Herpes Simplex Encephalitis
Does Interferon care?

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Introduction

Herpes simplex encephalitis (HSE) is an acute, life-threatening disease, requiring prompt intervention. Defects of the TLR3-interferon (IFN) axis in the antiviral innate immune response against HSV-1 and defects of some genes of the TLR3 pathway (TLR3, UNC93B1, TRAF3, TRIF, TBK1) probably play an important role in HSE pathogenesis.

Methods

Descriptive study between January 2007 and December 2012. HSV-1 was detected by PCR from CSF samples. PBMC and fibroblasts were studied for their IFN responses to TLR3, after stimulations of poly(I:C), that is thought to be TLR3-dependent and virus stimulations. Coding exons of the known HSE-associated genes were sequenced.

Results n = 6

**ALPHA INTERFERON 2B 10 MILION IU SUBCUTANEOUS**

| Patient 1  | 8M, M | IFN was stopped 7 days later for bycitopenia (Hb 6.3 g/dL, Neutrophils 450 μL) | 5.5 years follow-up | Severe global Developmental Delay | Started IFN after D7 Tetraraphesis and cognitive delay |
| Patient 2  | 7M, F | Acyclovir started on D2 IFN started on D3 | 3 years follow-up | NO SEQUELAE | Lower tolerance for frustration No motor or cognitive dysfunction. |
| Patient 3  | 11Y, M | Acyclovir started on D3 IFN started on D5 | 2,3 years follow-up | Minor behavior disorder | Right sided hemiparesis with pyramidal signs No cognitive deficits |
| Patient 4  | 20M, F | Acyclovir started on D3 IFN started on D5 | 2,3 years follow-up | Moderate motor deficit | No motor deficits Cognitive function below average |
| Patient 5  | 12M, M | Acyclovir started on D2 IFN started on D3 | 2 years follow-up | Epilepsy Not severe | No motor deficits |
| Patient 6  | 11M, F | Acyclovir started on D7 IFN started on D7 | 1 year follow-up | Epilepsy Not severe | |

Heretofore functional studies were normal EXCEPT for Patient 3 whose fibroblasts displayed impaired IFN-lambda production after stimulations of poly(I:C). No mutation was found in the sequenced coding exons of UNC93B1, TLR3 and TRAF3.

Conclusion

- None of the 5 patients who started IFN until the 7th day of illness had severe motor or cognitive sequelae.
- Only patient 1, who started IFN after the 7th day of illness, had the classic pattern of HSV encephalitis motor and cognitive sequelae.
- In spite of the small size of the sample studied, our results suggest that IFN treatment should be considered in patients suffering from HSE.

References