

Human bocavirus is not detectable in bone marrow from patients with myelodysplastic syndromes

Verena Schildgen,^a Jessica Lüsebrink,^a Ramona Liza Tillmann,^a Michael Wulfert,^b Norbert Gattermann,^b Oliver Schildgen^{a,c}

^aInstitut für Pathologie, Kliniken der Stadt Köln gGmbH, Hospital of the Private University Witten/herdecke, Cologne, Germany. ^bUniversity Hospital Düsseldorf, Clinics for Hematology, Oncology, and Clinical Immunology, Düsseldorf, Germany. ^cHospital of the Private University Witten/herdecke, Fakultät für Gesundheit.

Correspondence: Oliver Schildgen, Kliniken der Stadt Köln gGmbH, Hospital of the Private University Witten/herdecke, Ostmerheimer Street 200, D-51109 Köln/Cologne, Germany. E-mail: schildgeno@kliniken-koeln.de

Accepted 14 November 2010. Published Online 31 January 2011.

Keywords Human bocavirus, HBoV, myelodysplastic syndromes, MDS.

To the editor:

The human bocavirus (HBoV) was discovered in 2005 and, depending on the subtype, is associated mainly with respiratory infections and gastrointestinal disorders.^{1–3} However, the final proof that HBoV is in fact a pathogen is still missing. It also remains unclear if HBoV modifies the pattern of other diseases.⁴

Human bocavirus is the second-known human pathogenic parvovirus and as such related to parvovirus B19, which has been known for decades and can cause severe clinical complications such as *hydrops fetalis*. Parvovirus B19 has a marked tropism for erythropoietic progenitor cells and can trigger aplastic crisis in patients with chronic hemolytic anemia. In this context, parvovirus B19 has also been shown to be present and eventually persist in multiple tissues including bone marrow (reviewed in Ref. 5). Based on the relationship between HBoV and B19, the fact that HBoV particles can be found in the lung but also in the serum as they are released from infected tissues,^{6–8} and the observation that HBoV infection may be most severe in patients with haemato-oncological disease,^{9,10} we addressed the question whether HBoV is associated with a group of hematological disorders typically presenting with anemia attributable to inefficient erythropoiesis. These disorders, called myelodysplastic syndromes (MDS), are clonal bone marrow diseases which are characterized by ineffective hematopoiesis and a risk of leukemic transformation.¹¹ Although the MDS clone often carries acquired genetic and epigenetic abnormalities, a disturbed bone marrow micro-environment is thought to contribute to disease pathology, and infectious triggers have also been suspected.¹²

We investigated 25 patients with different types of MDS (Table 1). Total DNA was isolated from bone marrow aspirates as previously described and subjected to a PCR specific for human bocavirus, using a previously published protocol.¹⁰

Human bocavirus DNA was detected in nasal swabs previously tested HBoV positive but not in any of the MDS samples. Therefore, although a causative role in myelodysplastic syndromes appears unlikely as the virus was not detected in bone marrow, a 'hit-and-run' mechanism remains possible. This conclusion is supported by the fact that in 2007 Manning *et al.*¹³ have also not detected HBoV-DNA in the bone marrow of HIV positive and HIV negative patients, which in turn may allow the conclusion that HBoV lacks a tropism for bone marrow.

Clinical relevance of HBoV in the field of hematology may be restricted to its possible role as a cause of pneumonia in patients whose general condition is weakened by a hematological malignancy.

Acknowledgement

This work was supported by a grant (2009_A95) from the Else Kröner-Fresenius Stiftung, Bad Homburg, Germany.

Ethical statement

This work was performed under a vote from the local Ethical Committee from the University of Düsseldorf. All patients enrolled in this study agreed with the work performed by written informed content.

Table 1. Patients with myelodysplastic syndromes (MDS) included in the analysis

Patient (gender)	MDS type	Age
1 (f)	RAEB-I	59
2 (m)	CMML	–
3 (m)	5q-	63
4 (m)	RAEB-I	75
5 (f)	CMML	59
6 (f)	RCMD-RS	83
7 (f)	RAEB-II	77
8 (m)	RAEB-I	72
9 (m)	RCMD	67
10 (f)	RCMD-RS	79
11 (f)	RCMD-RS	57
12 (f)	RAEB -II	65
13 (m)	RAEB -I	71
14 (f)	RAEB -I	62
15 (m)	RCMD	64
16 (m)	CMML-I	63
17 (f)	RCMD-RS	76
18 (m)	RCMD-RS	60
19 (m)	CMML-II	69
20 (m)	CMML-II	64
21 (m)	RCMD	68
22 (m)	RAEB-II	77
23 (m)	RAEB-II	74
24 (f)	RAEB-II	67
25 (m)	RCMD	49

RAEB, refractory anemia with excess of blast cells; RCMD, refractory cytopenia with multilineage dysplasia; RCMD-RS, RCMD with ring sideroblasts; CMML, chronic myelomonocytic leukemia; 5q-, MDS with deletion of 5q as sole chromosomal abnormality.

Conflicts of interest statement

Nothing to declare.

References

- Allander T, Tammi MT, Eriksson M, Bjerkner A, Tiveljung-Lindell A, Andersson B. Cloning of a human parvovirus by molecular screening of respiratory tract samples. *Proc Natl Acad Sci U S A* 2005; 102:12891–12896.
- Arnold JC, Singh KK, Spector SA, Sawyer MH. Human bocavirus: prevalence and clinical spectrum at a children's hospital. *Clin Infect Dis* 2006; 43:283–288.
- Arthur JL, Higgins GD, Davidson GP, Givney RC, Ratcliff RM. A novel bocavirus associated with acute gastroenteritis in Australian children. *PLoS Pathog* 2009; 5:e1000391.
- Schildgen O, Muller A, Allander T *et al.* Human bocavirus: passenger or pathogen in acute respiratory tract infections? *Clin Microbiol Rev.* 2008;21:291–304, table of contents.
- Söderlund-Venermo M, Hokynar K, Nieminen J, Rautakorpi H, Hedman K. Persistence of human parvovirus B19 in human tissues. *Pathol Biol (Paris)* 2002; 50:307–316.
- Dijkman R, Koekkoek SM, Molenkamp R, Schildgen O, van der Hoek L. Human bocavirus can be cultured in differentiated human airway epithelial cells. *J Virol* 2009; 83:7739–7748.
- Fry AM, Lu X, Chittaganpitch M *et al.* Human bocavirus: a novel parvovirus epidemiologically associated with pneumonia requiring hospitalization in Thailand. *J Infect Dis* 2007; 195:1038–1045.
- Tozer SJ, Lambert SB, Whitley DM *et al.* Detection of human bocavirus in respiratory, fecal, and blood samples by real-time PCR. *J Med Virol* 2009; 81:488–493.
- Koskenvuo M, Mottonen M, Waris M, Allander T, Salmi TT, Ruuskanen O. Human bocavirus in children with acute lymphoblastic leukemia. *Eur J Pediatr* 2008; 167:1011–1015.
- Kupfer B, Vehreschild J, Cornely O *et al.* Severe pneumonia and human bocavirus in adult. *Emerg Infect Dis* 2006; 12:1614–1616.
- Tefferi A, Vardiman JM. Myelodysplastic syndromes. *N Engl J Med* 2009; 361:1872–1885.
- Shetty V, Hussaini S, Alvi S *et al.* Excessive apoptosis, increased phagocytosis, nuclear inclusion bodies and cylindrical confronting cisternae in bone marrow biopsies of myelodysplastic syndrome patients. *Br J Haematol* 2002; 116:817–825.
- Manning A, Willey SJ, Bell JE, Simmonds P. Comparison of tissue distribution, persistence, and molecular epidemiology of parvovirus B19 and novel human parvoviruses PARV4 and human bocavirus. *J Infect Dis* 2007; 95:1345–1352.