Defective HBsAg as risk factor for HBV reactivation in kidney transplant Abstract n. EV1058

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Objectives

HBV surface antigen (HBsAg) variant is a health concern because of risk of false negative detection. We describe a probable HBV reactivation due to a mutated strain in a renal transplanted patient.

Methods

A renal transplantation was performed in a male in November 2012; HBV serology and HBV-DNA were carried out at the time of transplantation and later on: serological markers were negative out of a not protective anti-HBs level (8 IU/ml), and no plasma viremia was detected.

In January 2014 the patient was admitted to the Padua Hospital presenting acute kidney failure, thrombocytopenia, jaundice, hypertransaminasemia and ascites. He was treated with everolimus, tacrolimus, metilprednisolone. HBV virological data are summarized in Table 1. A molecular analysis by in-house sequencing of RT region (5-245 bp) and HBsAg coding region (1-227 bp) was performed.

Table 1: HBV serology and plasma HBV-DNA (quantitative HBsAg cut off <0.05 IU/ml, HBsAb cut off 10 IU/L, NAT HBV-DNA cut-off 2.3 IU/ml, HBV-DNA cut-off 6.4 IU/ml).

Test	201112	301112	171212	230113	070114	210114	230114	250114	270114	280114
HBsAg[1]	neg	neg	neg	neg	neg	neg	neg	neg		
HBsAg[2]	-	-	-	-	-	-	neg	neg		
Quantitative HBsAg (IU/ml)	-	-	-	-	-	-	**0.07**	**0.09**		
HBsAb (IU/L)	8	4.97	4.49	2.78	0.8	0.74	**77**	**72**		
HBeAg	-	-	-	-	-	-	**pos**	**pos**		
HBeAb	-	-	-	-	-	-	neg	neg		
HBcAb IgM	-	-	-	-	-	-	neg	neg		
HBcAb	neg	neg	neg	neg	neg	neg	neg	**pos[3]**		
HBV-DNA NAT (IU/ml)		neg					**pos**			
HBV-DNA (IU/ml)		neg	neg	neg				**> 1x10^9**	**> 1x10^9**	**> 1x10^9**

[1] Chemiluminescent Micropartical Immunoassay, Architect, Abbott
[2] enzyme linked fluorescent assay (ELFA, VIDAS Anti-HBc Total II, bioMérieux, Lyon, France)
[3]data on the threshold value

Results

A Genotype D was identified, with L109GIRV, I110HKNPQT, S117ST, T118HNPT, P120KR, T126ST, Q129DH, T131ILMPT, S132PS, M133IT, Y134GISW, C137CGW, D144E. The strain was classified as HBsAg escape mutant. To investigate the origin of infection, as acute acquisition from a behavioral risk or reactivation, a stored plasma sample of the kidney donor was studied; an HBV-D genotype was revealed, with L109I, T118R, G119R, T123N, Q129H, M133I, D144E. Complete genome sequencing is ongoing, but a close phylogenetic relationship among the two strains was demonstrated, suggesting a trasmission as plausible. The index patient died due to a septic shock.

Conclusion

- A misclassification of the kidney donor as HBsAg negative at screening is conceivable, but an analyzable virus would have been detectable: the HBcAb negative result in the recipient may be explained, and was already reported in literature in immunosuppressed subjects.
- The recognition of escape mutants closely related in both donor and recipient suggests that HBV-DNA testing should be added to the pre transplant evaluation.

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