BK VIRUS- NEPHROPATHY IN PEDIATRIC PATIENT WITH MYELODYSPLASTIC SYNDROME AND HEMATOPOIETIC STEM CELL TRANSPLANTATION

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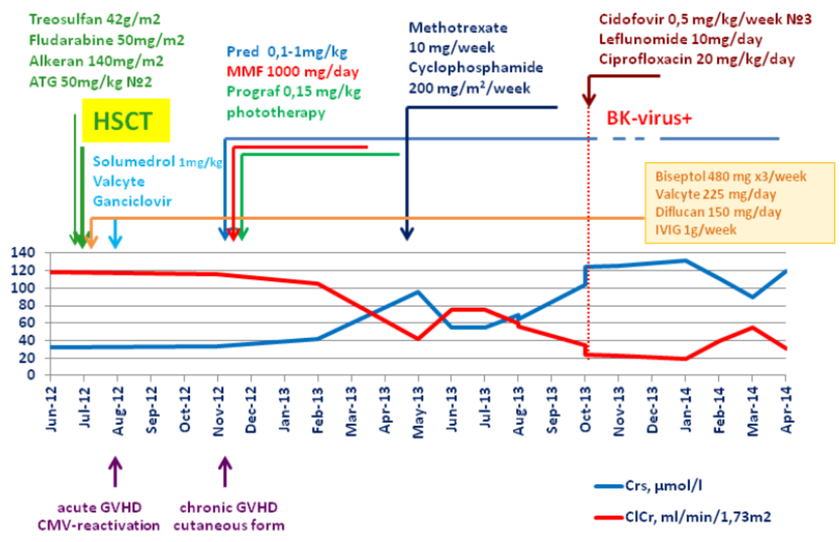
BACKGROUND

BK virus-nephropathy (BKVN) is estimated to cause a progressive kidney transplant injury in 1-10% of renal transplant recipients, but it's rarely diagnosed in case of non-renal transplantation [1,2].

There are few clinical observations of BKVN in patients with heart, liver and hematopoietic stem cell transplantation (HSCT) to date [3,4,5].

It's possible that the actual incidence of BKVN is much higher in these patients.

Fig.1 Clinical-laboratory data of the patient



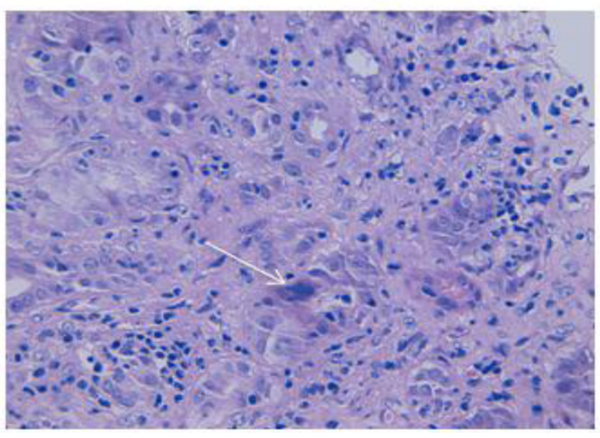


Fig.1A
H&E; magnification x100
Mild inflammatory infiltrates in the interstitium, interstitial fibrosis and tubular atrophy; many tubular epithelial cells have large, homogenius, intranuclear inclusions (arrow) with a ground-glass appearance, representing aggregations of viral particles in the nucleus

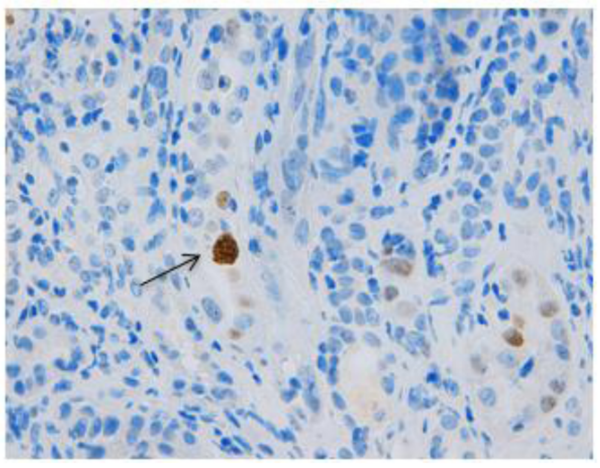


Fig.1B
Immunoperoxidase staining against SV40 T-antigen; paraffin/microwave techniques; magnification x400
A positive immunohistological reaction with BK-specific determinants (arrow).

CASE DIAGNOSIS/TREATMENT

Our patient was presented with severe anemia at first year of age. The multilinear myelodysplasia was diagnosed, and HSCT was performed to the patient at 6 y.o.(28.06.2012). Engraftment was observed at +26 day after HSCT. The function of transplant was sufficient during the whole period of observation. The girl suffered from chronic relapsing steroid-dependent skin form of graft-versus-host disease grades II-III. That why she was treated with prednisone 1mg/kg/day (07.08.2012-01.04.2013), Mycophenolate mofetil 25mg/kg/day (25.10.2012-01.04.2013), Prograf 0,12mg/kg/day (07.11.2012-24.05.2013) (Fig.1). Considering low serum IgG level (1,5-3,6 g/l) she received IVIG. The patient's immunosuppression was converted to Methotrexate (0,6 mg/kg/week from 24.05.2013) and Cyclophosphamide (200 mg/m^2/week from 21.06.2013) because of stem cell transplant's hypofunction and acute nephrotoxicity (reversible rising of blood creatinine to 80 µmol/l).

One month later (28.07.2013) the gradual deterioration of renal function was noted: in 2 mo serum creatinine rose from 58 µmol/l to 120 µmol/l, urine specific gravity was 1005-1008. Urinalysis and renal US were normal. BK-virus PCR analysis revealed 6,7 $x10^6$ copies/ml in urine and $2x10^6$ copies/ml in blood. A renal biopsy was performed. There was advanced chronic tubulointerstitial injuary, mild lymphocytic infiltration and many intranuclear inclusions typical for BK-polyoma virus infection (Fig.2A) with positive immunostaining for SV40 T-antigen (Fig.2B). Immunosuppression was discontinued, therapy with Cidofovir 0,5 mg/kg/week, leflunomide (Arava) 10mg/day, Ciprofloxacin 20 mg/kg was started. Despite BK-virus clearance of blood and decline of BK-virus level in urine, there was no improvement of renal function after 6 weeks of treatment: Cr_s=136µmol/l, Cys-C=3,36mg/ml, $eGFR_{Cys-C}$=22 ml/min [6].

CONCLUSIONS

Renal dysfunction in HSCT recipient traditionally has been attributed to use of nephrotoxic drug. But our clinical case and literature data demonstrate that BK virus PCR testing and renal biopsy would be performed in all pediatric non-renal transplant and immunosuppressed patients with unexplained rising of serum creatinine. These patients may benefit from early detection and treatment of BKVN and modification of immunosuppressive therapy.

REFERENCES

1. Hirsch H, Drachenberg C, Steiger G, al Poliomaviruses and human diseases. Landes Bioscience, Georgetown 2006:117-147.
2. Costa C, Cavallo R Polyoma-associated nephropathy. World J Transplant 2012; 24:84-94.
3. Vergese P., Finn L., ENGLUND J. BK nephropathy in pediatric hematopoietic stem cell transplant recipients Pediatr Tramsplant 2009;13:913-918.
4. O'Donnell P, Swanson K, Josephson M, Artz A, BK virus infection is associated with hematuria and renal impairment in recipients of allogenic hematopoietic stem cell transplants Biol Blood Marrow Transplant 2009;15:1038-1048.
5. Stracke S., Helmchen U., Von Müller L. Polyoma virus-associated interstitial nephritis in a patient with acute myeloic leukaemia and peripheral blood stem cell transplantation Nephrol Dial Transplant 2003;18:2431-2433
6. Filler G.,al Should the Schwartz formula for estimation of GFR be replaced by Cystatin C formula? Pediatr Nephrol 2003; 18:981-985.

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