Pilot Study of the Effects of Thymus Protein on Elevated Epstein-Barr Virus Titers

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Abstract

Six patients with chronically elevated Epstein-Barr virus early antigen antibody titers were treated for 60 days with purified Protein A from calf thymus cell culture (BPTPA). There was a statistically significant reduction of antibody titers after treatment. The thymic protein was well tolerated and increased energy was reported by most of the participants. These results suggest that BPTPA may be useful in the treatment of patients with persistently elevated Epstein-Barr virus early antigen antibody titers.

Background

Epstein-Barr virus (EBV) infection is extremely common, approaching 100% by the age of 10 in some parts of the world. EBV is thought to be spread via the respiratory route, and is the causative agent of infectious mononucleosis.[1]

After acute infection, EBV has been shown to establish a latency state within B lymphocytes, salivary gland epithelium, and oropharyngeal epithelial cells.[2] Like other herpes viruses, EBV can reactivate. Primoinfection and reactivation of EBV have been associated with several disease states, including chronic fatigue syndrome (CFS), Burkitt's lymphoma,[3] nasopharyngeal carcinoma,[4] aplastic anemia,[5] Hodgkin's disease, several lymphoproliferative disorders,[6] and neurological disorders.[7] In addition to primoinfection and reactivation, a chronic-active EBV infection has been described.[8]

EBV infection occurs more frequently in immunocompromised hosts,[9,10] and has been reported to be immunopathologic in presumably immunocompetent hosts.[11,12] A cytotoxic T-lymphocyte (CTL) response is responsible for resolution of EBV infections.[13]

Purified protein A from calf thymus cell culture Thymic Protein A™ is a patented, over-the-counter supplement which contains a polypeptide that has shown the ability to stimulate mature T lymphocytes and enhance mammalian immune response to infectious agents and to malignancies.[14] This polypeptide was first studied at UCLA in 1979. Since that time, a bovine thymus cell line which produces the protein has been established. The protein is chromatographically purified from a medium used to culture the cell line. It is now commercially available in a base of maltodextrin, and is taken sublingually (4 mcg/dose).

Quantitation of IgG antibodies to EBV early antigen (EBV EA) is commonly used to detect recent or chronic-active infection. Elevated serum viral capsid (EBV VCA) antibodies indicate previous infection and can remain elevated for life.

Objective

The objective of this study was to determine what effect BPTPA, a T lymphocyte stimulant, had on chronically elevated EBV EA titers.

Methods

Seven patients meeting the criterion of having persistent (>6 months) EA titers of greater than or equal to 1:80 (Negative <1:20) were recruited to participate in the study for 60 days. Participation was entirely voluntary, and informed consent was received from all participants. The study protocol was approved by our Institutional Review Board and was carried out with the ethical standards set forth in the Helsinki Declaration of 1975.

Participants were provided with 4 mcg. packets of Thymic Protein A, which were taken sublingually, three times per day, for a period of 60 days. At the end of the study period, EBV EA and EBV VCA levels were re-tested.

Participants were also requested to complete a symptom questionnaire before and after the study. The questionnaire contained 86 current symptom questions which were ranked by the participants on a scale of 1-7 (1=no symptom, 7=severe symptom). The pre- and post-treatment scores were compared using the student T-test.

Determinations of EBV EA (IgG) and EBV VCA (IgG) were performed by Laboratory Corporation of America, Wichita, Kansas. EBV EA (Negative:

Table 1. Age, sex, and diagnoses of patients.

Pt #	Age	Sex	Diagnosis 1	Diagnosis 2	Diagnosis 3	Diagnosis 4
1	67	M	CFS	EBV		
2	15	M	Hodgkin's lymphoma	Intestinal parasites	Dermatitis	
3	68	M	Hepatitis C	EBV	CFS	
4	50	M	EBV	Leukopenia	Glossitis	CFS
5	57	F	EBV	Rheumatoid arthritis	CFS	
6	58	M	Non-Hodgkin's lymphoma	EBV	Back pain	CFS

<1:20) was quantified using indirect fluorescent antibody, and EBV VCA (Negative: <20 arbitrary units) was determined using enzyme immunoassay. The pre- and post-treatment scores for both assays were compared using the student T-test.

Results

Of the seven patients enrolled, six completed the study. One patient discontinued use after 7 days after experiencing flu-like symptoms which resolved within three days of discontinuation. No adverse side effects were reported by the other six participants. Four participants completed both before and after symptom questionnaires. Compliance was good, with greater than 90% of doses taken. Table 1 shows the ages, sexes, and diagnoses of the six participants.

The results of the study are summarized in Table 2. After treatment the EBV EA levels of four of the six participants were reduced. The reduction was significant (p<.03). There was no reduction of the EBV VCA levels after treatment.

The overall trend of the symptom profiles was toward a reduction in symptoms. Of the four before and after profiles completed, two showed significant (p=.04) reduction in symptoms after treatment (Table 3).

In post-study interviews, all of the 5 participants with a diagnosis of CFS reported increased energy and a decrease in hours slept after the 60 day treatment.

Also of note was that elevated liver enzymes (ALT, AST, and GGT), and cholesterol in patient number 3, who had a concomitant diagnosis of hepatitis C, and leukopenia in patient number 4, were all normalized by the end of the study.

Discussion

Although this was a non-blinded pilot study, the fact that a significant reduction of EBV EA titers occurred in a group of patients who had persistently elevated titers suggests that BPTPA may play a role in modulation of chronic-active EBV infection.

Conclusion

The role of BPTPA in the management of fatigue and chronic-active EBV infection should be studied further.

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Table 2 Pre- and post-treatment Epstein-Barr virus titers.

Pt #	EBV EA Pre-Tx	EBV EA Post-Tx	EBV VCA Pre-Tx	EBV VCA Post-Tx
1	**1:160**	**1:160**	*170*	*170*
2	**1:160**	**1:80**	*102*	*119*
3	**1:320**	**1:160**	*170*	*170*
4	**1:320**	**1:80**	*170*	*138*
5	**1:80**	**1:80**	*170*	*170*
6	**1:320**	**1:80**	*170*	*170*
t-test	**p<.03 significant**		*p=.88 not significant*	

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Table 3. Pre- and post-treatment (Tx) questionnaire results.

Pt Number	Pre-Tx	Post-Tx	p value	**significant
2	1.27	1.26	0.87	
3	2.07	1.63	0.04**	
4	3.14	3.09	0.87	
5	1.67	1.31	0.04**	