014).

Conclusion: In the present study, a realistic comprehensive picture of the nephrectomy reasons in a central children's hospital has been provided and it was discussed whether early diagnosis and adequate medical treatment can prevent nephrectomy in some of these disorders as well as the possible reasons of high XGP percentage in our series. It is also concluded that kidney size may be used as a specific clue for preoperative differential diagnosis of XGP.

Key words: childhood, non-neoplastic reason, nephrectomy, xanthogranulomatous pyelonephritis.

Introduction

Nephrectomy in childhood is an ultimate indication which is generally realized in neoplastic involvement of the kidney. The recognition that the pediatric kidney has a remarkable ability to recover its function after reconstructive surgery has led to a more conservative approach. Children with antenatally detected congenital urinary system malformations such as pelvi-ureteric junction obstruction (PUJO) or multicystic dysplastic kidney (MCDK) have recently been advocated reconstructive surgery instead of nephrectomy. Similarly in some infection related disease, the nephrectomy can be avoided with early diagnoses and adequate treatment. But still severe

deterioration of the renal function may occur in some congenital or acquired disorders in which nephrectomy becomes necessity. Fortunately, the annual incidence of ESRD in the childhood is very low, approximately 1–2 children per million in general population or 4–6 children per million in childhood population.[1–4]

Xanthogranulomatous pyelonephritis (XGP) is an uncommon chronic, inflammatory disease accounting for 6/1000 surgically proved cases of chronic pyelonephritis. It is observed less frequently in children and etiology is still obscure due to the limited number of the cases. Its manifestation mimics a neoplastic disease because of extensive adhesions to the surrounding structures and ill-defined margins in radiological investigations.[5–7]

We think that providing a panorama of the childhood nephrectomy reasons could be useful to reduce the non-tumoral nephrectomy incidence in children. In this study, we aimed to document and categorize the reasons of pediatric non-tumoral nephrectomies, and compare the differences with literature findings. By this way, we tried to determine the percentage of some disease in which nephrectomy can be prevented. As well as, the etiology of XGP and the probabilities of environmental differences or genetic susceptibilities were discussed because of the high percentage of this disease in our series corresponding to the rates published in many other countries.[8–10]

Material and Methods

The hospital records and pathological slides of 74 consecutive nephrectomies for non- neoplastic conditions performed during the period of 1991 to 2003 were reviewed. The hematoxylin-eosin stained slides were retrospectively examined by four pathologists.

Reason(s) of nephrectomy, weight of kidneys, findings in radiological and scintigraphic investigations, presence of urinary infection at operation time, age and sex of patients and the correlations of all these parameters were assessed.

The pathological slides of the infection-related diseases were carefully reviewed to found focal or diffuse XGP. Two slides representing the lesion of these cases were stained with Erlich-Ziehl-Nielsen and periodic asit Shiff (PAS) stains for excluding the specific etiologic agents.

The changes in kidney weight were evaluated quantitatively according to normal weight scales[11] and results were classified as small, normal or large. The presence of urinary infection at operation time was searched by both direct microscopic examination and recorded urine culture results for each case. Radiological investigations were consisted of intravenous pyelography, retrograde pyelography, ultrasound scan and computerized tomography (CT), while scintigraphic studies were of conventional renal scans with Tecnetium 99m diethylenetri-aminepentaaseticacid (DTPA) and Tecnetium 99m dimercaptosuccinicacid (DMSA).

Descriptives and frequencies of parameters were evaluated by Pearson Correlation Analysis and Chi-square test. P values less than 0.05 were considered as statistically significant.

Results

Forty-five (60.8%) patients were male and 29 (39.2%) were female. Left and right kidneys were involved in 35 (47.3%) and 39 (52.7%) patients, respectively. The mean age was 6.01 years (±4.16) ranging between 1 month to 15 years.

In all patients, loss of renal function more than 90-95% was detected by the scintigraphic studies, especially renal scan with DTPA.

The etiology of renal failure leading to surgery was infection in 44 cases (59.5%); trauma in 4 cases (5.4%); renal calculi in 5 cases (6.7%) and congenital malformations in the remaining 21 cases (28.4/%) such as MCDK (n: 11), hydronephrosis associated with congenital urinary tract obstruction (CUTO) or reflux (n: 6), horseshoe kidney (n: 2) and renal duplication (n: 2) (Figure 1). The focal or diffuse XGP was found in 8 (10.8%) cases (Figure 2). These lesions were consisted of granuloma-like collection of histiocytes and other inflammatory cells (Figure 3) in which a specific etiologic agent could not be demontrasted either histopathologically or microbiologically. The clinical features of these patients are summarized in Table 1.

It is found that the number of nephrectomies secondary to acquired disorders is declining during the

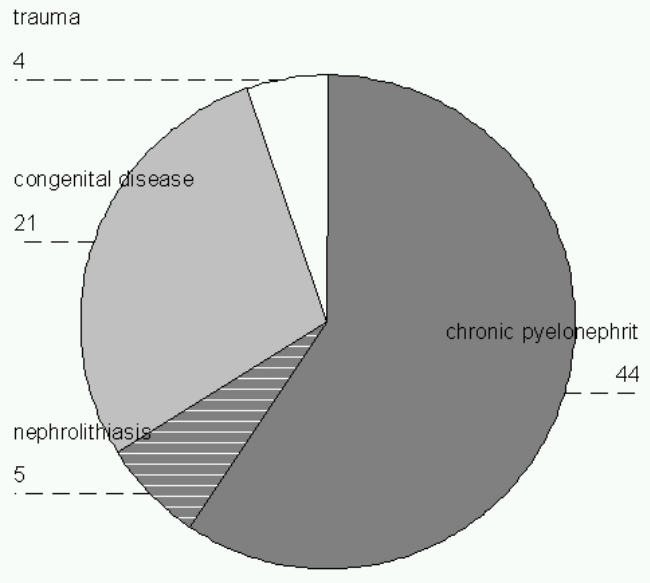

Figure 1. Distributions of the cases according to nephrectomy reasons.

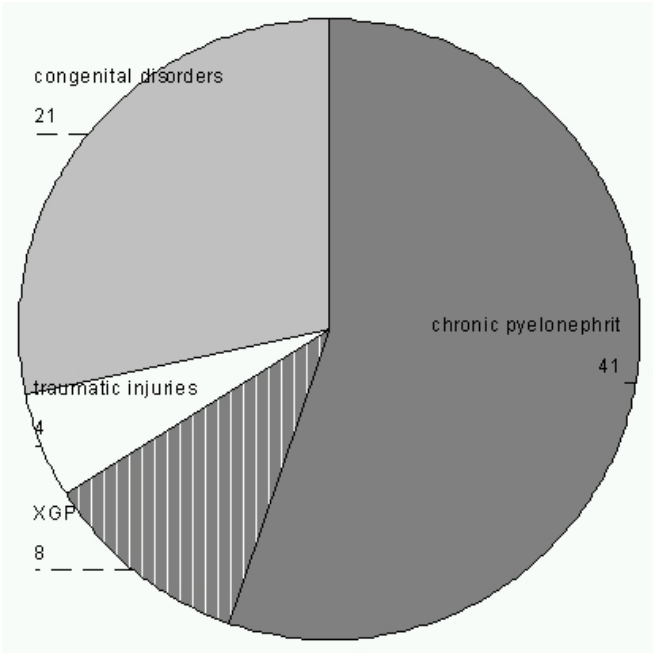

Figure 2. Distributions of the cases according to the pathological diagnosis.

last few years (Figure.4). The mean case number per year have decreased from 7.28 in 1991-1997 to 3.80 in 1998-2003. On the other hand, the higher incidence of nephrectomy for congenital diseases is relatively persistent. While the rate of nephrectomy for acquired disorders decreased from 73.7% to 58.3% to date, the decrease for congenital disease is found to be only from 29.4% to 26%. A similar decrease with age is also observed in the frequency of congenital disorders leading to nephrectomy (Figure 5).

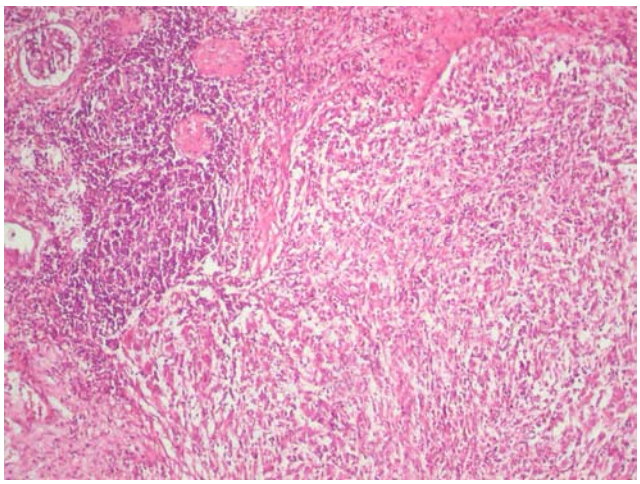

Figure 3. Microscopic appearance of granulomatous infiltration of renal parenchyma by histiocytes with a relatively intact glomerulus and two sclerotic glomeruli (HEX 100).

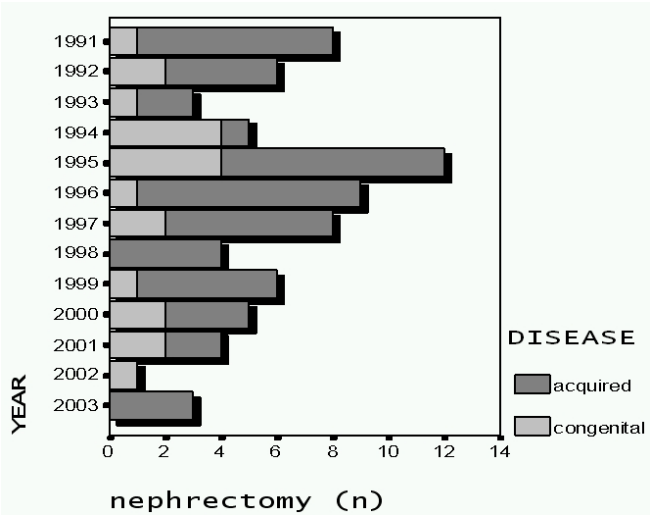

Figure 4. The annual incidence of nephrectomy for congenital and acquired diseases.

Kidney size was normal in 21 cases (28.4%), small in 25 cases (33.8%) and large in 28 cases (37.8%). Kidney size was found to be as normal or small in 62.2% of all cases. Contrary, it was found as large in 75% of XGP. In 31 cases (41.9%) urinary infection was detected at the operation time. Urine culture was positive for E. coli in 27 cases (87 %), for P. mirabilis in 2 cases (6.6%), for Klebsiella spp and Staphylococcus epidermidis in others. Non-functioning kidney with or without calcifications was the most frequent finding in radiological investigations. Only one case (1.35%) presented high blood pressure.

Table 1. The clinical features of the cases with XGP.

Patient	Year	Sex	Age	Kidney side	Kidney size	Renal calculi	Urinary infection (Isolated bacteria)
1	1991	Male	6	left	large	–	*E. coli*
2	1994	Male	5	left	large	_	_
3	1996	Male	4	right	large	_	_
4	1997	Male	3	right	large	_	_
5	1999	Male	8	right	large	–	*Proteus mirabilis*
6	1999	Female	14	left	large	+	*E. coli*
7	1999	Male	10	right	normal	_	–
8	2003	Male	8	Left	small	_	*E. coli*

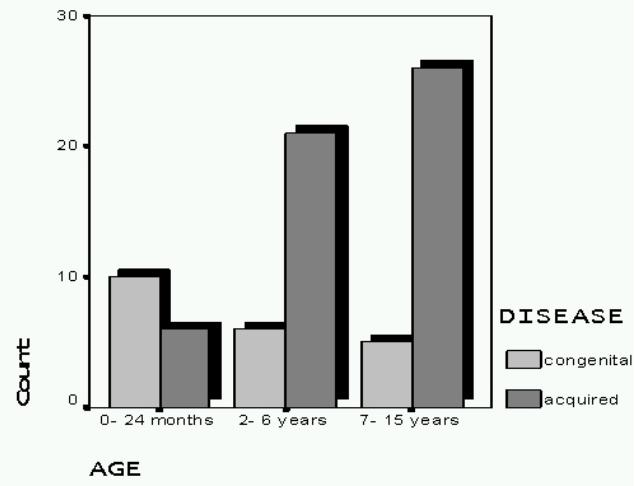

Figure 5: Distribution of diseases according to patient age.

In Pearson correlation analyses, increase of kidney size was found to be associated with urinary infection (p=0.04). In Chi-Square test, there was also a statistically significant association between large sized kidneys and XGP (p=0.014).

Discussion

Many reports suggested that the rate of nephrectomy for benign conditions has declined during the last few years in comparison with malignant conditions. Similarly, the rate of acquired disorders leading to nephrectomy has decreased. But, in spite of the development of antenatal diagnostic methods, the higher incidence of nephrectomy for congenital diseases still persists. Because of the relatively high frequency in society, there is a great deal with the congenital malformations of urinary system. If all malformations are considered, ranging from incidental findings to lethal anomalies, it is estimated that congenital urinary tract malformations are present in 10% of newborns.[10,12–14]

It is debatable whether nephrectomy or only careful follow up is the more appropriate menagement of children with congenital malformations leading to severe impairment of renal function. The review of the literature reveales that, there is minimal risk for hypertension and infection in non-obstructive congenital disorders. The most important risk is the development of Wilms' tumor in the left kidney. This is 3 to 10-fold of the general pediatric population risk of 0.001. Therefore, in conservative approach, following up of these children with radiological investigations until 8 years age is necessary. Early nephrectomy seems to be more cost-effective than these procedures. On the other hand, if it seems not possible to follow up these children frequently, nephrectomy may be a more reasonable choice of treatment.[1,2,15]

There are more grave complications such as high blood pressure and acute pyelonephritis in CUTO. Although specialized diagnostic techniques are well-developed, efforts for early detection of the disease remain unsatisfactory. The reason for this is not only the atypical course of early hydronephrosis but also the absence of pathognomonic symptoms. Approximately half of patients undergo primary nephrectomy. Some of these procedures are performed following earlier plastic operations. Considering the current literature, unfortunately, it seems that the relatively higher

incidence of nephrectomy in congenital malformations will persist for a long time.[3,4,9,16,17] Similarly, the present study showed that while the decrease in nephrectomy rate secondary to acquired disorders is 25.4% (from 73.7% to 58.3%), it is only 3.4% (from 29.4% to 26%) in congenital diseases.

Chronic pyelonephritis is the second commonest cause of end-stage renal failure after chronic glomerulonephritis.[18] But in our series, inflammatory conditions are restricted with renal parenchymal infections. As our center can not perform renal transplantation, patients who have bilateral renal failure secondary to glomeruler disease are not admitted.

It is usually believed that recurrent infections are the basic cause of chronic pyelonephritis. But there is little evidence that urinary-tract infection (UTI) causes progressive renal damage without vesicoureteric reflux in infants and children or without obstructive uropathy in adults. Cystitis accounts for the vast majority of UTIs and pyelonephritis occurs less frequently. Many bacteria are capable of causing either of these infections; however, it is not known why cystitis develops in one individual and acute pyelonephritis develops in another. Are there specific genotypic or phenotypic features of the infecting bacterium, or do host factors dictate the outcome of cystitis or pyelonephritis? What trait of a bacteria strain makes it a cystitis-causing strain as opposed to a pyelonephritis-causing strain? More recent works have suggested that the ordinary bacteria have required some organelles for binding to uroepithial cells. Type I and P-fimbriae are hair-like projections that extend from the surface of Escherichia coli and other genera of the Enterobacteriaceae. Indeed, the presence of type I fimbriae increases the number of E.coli successfully infecting the urinary tract, as well as enhancing the persistence of the bacteria.[19–21] In the present study, the most isolated etiologic agent of UTIs was *E. coli*, but phenotypic differentiation could not be done.

XGP is a rare inflammatory disease accounting for 0.6% of chronic pyelonephritis. It is observed more frequently in adults. Etiology is not still enlightened. However, several etiological factors are thought to be responsible for the pathogenesis of XGP. These include urinary obstruction, ineffectively treated urinary infection, chronic renal ischemia and immune deficiency. In this study, the rate of XGP was higher than other series and all of them was diffusely affected the kidney. As focal XGP was reported to be more common in children,[5,7] we think that XGP could easily be overlooked in children with localized disease if only tru-cut biopsy or partial nephrectomy were performed. Adding the conservative management of severe deterioration of the renal function in children as a recent choice of treatment, it can be concluded that the actual incidence of XGP in children may be higher than diagnosed.

It is known that untreated infections can also somehow allow XGP to develop.[22] As social-economical status of most admitted patients to our hospital was low, they have probably exposed to insufficient care and treatment for ordinary UTIs.

In pediatric renal diseases except from hydronephrosis, nephromegaly usually is not determined. XGP can appear as a solid mass because of its large size. It mimics a malignant disorder especially with extensive adhesions to the surrounding structures and ill-defined margins in radiological investigations. Secondary cyst formation may be observed and it is often misdiagnosed preoperatively. Therefore, XGP must be considered in the differential diagnosis of renal neoplasm in childhood, particularly cystic Wilms' tumor or Wilms' tumor with significant intratumoral hemorrhage.[23] In this study, while kidney size was found as normal or small in 62.2% of all cases, it was large in 75% of XGP. But extensive adhesions or ill-defining margins were not determined and malignancy was not suspected in any patients.

We conclude that children presenting with multinodular nephromegaly and renal failure, watchful eyes would be kept open for the possibility of xanthogranulomatous pyelonephritis. Nephromegaly may be used as a criterion to predict XGP instead of other chronic pyelonephritis and this finding may be helpful in the differential diagnosis with malign conditions as well as for therapeutic decisions.

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