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Surveillance and management of ventriculitis following neurosurgery

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SUMMARY

Ventriculitis is an important complication following neurosurgery and is often associated with the use of an external ventricular drain (EVD). The incidence varies from <5% to 20%, partly due to variations in the definitions used for diagnosis. Staphylococci are the most important causes but the isolation of coagulase-negative staphylococci from a cerebrospinal fluid (CSF) sample needs to be interpreted with caution as it may represent contamination. Risk factors for ventriculitis include advanced age, the duration of EVD placement, the number of manipulations and the presence of intraventricular haemorrhage. Prevention strategies increasingly focus on the implementation of a care bundle that includes aseptic technique at the time of insertion and during any manipulations, skin preparation, prophylactic antibiotics, and appropriate dressings at the site of the EVD. The use of EVDs impregnated with antimicrobial agents is increasing but, whereas some studies show that these are effective, it is not clear whether they provide added benefit when there is compliance with other measures. Antimicrobial treatment is challenging as many widely used agents do not penetrate into the CSF and causative bacteria are increasingly multidrug resistant. Often a combination of high-dose intravenous and intraventricular agents is required, especially for Gram-negative infections. Large trials in this area are challenging to conduct; therefore, to better inform preventive strategies and to optimize management of this important condition, ongoing national surveillance and pooling of data on treatment approaches and outcomes are needed.

Introduction

Patients undergoing neurosurgery are at increased risk of healthcare-associated infections (HCAIs). In the four-country HCAI prevalence survey in 2006, the prevalence rate in the neurosurgical patients was 10.5%.[1] In the USA, a multistate point-prevalence survey found that central nervous system infection ranked 11th, at 0.8% of all HCAI (pneumonia and surgical site infection were equal first at 21.8% each).[2] In incidence studies targeting neurosurgical units in Italy and Germany, the overall HCAI rate was 22% and 24%, respectively, with meningitis occurring in 4–8% of patients.[3,4] Many HCAIs in neurosurgical patients, such as surgical site infection or respiratory tract infection, are similar to those in other patients. Although not as prevalent, meningitis and ventriculitis have important sequelae. In the recent US multistate point-

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prevalence survey of HCAI, it was calculated that in 2011 there were between 700 and 20,000 cases of central nervous system infection, many of which would have been meningitis and/or ventriculitis.[2] The consequences of ventriculitis/meningitis include death, impaired intellectual capacity, and prolonged hospital stay.

Many cases of ventriculitis/meningitis occur in patients who are already very ill, such as following a large subarachnoid haemorrhage. However, there is very little ongoing surveillance of meningitis/ventriculitis in neurosurgery and the risk factors associated with it. Furthermore, the management of these conditions is challenging in terms of optimal strategies for prevention and antibiotic treatment. We review here the literature from the last ten years on aspects of ventriculitis following neurosurgery with an emphasis on prevalence, risk factors, microbial aetiology, prevention, and treatment. Much of the literature consists of case-series, and retrospective/observational studies, with few randomized controlled trials. There is therefore a need for well-designed multicentre trials or the pooling of well-collected data from many units, as few if any centres have enough cases on their own to determine the efficacy of interventions.

Risk factors

Postoperative meningitis/ventriculitis usually occurs when an external ventricular drain (EVD) is inserted to monitor or control intracranial pressure. As with any other prosthetic device, there is an associated increased risk of infection. In a retrospective review between 2005 and 2010 of 410 patients, 10.2% of patients surveyed developed ventriculitis.[5] Univariate analysis indicated that female gender, older age, positive blood culture, duration of EVD and the number of cerebrospinal fluid (CSF) samples taken were associated with ventriculitis. However, after multivariate analysis, only the number of CSF samples and female gender remained statistically significant.[5] In a smaller study from the Middle East of 84 patients, the rate of ventriculitis was 14%; after multivariate analysis, repeat insertion of the EVD was associated with all causes of ventriculitis.[6] The insertion of the EVD outside the operating theatre was a significant risk factor for Gram-positive infection.[6]

A Medline literature search of ventriculitis/meningitis by Beer *et al*. found rates of infection between 5% and 20%.[7] This wide variation may relate to the diagnostic criteria used (see below). Among the risk factors they identified from the studies included were: the duration of EVD, especially more than 11 days; the frequency of EVD manipulations such as the taking of CSF samples; the presence of intraventricular haemorrhage; and the surgical technique used in inserting the device (the rate is lower when the device is tunnelled through the skin before entry into the cranium).[7] There is no convincing evidence, however, that routinely changing EVDs prevents infection. But it is clear that any additional manipulation increases the rate of infection.

Challenges remain for diagnostic criteria for meningitis/ventriculitis in this setting. A wide variety of criteria are used, some of which are exclusively microbiologically based (positive CSF culture); whereas others include microbiology findings, clinical presenting features, and CSF abnormalities such as increased CSF leucocyte count and reduced glucose concentration.[8] In a retrospective Swiss study of 48 patients with EVD-associated meningitis/ventriculitis comparing findings at the time of insertion with those on presentation with infection, fever and meningism were more frequent at the time of diagnosis but the Glasgow coma scale was lower at the time of EVD insertion.[9] An increased CSF leucocyte count was predictive of infection but a raised serum C-reactive protein was the most predictive. Scheitauer *et al*. prospectively surveyed 1333 patients using the US Centers for Disease Control and Prevention definitions, which categorize meningitis/ventriculitis into definite and probable.[10] When coagulase-negative staphylococci (CoNS) were isolated from CSF, there were clinical signs of meningitis in only 13/41 (32%) patients, and a low CSF glucose level was found in only 15/41 (37%). However, in meningitis caused by *Staphylococcus aureus*, *Enterococcus faecalis*, and Gram-negative bacilli, the CSF glucose was low in all cases.[10] For surveillance purposes, it is best not to rely on a definition invoking a decision to treat with antibiotics where suspicion of meningitis/ventriculitis is based solely on deterioration of a patient with an EVD, as this situation may be mimicked by other conditions, such as a further intracranial haemorrhage. Another challenge relates to denominator data. The total number of patients with EVDs is often used as the denominator, but the number of EVD drainage days is preferable (analogous to calculating device-related bloodstream infections) since the risk of infection generally increases the longer the EVD is *in situ*. However, monitoring the number of drainage days, and when and how often the EVD is manipulated (another risk factor for infection) requires a well-resourced surveillance programme.

Whereas some individual centres routinely or periodically carry out surveillance, national surveillance appears to be limited to those countries, one of which is The Netherlands, with a comprehensive system of HCAI surveillance. A retrospective cohort study was used to validate and update a previously developed multivariate prediction model for the detection of EVD-related meningitis.[11] Significant factors predictive of meningitis included abnormalities of the CSF such as raised white cell count, the type of drain, and whether admission to an intensive care unit was required.[11]

Microbial aetiology

Many of the causes of meningitis/ventriculitis are skin organisms: staphylococci, particularly *Staphylococcus epidermidis* and *S. aureus*, account for nearly 80%. A variety of other organisms, including aerobic Gram-negative bacilli and occasionally fungi, are less likely causes.[7] The isolation of *S. epidermidis* or other CoNS in the CSF needs to be interpreted with caution (see above) as this may represent contamination and can result in overtreatment. Huang *et al*. have suggested a hierarchy of diagnosis for patients with CoNS in the CSF from definite (positive culture in at least two specimens together with appropriate clinical signs and symptoms, as well as abnormalities of the CSF) to probable/possible (when only one CSF sample is positive but there are clinical features and/or changes in the CSF).[12] The same approach should be adopted for other skin commensals such as *Propionibacterium acnes*. There is a complex interplay between CoNS, the device, and the production of biofilm, which facilitates EVD colonization and subsequent meningitis. For example, the genotype of some

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