Reactivation of polyomavirus in bone marrow transplant recipients

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Abstract

Polyomavirus was detected in the urine samples of 12 (48%) out of 25 patients within three months of receiving a bone marrow transplantation. The virus was first detected 11 to 46 days after the transplantation and excretion persisted for up to 42 days. Detection of the virus was not associated with symptoms and it seemed to be a marker of immunosuppression.

Detection of polyomavirus in patients' urine after bone marrow transplantation (BMT) has been described in association with hepatic dysfunction and haemorrhagic cystitis. O'Reilly et al., using electron microscopy, detected polyomavirus in 17 out of 45 patients after BMT. A review of the patients' clinical course suggested that there was an association between mild hepatic dysfunction and virus excretion. Arthur et al. used an enzyme linked immunosorbent assay (ELISA) and DNA hybridisation to monitor the presence of BK and JC virus after BMT. They found BK virus in about 50% of patients, in whom it was associated with severe haemorrhagic cystitis. JC virus, less frequently detected (7%), was not associated with symptoms. Arthur et al. did not find any association between either virus and hepatic dysfunction. Apperley et al. described eight patients with papovavirus after BMT, three of whom had haemorrhagic cystitis.

In this study electron microscopy was used to examine four or more urine samples (mean eight per patient) from 25 patients in the three months following BMT for haematological malignancies. Urine samples were received either neat (70 out of 200) or diluted in an equal volume of virus transport medium (VTM) and 2 ml aliquots were ultracentrifuged at 65 000 g for one hour at +8°C. The resulting pellets were resuspended in distilled water. A pioloform-coated copper grid was floated on a drop of suspension and, after blotting, negative staining was performed using 3% aqueous phosphotungstic acid at pH 6.3–6.5. Polyomavirus was easily detected, being present in large numbers, even when the urine had been diluted in an equal volume of VTM. The virus was detected by electron microscopy in 34 urine samples from 12 (48%) of the patients and was first seen between 11 and 46 days (mean 29 days) after BMT. Twenty two of the 34 electron microscopy positive urines were received in VTM and these were also cultured in MRC fibroblasts. A cytopathic effect was seen in 15 (68%) specimens after nine to 48 days. The cytopathic effect occurred mainly at the edge of the cell sheet and consisted of isolated, large, round, slightly refractile cells. In the nine patients in whom virus was found in more than one urine sample it persisted for seven to 42 days. These results are very similar to those of other workers. No association was found between virus excretion and either haemorrhagic cystitis or hepatic dysfunction.

There is a high prevalence of antibodies to human polyomavirus in the general population. Thus the virus seen in the present study was considered to be due to reactivation. It is difficult to attribute symptoms to any one cause after BMT, as cytotoxic treatment, graft versus host disease, and infection may all lead to morbidity. It may be that this multiple pathology obscured the part played by polyomavirus in our patients' symptoms, but an alternative explanation is that there may have been subtle differences in our patient group or in their treatment that limited the pathogenicity of polyomavirus. In spite of the large amount of virus excreted in the urine, polyomavirus in our patients seemed to be a marker of immunosuppression which did not cause any associated morbidity.