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On the Cover
What's the diagnosis?
A 55-year-old man underwent a 3 month protocol biopsy after living donor transplantation. Recently, he has suffered from diarrhea but was otherwise healthy. At the time point of biopsy, a slight increase in creatinine (+40 μmol compared to baseline) as well as >0.5 million CMV-copies (previously negative) were documented. He was still on antiviral prophylaxis with valganciclovir when the primary infection was diagnosed. CMV-infection of the transplanted kidney was diagnosed by biopsy. The patient was successfully treated with intravenous ganciclovir. Image Description: Kidney biopsy revealed viral nuclear inclusions in the glomeruli without significant glomerular inflammation (Figure 1) as well as mild interstitial inflammation and tubulitis. CMV-immunohistochemistry revealed that the vast majority of infected nuclei were restricted to the glomeruli with only single positive cells in the interstitial compartment. Glomerular infection was not restricted to endothelial cells (Figure 2), but also affected cells of podocyte origin. Teaching Points: CMV-infection in kidney transplants is rare nowadays, since prophylactic therapy is the standard. However, it still exists, even under ongoing prophylaxis, and can be morphologically a very subtle finding lacking prominent inflammatory reaction. It is important to be aware of the histological changes induced by CMV and to utilize CMV-immunohistochemistry in suspect cases.

Figure Legend: 1. Glomerulus with viral nuclear inclusions (arrows). At the lower right nuclei are localized intracapillarly going in line with cells of endothelial origin, at the upper left (arrow) a cell with viropathic changes is localized at the outer aspect of the glomerular capillary best fitting a podocyte origin (hematoxylin and eosin, x630). 2. Immunofluorescence double staining for cytomegalovirus (CMV) antigens (red) and the endothelial transcription factor ERG (green) prove the endothelial origin of a subset of cells infected (bottom, double arrow), but also shows one CMV-infected cell not belonging to the endothelial cell pool (top, single arrow, original magnification, x630 blue: nuclear counterstaining with DAPI).

(Images and text provided by Simon P. Parmentier, University Hospital Carl-Gustav-Carus, Department of Medicine III, Division of Nephrology, Dresden, Germany and Maike Büttner-Herold, Department of Nephropathology, Institute of Pathology, University Hospital Erlangen, Friedrich-Alexander-University Erlangen-Nürnberg, Erlangen, Germany)