Chicken Pox in Adult Renal Transplant Recipients

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Two out of 90 renal transplant recipients developed chicken pox 3 and 52 months after transplantation. Both patients were receiving triple therapy with prednisone, azathioprine and cyclosporin. The azathioprine was stopped temporarily and both received intravenous acyclovir. Renal function remained normal and both patients survived with full clinical recovery. Chicken pox has been reported to be associated with a severe and often fatal course in immunosuppressed adult renal transplant patients. We describe the successful course of two renal transplant patients who developed chicken pox and were treated with intravenous acyclovir.

Primary varicella is a benign disease in the healthy but in adult renal transplant recipients immunosuppressed with prednisone and azathioprine it has been reported to have a grave prognosis with high mortality despite acyclovir therapy. A more favourable outcome was seen in patients on prednisone and cyclosporin only, with the suggestion that cyclosporin-treated patients have a better prognosis in chicken pox than azathioprine-treated patients in view of the more selective immunosuppressive action of cyclosporin. Looking at the results carefully, however, it would seem that early and optimal doses of acyclovir significantly contributed to the favourable prognosis.

Two of our adult renal transplant recipients receiving triple therapy with prednisone, azathioprine and cyclosporin developed chicken pox. They therefore represented a different immunosuppressed population to the above reported cases. We report their successful course with intravenous acyclovir therapy.

Methods

At Al Hada Hospital 90 renal transplant recipients are being followed up. Two of these patients developed chicken pox between 3 and 52 months after transplantation. In view of the characteristic skin eruption and history of exposure in the previous 2–3 weeks, it was felt unnecessary to perform specific sophisticated diagnostic tests (identification of the varicella zoster virus [VZV]) by electron microscopy or by elevated antibody titres to VZV).

Case 1

A 16-year-old female who had received a cadaveric renal transplant 52 months previously and who was maintained on prednisone 0.1 mg/kg, azathioprine 1.6 mg/kg and cyclosporin 2.2 mg/kg (whole blood level 345 ng/ml) was admitted to hospital with a 3-day history of fever and generalized malaise. On the second day of admission she developed a characteristic chicken pox rash and gave a history that three of her siblings, who lived at home with her, had suffered from chicken pox within the previous 3 weeks. Prednisone and cyclosporin were continued but the azathioprine was stopped. Intravenous acyclovir was started at 5 mg/kg every 8 h and continued for 5 days. The chicken pox rash started to regress by the third day of therapy and the azathioprine was reintroduced on the fifth day. Renal function remained normal and the patient made a full recovery and was well at her last follow-up 15 months later.

Case 2

A 31-year-old female received a live non-related renal transplant in early February 1989. She was taking prednisone
Discussion

Chicken pox is a serious disease in immunosuppressed adults with renal transplants. Zoster immune globulin has been shown to prevent or modify the course of chicken pox in immunocompromised patients when given during the incubation period\(^6,5\) but the majority of patients present beyond that period and hence would not benefit from it. The recommended dose is 125 units/10 kg intramuscularly\(^6,5\) and recently a preparation for intravenous infusion (1 ml/kg) has also become available.

In immunosuppressed children acyclovir has been shown to be helpful against varicella infection\(^6\) especially when given early in the course of infection.\(^3\) In another study acyclovir was also found to halt progression of herpes zoster in immunocompromised patients.\(^7\)

Both our patients were on triple therapy. Prednisone and cyclosporin were continued and azathioprine stopped as soon as the diagnosis was made. Our experience and that of others\(^9\) show no loss of graft function from stopping the azathioprine temporarily.

Mild and transient elevation of liver enzymes is common in routine cases of chicken pox but marked elevation in addition to thrombocytopenia tends to be associated with severe infections as seen in Case 2. Pneumonitis was not seen in our patients although it has been reported in association with severe varicella infection.

Acyclovir therapy is well tolerated in the recommended dose of 10 mg/kg (or 500 mg/m\(^2\)) every 8 h.\(^9\) In patients who are inadequately hydrated or have impaired renal function, it has been claimed that intravenous acyclovir can accumulate in the collecting system of the kidney to cause reduction in renal function.\(^3\) In view of slight dehydration in our patients, we started with the smaller dose of 5 mg/kg every 8 h.

The total white count dropped in our patients. In Case 2, however, this occurred 2 days after increasing the intravenous acyclovir to 10 mg/kg and started to rise 2 days after resuming the smaller dose of 5 mg/kg. Whether this drop in white count was due to the severe varicella infection or was related to the increase in the acyclovir dose is difficult to ascertain. A transient drop in white count following intravenous acyclovir was also reported previously\(^10\) but other complicating factors in that case preclude firm indictment of acyclovir as the responsible agent.

The rapid improvement in Case 1 when the patient received acyclovir on the first day of the rash is in keeping with previous reports stressing the need for early administration of acyclovir\(^9\) and might also be related to the much smaller maintenance dose of prednisone at the time of varicella infection in contrast to Case 2.
Renal transplant patients with no previous history of chicken pox should be instructed to report any contact with such cases immediately. If they present during the incubation period they should receive zoster immune globulin. If, however, as is usual they present after the onset of chicken pox they should be hospitalized and intravenous acyclovir started as early as possible. Hydration is important and renal function and white cell count should be regularly monitored. Prednisone and cyclosporin should be continued but azathioprine can be stopped temporarily without apparently precipitating graft rejection. The recent development of a varicella vaccine\(^{11}\) may prove useful in preventing infection in high risk patients.

Second attacks of chicken pox are rare,\(^{12}\) but in view of the severity of the disease in immunosuppressed renal transplant recipients, even those with previous history of chicken pox should be advised to report contact with fresh cases. They should be carefully observed and acyclovir given at the earliest indication of onset of chicken pox.

References