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ORIGINAL ARTICLE

Long-term outcome of biopsy-proven minimal-change nephrotic syndrome in Chinese children

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KEYWORDS
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Summary *Background:* Previous studies have shown that up to 40% of childhood-onset minimal-change nephropathy (MCN) cases persist after puberty. However, data are scarce concerning the long-term renal prognosis and prevalence of treatment-related complications of this group of patients after they become adults.
Materials and methods: The clinical records of 55 consecutive pediatric patients with biopsy-proven MCN treated in our hospital from 1984 to 2004 were reviewed to evaluate the disease pattern, treatment regimen, and the development of treatment-related complications.
Results: Of the 55 patients treated, 35 were followed after age 18 years; 13 (37%) had relapses during adulthood. Treatment-related complications were observed in 20 patients (57%), including being overweight (23%), impaired fasting glucose (14%), infertility (14%), persistent low grade proteinuria (11%), fracture (9%), and hypertension (9%). All patients had normal renal function when last assessed.
Conclusion: A substantial proportion of patients with childhood-onset MCN continued to have relapse after they became adults. Although almost all patients have normal renal function, prolonged use of steroid and immunosuppressive agents results in a considerable risk of treatment-related complications. Life-long follow-up seems advisable for this group of patients, not only for detecting relapses, but also to allow timely diagnosis of treatment-related complications.

背景：之前的研究顯示，童年病發的微小變化型腎病變(MCN)有高達40%會持續至青春期之後；然而，對於這類病情延續至成年的患者，至今少有研究對其長期腎臟預後及治療相關併發症比率作出報告。
方法：針對經活檢證實的MCN兒童患者，我們回顧了55位於1984至2004在本院接受治療的連續個案，從而對其病情發展、治療用藥、及治療相關併發症作出瞭解。
結果：在所有55位兒童病人中，35人持續接受追蹤至成年期。在成年階段中，13人(37%)出現復發，20人(57%)發生治療相關併發症，後者包括過重(23%)、空腹血糖過高(14%)、不孕症(14%)、持續性輕度蛋白尿(11%)、骨折(9%)、及高血壓(9%)。在最後追蹤中，所有人均呈現正常的腎功能。

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結論：不少的童年病發MCN患者會在成年期復發，即使幾乎所有人的腎功能正常，持續使用的類固醇及免疫抑制劑所導致的治療相關併發症風險卻不容忽視。對於這些病人，似乎應予以終生的追蹤，以利於病情復發及治療相關併發症的及早發現。

Introduction

Minimal change nephropathy (MCN) is the major cause of steroid-sensitive nephrotic syndrome in childhood.[1] It was previously believed that MCN runs a benign course in childhood, and most cases remit prior to or at puberty.[2] However, more recent studies have revealed a higher rate of disease relapse during adulthood despite the availability of more potent immunosuppressive agents.[1,3] More importantly, a prolonged course of the disease implies that patients are exposed to high cumulative doses of corticosteroid and, sometimes, other immunosuppressive agents, and the risk of developing adverse effects increase correspondingly. Although there have been many studies on the disease course and treatment response in children suffering from steroid sensitive nephrotic syndrome or MCN, few studies have explored the outcome when those children reach adulthood. Even in the largest series by the International Study of Kidney Disease in Children (ISKDC),[4] where 389 biopsy-proven children with MCN were followed for up to 17.6 years, no data were provided on those patients who were continued to be followed after puberty.

Since cyclosporine was introduced in the late 1960s, the outcome of MCN patients with frequent relapse changed dramatically. In addition to the availability of cyclosporine to our therapeutic armamentarium, there have been many concomitant changes in the clinical nephrology practice during this period. In the past decade, a few case series reported the clinical course of adult western patients who had childhood-onset MCN.[1,3,5] The overall rate of relapses during adulthood ranges from 29% to 42%. In the study by Fakhouri et al,[1] more than 40% of patients were identified as adulthood relapsers, one-third of the patients relapsed during adulthood in the report by Rüth et al,[3] whereas 29% patients in the study by Kyrieleis et al relapsed as adults.[5] In the present study, we evaluate the long-term outcome of Chinese children with biopsy-proven MCN after they became adults.

Materials and methods

There were 55 pediatric patients (age $<$ 18 years) identified with biopsy-proven MCN treated in our hospital from 1984 to 2004. Out of the 55 patients, 35 were followed after age 18 years. The clinical records of these patients were reviewed; relevant data on the course of disease, treatment regimen and response, disease outcome, as well as complications were collected.

Treatment protocol

The standard regimen in our hospital for the initial episode of nephrotic syndrome diagnosed in childhood was similar to that outlined by international guideline,[6] and was generally prednisolone, at a starting dose of 60 mg/m^2. This regimen was continued and tapered in 8—12 weeks when proteinuria disappeared. Further relapses were treated with repeated high doses of prednisolone until proteinuria subsided. In patients with frequent relapses or those dependent on steroid or in those with substantial steroid-related adverse effects, second line agents such as cyclophosphamide, cyclosporine, or levamisole were used.

Definitions

The definitions of treatment response have been previously described.[5] Briefly, complete remission of nephrotic syndrome is defined as: a reduction in urinary protein excretion rate to $<$4 mg/m^2/hour; proteinuria $<$0.2 g/10 mM creatinine; or zero to trace albuminuria on dipstick for 3 consecutive days. Partial remission is defined as protein excretion between 0.2 g/10 mM and 2 g/10 mM creatinine without hypoalbuminemia. A relapse-free period of a minimum of 2 years without immunosuppressive medication is defined as a permanent remission. Patients were classified as frequent relapsers when they experienced four or more relapses within a 12-month period.

Complications

The long-term complications of nephrotic syndrome and immunosuppressive medications were also reviewed. Parameters reviewed include renal function, short stature, being overweight or obese, osteoporosis, hypertension, ocular complications, and fertility. Short stature was defined as a height less than 2.5 standard deviation compared with normal stature for age and gender in the local population. Overweight was defined as a body mass index $>$ 23 kg/m^2; obesity was defined as a body mass index $>$ 26 kg/m^2.[7] Hypertension was defined as an office blood pressure of over 140/90 mmHg or the need of antihypertensive treatment.[8]

Statistical analysis

Statistical analysis was performed by SPSS for Windows software version 17.0 (SPSS Inc, Chicago, IL, USA). Data are expressed as mean $\pm$ standard deviation if normally distributed, or median (range) if not. Groups were compared by unpaired Student *t* test, Chi-square test, or Fisher's exact test as appropriate. A *p*-value of $<$0.05 was considered significant. All probabilities are two-tailed.

Results

Clinical features

Of the 55 patients identified, 35 were followed into adulthood. Their average age at presentation was 8.8 $\pm$ 3.2

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