4.2 Prognosis

Practice Point 4.2.1: The prognosis for childhood nephrotic syndrome is best predicted by the patient's response to initial treatment and frequency of relapse during the first year after treatment. Therefore, a kidney biopsy is not usually needed at initial presentation, and instead is reserved for children with resistance to therapy or an atypical clinical course.

Nephrotic syndrome is the most frequent glomerular disease in children, with an incidence of 1.15–16.9 per 100,000 children.[207] Before the availability of antibiotics and glucocorticoids, about 40% of children with NS died of infection, kidney failure, and occasionally thromboembolism.[208] If the children survived, sustained spontaneous remission was observed only after years of disease activity. Antibiotics reduced mortality, but it was the introduction of glucocorticoid use in the 1950s that changed the natural history of the condition.[208] Since the 1970s, following onset of disease, children are treated with a standard dose of glucocorticoids. Response to this standard dosing regimen and the number of relapses in the subsequent year allows classification of the child's NS, and this classification holds more prognostic value than a kidney biopsy, which is therefore not routinely performed at disease onset. In general, it is assumed that children with steroid-sensitive forms of NS, if biopsied, would most frequently be found to have MCD, though mesangial proliferation with IgM and FSGS (the lesion most frequently associated with steroid-resistant forms of NS) has also been described.

In children with steroid-sensitivity receiving timely and appropriate treatment, kidney function is always maintained, and prognosis is correlated with the morbidity of prolonged exposure to glucocorticoids and to second-line glucocorticoid-sparing agents that are prescribed in frequently relapsing and especially in steroid-dependent forms of disease. The disease has a chronic, relapsing–remitting course, which tends to resolve spontaneously following puberty. However, in 15%–25% of cases, it may progress to adulthood, maintaining the peculiar features of the childhood-onset NS with rapid response to glucocorticoids in case of relapse. Moreover, a small percentage of children may, in subsequent relapses, become secondarily steroid-resistant. These children have a high chance of both progressing to kidney failure and relapsing post-transplantation.

A kidney biopsy is therefore performed at onset only in children with atypical features and in all children with steroid-resistance (Figure 43). Subsequently, during the disease course, it may be advisable to perform or repeat a kidney biopsy in children who have had a prolonged (>2–3 years) exposure to CNIs or who have secondary steroid-resistance.

In children with steroid-sensitive (SS) and steroid-resistant (SR) but calcineurin-responsive forms of NS, the optimal treatment strategy is therefore aimed at employing the lowest cumulative doses of glucocorticoids and the safest and most effective glucocorticoid-sparing agents to maintain remission. The use of vitamin D/calcium, gastroprotection, and an appropriate vaccination strategy are also important to minimize morbidity.

In children with resistant forms of NS, prompt genetic testing to allow appropriate management of the kidney disease and, when present, extrarenal features, is mandatory. Optimal conservative therapy to minimize the side effects of prolonged proteinuria and treatment with dialysis and transplantation must be performed in centers that have specific expertise in pediatric nephrology.

4.3 Treatment

A schematic approach to treatment is outlined in Figure 40.