EDITORIAL

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Old problem may have new solution

In this issue of the journal we published a paper entitled "Long-term outcome of acute central nervous system infection in children" written by the team led by Dr. Gang Liu.[1] The publication of this article itself reflects that the authors, the editors and the reviewers all consider that this topic and the body of this article are important. The reasons may involve the following.

1. The number of patients who survive acute central nervous system (CNS) infections but have various long-term sequelae may be quite large. Acute CNS infections in fact include more than those mentioned by Dr. Chen et al[1], i.e., meningitis, encephalitis, and to a lesser extent, myelitis and abscesses in the CNS caused by various microorganisms and some parasites such as protozoa. There are no easily available statistics of incidences of these CNS infections in general in terms of the pathogens as well as the whole age range of children. However, previously reported data may have some useful implications. The incidence of bacterial meningitis among 100 000 children 0–5 years of age was 30–50 in Australia.[2] However in the United States, the incidence of *Neisseria meningitidis* infection was 4–5 cases and that for *Streptococcus pneumoniae* was 2.5 cases per 100 000 children of the same age group after 1980.[3] As to the prevalence of long-term sequelae, there are great diversity because many factors influence the statistics. In Dr. Liu's report, 15% of their cases were moderately or severely impaired, and two cases were in vegetative status. More than a decade ago, it was observed that as high as 10%–20% of children recovering from bacterial meningitis developed severe neurodevelopmental sequelae.[4] Sensorineural hearing loss was regarded as the most common long-term sequelae of bacterial meningitis, as high as 30% of children with pneumococcal meningitis, 10% of meningococcal meningitis and 5%–20% of those with Hemophilus influenzae type b meningitis suffered from this problem.[4] A recent systematic review and meta-analysis involving 1018 children with infective encephalitis reported by Khandakere et al[5] pointed out that 42% of the patients had incomplete recovery; 10% to 35% of the patients had the problems of seizures, motor impairments and abnormal behaviors etc. As high as 52%, 48% and 43% of survivors of infants with Salmonella meningitis had long-term sequelae of language disorder, motor disability and lower intelligence quotient.

2. Some of the long-term sequelae could be prevented or reduced if more efforts are made. Recent studies suggest that appropriate treatment of acute CNS infections may prevent or reduce severity of certain neurological complications and death. The important question is: would treatment during the acute phase of the diseases possibly reduce the frequency and/or severity of the long-term sequelae? Namani et al[6] reported that the outcome of bacterial meningitis in children was related to the initial treatment of the disease. The occurrence of neurological complications and mortality in children treated with ceftriaxone and chloramphenicol was higher (43% and 8%) than those of children treated with penicillin G and chloramphenicol (13% and 3%).

3. Predictors of long-term sequelae might be helpful in early finding, early and effective management of long-term sequelae in children with viral encephalitis.[7-9] Although the incidence of Japanese encephalitis B (JEB) has been dramatically reduced since the vaccines against the disease became available, the disease is still a problem in some areas in Asia. Of 44 survivors of children with JEB, 31% had severe neurological sequelae, and results of assessment during the first 3–6 months after discharge from hospital could predict long-term outcome of the patients.[7] Survivors of Nipah virus encephalitis often have long-term neurological and functional morbidities.[9]

Seizures, cranial nerve palsy, abnormal deep tendon reflexes and low scores at Glasgow coma scale etc. at admission were significantly associated with sequelae.[10] In a report on transverse myelitis in children, it was found that persistent motor deficit could predict long-term bladder dysfunction.[11]

On the other hand, in addition to clinical manifestations, certain laboratory markers related to inflammation, such as cytokines detected during the acute phase of the CNS infections may help predict occurrence of long-

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term sequelae. Fowler et al[12] reported that high levels of cytokines in the cerebrospinal fluid of patients with tick-born encephalitis that associated with severity of inflammation, including interferon gamma, interleukin (IL)-4, -6 and -8 possibly indicate a risk of incomplete recovery. It is reasonable to postulate that if the diagnosis of CNS infections is made early enough, before some of the predictors of long-term sequelae appear, and if the effective therapies are applied early enough, some of the long-term sequelae might be prevented or reduced.

Together with Dr. Liu[1] and her colleagues' evidences and all the other observations mentioned above demonstrated that quite high proportions of patients with either bacterial meningitis or viral encephalitis suffer from various neurological, intellectual, behavioral and other functional sequelae, especially hearing impairments. It is clear that many of the sequelae are predictable, and there are some laboratory parameters that can help predict occurrence of some long-term adverse outcomes. We need to do much more work to find out more predictors in number and in reliability to help recognize and try to reduce long-term sequelae of CNS infections.

To substantially reduce the long-term sequelae of acute CNS infections, much more clinical and laboratory studies need to be done, which include 1) early and accurate diagnosis; 2) early and effective treatment; 3) specific treatment for prevention of the long-term adverse outcomes; last but not least, 4) rehabilitative therapies for the neurological, intellectual and other sequelae.

For studies on long-term outcomes of the CNS infections, prospective, large-scale, and longer follow-up studies would be more helpful to identify more valuable evidences for predicting and managing long-term adverse outcomes.

For many of the bacteria causing meningitis, including *Mycobacterium tuberculosis*, other bacteria, and viruses that cause encephalitis, efforts for prevention, esp. research and development of highly effective and safe vaccines, should be taken into account. During the recent years, more and more reports have shown that *Mycoplasma pneumoniae* infections seem to be causing more severe and frequent problems clinically, although there are effective and safe antibiotics for this pathogen, development of effective and safe vaccine against this organism seems to be necessary.

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CONFLICT OF INTEREST

I have no conflicts of interest to declare regarding this manuscript.

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