Current trends in the management of subacute sclerosing panencephalitis

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Current Trends In The Management Of Subacute Sclerosing Panencephalitis

Abstract

Subacute sclerosing panencephalitis (SSPE) is slow viral encephalitic sequelae occurring secondary to measles infection. Symptoms occur insidiously and progresses to coma and death. This condition carries a very high mortality. This article discusses the various drug therapies tried in this condition. The currently proven drug regimens include Isoprinosine, Interferon alpha and their combination.

Introduction

Subacute sclerosing panencephalitis (SSPE) is slow viral encephalitic sequelae occurring years after infection with measles virus. The prevalence proportionately follows the incidence of measles. The exact pathophysiology of the disease is not completely known; however it is believed that factors causing a selective humoral over cellular immune response against the virus may play a role. A defective virus structure secondary to immature immune response mounted is also believed to play a role. The clinical features occur on an average of 6 years after measles virus infection and includes insidious onset of behavioral changes, myoclonus and involuntary movements progress sing to coma and death. The diagnosis is made clinically, supported by periodic complexes on electroencephalography, brain imaging suggestive of demyelination, and immunological evidence of measles infection.

Review

The pharmacologic management of SSPE includes symptomatic therapies and disease modifying agents. Many different anticonvulsants have been tried and no single agent has emerged as the best. With current evidence carbamazepine has been effective in few settings. There are case reports of successful treatment of myoclonus with trihexyphenidil and ketogenic diet. In the disease modifying drugs, Isoprinosine (inosiplex) and interferon have been studied in detail. Isoprinosine is an immune modulating substance which promotes lymphocyte proliferation, production of immunoglobulin and lymphokines that facilitates lymphocyte immune function once triggered by a viral antigen. It has been found to be effective in numerous trials. Interferon acts by activating Natural Killer cells and directly inhibiting virus replication. IFN alpha is administered intraventricularly and has found to be effective. Beta-interferon has also been successfully used in treating seven patients in a case series. Combined use of both Isoprinosine and IFN alpha has been found to be effective in a large multicentric trial, although conflicting reports of it being ineffective in the early stages of SSPE are present.

Other immune-modulating medications tried in SSPE include Cimetidine and thymus extract in combination with Isoprinosine, but not found to be effective. Ribavirin has been used as adjunct therapy, in addition to intra-ventricular IFN alpha, with minimal success. There are isolated reports claiming success with IVIF, amantadine, steroids and acyclovir, but none proven in multicentric trials. Rituximab (anti CD 20 antibody) has been tried in SSPE with no success. Flupirtine, an anti apoptotic agent which has been used with limited success in Alzheimer's and prion diseases has been hypothesized to halt the disease progression in SSPE, but no clinical data is available yet.

Conclusion(s)

With the current available evidence only Isoprinosine, Interferon alpha and their combination appears to be effective in slowly the progression of SSPE. Irrespective of recent insights into the possible treatment options, prognosis is uniformly dismal. Therefore, the most successful strategy in the management of SSPE is the prevention of the primary disease by means of immunization.

Abbreviation(s)

SSPE -- Subacute sclerosing panencephalitis.
References

Reviews

Review 1

Review Title: Comments on

Posted by Dr. Generoso Gascon on 07 Apr 2011 08:26:21 AM GMT

Rating: 8

Comment:
This is an updating brief review, and as such, serves satisfactorily as an introduction to the subject. The emphasis on treatment is appropriate for the general physician and up-to-date. Some of the spelling and grammar needs editing/refinement. There are no tables.

In countries where measles immunization has not reached 80% of children, suspicion for SSPE should have a low threshold. Any early decline in behavior, school performance, even appearing like ADHD, should raise Stage 1 SSPE in the differential diagnosis. There should be no problem in clinically recognizing SSPE in Stage II, when periodic myoclonic spasms are obvious. In developed countries a history of early exposure to measles, before measles immunization, in either native or immigrant populations, should also raise the possibility. Unexplained retinopathy, whether discovered incidentally or because symptomatic, may precede clinical Stage I by years. Early diagnosis can also be done by astute clinical examination for periodic myoclonic spasms in someone with mental/behavioral change, by recording an EEG in the standing position, with video if possible, and looking for subtle eye blinks, or loss of posture of extended arms when standing in the Romberg position, coupled with periodic slow wave complexes. The key word is "periodic". One should count the number of seconds between abnormal involuntary movements and see that they are consistently every 10, or 12, or 8 seconds, whatever the period is. The diagnosis specifically is based on clinical history, elevated CSF IgG, and elevated CSF measles antibody titers. The periodic slow wave EEG complexes (they are not epileptiform discharges) early on may appear in sleep only, should be obvious in Stage II, and may disappear in late Stage III and Stage IV.

The review of treatments is brief but comprehensive. The symptoms and signs of SSPE are initially due to inflammatory responses during immunomodulatory treatment, which may slow rate of progression. But chronic progression is inevitable, which may last a decade or more, secondary to atrophy and neuronal loss. So far, no new therapies based on knowledge of the molecular pathophysiology of the disease have emerged.

Competing interests: No

Invited by the author to make a review on this article? : Yes

Experience and credentials in the specific area of science:
I directed the International Consortium on SSPE randomized treatment trial cited in the article, which was published in the Journal of Child Neurology. Prior to that, treated many SSPE patients in Saudi Arabia in the late 1980’s, early 1990’s, with several publications.

Publications in the same or a related area of science: No

How to cite: Gascon G. Comments on [Review of the article ‘Current trends in the management of subacute sclerosing panencephalitis’ by ].WebmedCentral 1970;2(4):REVIEW_REF_NUM647
Review 2

Review Title: subacute sclerosing panencephalitis

Posted by Dr. Garg RK on 07 Mar 2011 03:10:11 PM GMT

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Rating: 1

Comment:
This is a very brief review on the subject better articles on SSPE are available. Instead a illustrative case with video ansd EEG would have been more informative for readers of the areas where SSPE is rare.

Competing interests: None

Invited by the author to make a review on this article? : No

Experience and credentials in the specific area of science:
I have seen plenty of cases of SSPE.

Publications in the same or a related area of science: Yes

References: Can be seen in Pubmed

How to cite: RK G.subacute sclerosing panencephalitis [Review of the article ‘Current trends in the management of subacute sclerosing panencephalitis ’ by ].WebmedCentral 1970;2(3):REVIEW_REF_NUM553
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