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Absence of BKV T-antigen antibodies, in patients with leukemia and aplastic anemia

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SUMMARY — The presence of BKV T-antigen antibodies in sera and urine of patients with bone marrow graft and in subject controls was tested. Neither bone marrow graft patients neither aplastic anemia or leukemia patients had developed T-antibodies to BK virus, indicating lack of aetiological role of this human polyomavirus in blood malignancies.

INTRODUCTION

Human polyomaviruses transform cells *in vitro* and cause tumors in laboratory animals[2,6,14,15]. Animals bearing tumors induced by BK or JC viruses, develop circulating antibodies to a viral antigen present in the nucleus of the tumor cell, the T-antigen. It is expected that human bearing polyomavirus-induced tumors, will also develop T-antibodies.

Attempts to correlate BK and JC viruses to human tumors, through detection of T-antibodies and hybridization tests, have failed[1,3,5,7,10]. No reports on the investigation of T-antibodies in serum of patients with leukemia or aplastic anemia were found out, though, the presence of polyomaviruses in their urine samples[11,12], has strongly suggested to some authors, an important role of these viruses in those diseases[8,9]. To ascertain this, serum and urine samples of 123 patients with leukemia or aplastic anemia and of 63 healthy subjects, taken as control, were collected for the detection of T-antibodies to BKV T-antigen.

MATERIALS AND METHODS

The patients were followed up to three years. They were divided in three groups (table 1). Fifty urine samples were obtained from patients of group I, as well as, t serum, collected before and after bone marrow graft. serum sample was also obtained from each patient groups II and III. Briefly, BKV T-antigen was prepa by exposition of VERO cells to BK virus during 2 hou the medium was then replaced by a virus-free medium a the infected cells were maintained at 37°C up to 3 da The T-antigen was extracted with NONIDET P-40 TRIS-buffer solution, pH 8.0, for 20 minutes at 4°C a finally separated from the bulk of cells by ultracentrifug tion[4]. The detection of T-antibodies in serum and uri samples were done by complement fixation (CFT) and i direct immunofluorescence tests (IFI). A total of 380 se and 50 urine specimens were tested. CF tests failed to d tect antibodies in urines of these patients, although it ha detected BKV T-antibodies in serum of 12 patients, whic was not confirmed by immunofluorescence test. A tit equal to 1/16 was found in serum of 6 normal donors b CFT, which was not confirmed by IFI test (table II). Al CFT positive sera were absorbed with VERO cells before immunofluorescence test.

COMMENTS

Patients with marrow transplantation are heavily im munossupressed. Besides various drugs, they also receiv antilymphocyte serum, that acts not only on the immun logical reactions causing the rejection of allografts, but, a seen before[17], it markedly enhances the development o polyomavirus tumors in rats[16]. The same may happen t humans, that may develop T-antibodies to the T-antige present in the nucleus of virus-induced tumor. Sera o

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TABLE I
Group of patients studied

Groups	Nº patients	Disease		Sex		Age	Specimens	
		AA	Leuk.	M	F	years	Urine	Sera
I	94	20	74	58	36	3-58	45	288
II	29	5	24	21	8	3-52	—	29
III	63	—	—	39	24	3-61	5	63

Group I — patients with bone marrow transplantation.
Group II — patients without bone marrow transplantation and treatment.
Group III — healthy subjects (44 of them were the donors of marrow).
AA — aplastic anemia.
Leuk — leukemia.
M — male.
F — female.

TABLE II
Antibodies to BKV T-antigen in patients with leukemia, aplastic anemia, bone marrow graft and in control subjects

Patients	Nº	CFT titre (nº cases)		IFT*	CFT titre (nº cases)	IFT*
Group I	94	1/32	(3)	0	0 (45)	ND
Group II	29	1/32	(9)	0	ND	ND
Group III	63	1/16	(6)	0	0 (5)	ND

CFT — Complement Fixation Test.
IFT — Immunofluorescence Test.
* — All CFT positive sera were absorbed with VERO cells and then screened by IFT.
ND — not done.

immunossupressed patients with bone marrow graft, followed up to 3 years, did not show any change with respect to the development of T-antibodies to BKV T-antigen, even in those, who had suffered BKV infection. Urine samples of patients who develop BKV infection contain hemagglutinating inhibition (HAI) antibodies[13] and the bulk of the specific antibody belong to the IgG class. Since it is expected the presence of T-antibodies in serum of patients bearing virus-induced tumors, they would also be excreted in urines. Thus, 50 urines specimens were also tested by CFT, but with negative results.

The absence of T-antibodies in patients before transplantation strongly suggests that BKV is not aetiologically associated to leukemia or aplastic anemia. Also, these patients, among them those who had an acute polyomavirus infection, did not develop tumor caused by BK virus, at least, during the time lapse of this study. The results signify that human BK polyomavirus is not likely to cause blood malignancies as it has being proposed[8,9].

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RESUMO

A presença de anticorpos contra o antígeno-T produzido por vírus BK foi testada no soro e urina de pacientes com transplante de medula óssea e em controles. Nenhum paciente com transplante, nem com anemia aplástica ou leucemia, desenvolveu anticorpos antiantígeno T, indicando ausência de um papel etiológico do vírus BK (um polioma humano) em leucemia ou anemia aplástica.

REFERENCES

1. CORALLINI, A. — Antibodies to BK virus: structure and tumour antigens in human sera from normal persons and from patients with various disease, including neoplasia. Infect. Immun. 13: 1.684-1.691, 1976.
2. COSTA, J.; YEC, C.; TRALBA, T.S. & ROBSON, A.S. — Hamster ependymomas produced by intracerebral inoculation of a human papovavirus (MMV). J. Natl. Cancer Inst. 56: 863, 1976.
3. COSTA, J.; YEC, C. & ROBSON, A.S. — Absence of papovavirus T-antibodies in patients with malignancies, Lancet 2: 709, 1977.

4. DOUGHERTY, R.M. — A comparison of human papovavirus T-antigens. J. Gen. Virol. 33: 61-70, 1976.

5. FIORI, M. & Di MAYORCA, G. — Occurence of BKV DNA in DNA obtained from certain human tumors. Proc. Natl. Acad. Sci. USA 73: 4.662-4.666, 1976.

6. GREENLEE, J.E.; NARAYAN, O.; JOHNSON, R.T. & HERNDON, R.M. — Introduction of brain tumours in hamsters with BK virus: a human papovavirus. Lab. Invest. 36: 636-641, 1977.

7. GREENLEE, J.C. — Failure to demonstrate papovavirus tumour antigen in human cerebral neoplasia. Ann. Neurol. 3: 479-481, 1978.

8. HENRY, K.; BIRD, R.; WATSON, G. & HUGHES, K. — Aplastic anemia, bone marrow transplantation and polyoma and other virus infections. Lancet II: 695-696, 1977.

9. HENRY, K. — Some ultra-structural aspects of bone marrow transplantation: hitherts unrecognized manifestation of GVHR involving heart and polyomavirus infection in the children. Pathol. Biol. (Paris) 26: 55-56, 1978.

10. ISRAEL, M.A.; MARTIN, M.A.; TAKEMOTO, K.K.; HOLEY, P.M.; AAROSON, S.A.; SOLOMON, D. & KHOURY, G. — Evaluation of normal and neoplastic human tissue for BKV. Virology 90: 187-196, 1978.

11. LECATSAS, G.; SCHOEB, B.D.; PROZESKI, O.W.; PRETRIUS, F. & DE BEER, F.C. — Polyomavirus in urine in aplas anemia. Lancet I: 259-260, 1976.

12. PAUW, I. & CHOUFOER, J. — Isolation of a variant of BK with altered restriction endonuclease form. Arch. Virol. 57: 35-4 1978.

13. REESE, J.M.; REISSIG, M.; DANIEL, R.W. & SHAH, K.V. Occurence of BKV specific antibodies in the urine of patients r ceiving chemotherapy for malignancy. Infect. Immun. 11: 1.37 1.381, 1975.

14. SHAH, K.V.; DANIEL, R.W. & STRANDBERG, J.D. — Sarc ma in a hamster inoculated with BK virus, a human papovaviru J. Natl. Cancer Inst. 54: 945-950, 1975.

15. UCHIDA, S.; WATANABE, S.; AIZAWA, T.; KATO, K.; FURUNO, A. & MUTO, T. — Induction of papillary ependymon and insulinomas in the Syrian golden hamster by BKV, a huma papovavirus. Gan. 67: 857-865, 1976.

16. VANDEPUTTE, M. — Transplantation of polyoma tumors i rats. Nature 199: 391, 1963.

17. VANDEPUTTE, M. — The effect of heterologous anti-lymphocy tic serum on the oncogenic activity of polyomavirus. Life Sci. 7 855-865, 1968.