Neurocritical Care
Highlights from Two Austrian Meetings December, 1991

Neurocritical care is a rapidly developing discipline in neurology. There were numerous well-attended papers in this area at the Second PanEuropean Congress of Neurology in Vienna, December, 1991. Also, a workshop on neurocritical care, organized by Werner Hacke from Heidelberg and Dan Hanley from Baltimore, was held immediately afterwards in St. Christoph, Austria. The following is a synopsis of major developments in neurocritical care from these meetings:

Herpes Simplex Encephalitis

Sköldenberg found the polymerase chain reaction (PCR) useful for the detection of herpes simplex DNA in the cerebrospinal fluid (CSF) at the time of initial presentation.[1] Although she reported essentially 100% sensitivity and specificity, others have not found it as good. It remained positive for the first week in all cases and in some for up to 27 days. CSF serology using ELISA (enzyme-linked immuno-serological assay) was only useful after the first week at which point it was superior to PCR.

Magnetic resonance imaging (MRI) scanning is the imaging test of choice and often shows abnormalities in the medial temporal lobe and insula at the time of initial presentation.[2] Hexamethylpropyleneamine oxime (HMPAO) or iodoamphetamine-single photon emission computed tomography (IMP-SPECT) scanning is also useful in showing early increase in regional cerebral blood flow (rCBF). A thymidate kinase mediated radionuclide scan is being developed which may prove to be sensitive and specific.[3]

An EEG which shows periodic lateralized epileptiform discharges from one or both temporal lobes is still useful and fairly specific if there is an encephalitis.[3]

The use of brain biopsy is still controversial, but Hanley indicates that less than 10% of patients who receive acyclovir for presumed herpes simplex encephalitis actually have that disease.[3] Also, outcome seems better when specific diagnoses are made early.[3] Despite these statements, many participants recommended treating suspect cases promptly with acyclovir. Biopsy is then avoided unless other treatable diagnoses are serious contenders.

Acyclovir is still the anti-viral agent of choice; the dose is 30 mg/kg/day IV for 10 days. There is evidence for the role of cytokines, suggesting the usefulness of adjunctive anti-inflammatory therapy in treatment.[1]

Pneumococcal Meningitis

Strokes frequently complicate purulent meningitis and greatly contribute to mortality and morbidity. Controlled trials showed that patients with pneumococcal meningitis who were heparinized had significantly fewer complications and higher percentage survival than did those who were not anticoagulated.[4,5]

Pfister's [6] elegant set of experiments on pneumococcal meningitis in the rat, showed that: a) cerebral edema occurred within hours and was associated with a multifocal reduction in regional cerebral blood flow and an increase in intracranial pressure b) the above features could be prevented by dexamethasone c) Indomethacin also was beneficial, probably by prevention of prostaglandin production d) A continuous intravenous infusion of superoxide dismutase (which blocks superoxide radical formation) or infusions of desferroxamine (which blocks hydroxyl radical formation) were effective in preventing/offsetting cerebral edema and reduced rCBF, which indicates that free radicals may play a role in the morbidity and mortality of purulent meningitis e) transforming growth factor B prevented an increase in cerebral edema. This effect seemed to be independent of tumor necrosis factor production.

Post-traumatic Meningitis

Patients with a previous history of significant head trauma who develop meningitis in association with frontal sinusitis were divided into surgical and nonsurgical groups. Surgery revealed a sinus tract communicating with the meninges in 50% of cases. Those with surgical repair did much better in mortality and morbidity than those without surgery.[7]

Listeria Monocytogenes Meningitis

This is seen mainly in alcoholics and immunosuppressed patients. It is, however, less common than expected in AIDS patients. Mortality is high. Patients often show signs of intrinsic brainstem dysfunction. CSF shows initially a lymphocytic or mixed cytology and markedly elevated protein concentration. Hydrocephalus is a risk in those with very high CSF protein; shunts often block. External drainage is often used. Treatment is ampicillin 8-12 g/day intravenously; gentamycin 2 doses of 120 mg/day is often added. The duration of treatment is uncertain; most feel it should be continued until the CSF returns to normal cytology.[8]

AIDS in the ICU

It is reasonable to admit AIDS patients to the ICU if they still have the potential of a reasonable quality of life and who are suffering from a potentially treatable disease, such as opportunistic infections and CNS lymphoma.[9]

Lateralized hemispheric signs are more characteristic of opportunistic infections than HIV encephalitis. CD4 lymphocytes are usually very low with opportunistic infections.[10] Multiple rounded lesions on CT favor toxoplasmosis, while a single lesion favors lymphoma according to Einhaupl, but there are exceptions. Progressive multifocal leukoencephalopathy is characterized by white matter lesions which do not enhance.

CMV encephalitis is treated with gancyclovir 10 mg/kg/day for 2 weeks, then 5 mg/kg/day for 5 days out of each week as maintenance.

CNS toxoplasmosis is treated with norprimethamine 50-75 mg/kg/day for 3 days plus clindamycin 2.5 g/day and folinic acid 10 mg/day. This seems now to be preferable to sulfadiazine and pyramethamine. In many cases empiric therapy for toxoplasmosis is instituted, even without definitive proof.

CNS lymphoma is treated with dexamethasone and radiotherapy, the latter 40 Gy/day for 3-4 weeks.

Needlestick injuries to staff have been a major concern. Steps should be taken to prevent this from happening. Should it occur, bleeding should be induced at the puncture site and the wound should be thoroughly cleaned. AZT prophylaxis is indicated and the individual should be followed serologically. Everything should be carefully documented.

Neurological Complications of Sepsis

Critical illness polyneuropathy[11] and septic encephalopathy[12] each occur in about 70 per cent of patients with sepsis. There is a characteristic temporal profile, with the early (usually reversible) encephalopathy appearing first, followed by critical illness polyneuropathy and ventilatory failure. The encephalopathy resembles metabolic encephalopathy, but should be regarded as a diagnosis of exclusion (especially of meningitis). The neuropathy is axonal; motor fibres are affected more than sensory clinically. Ventilatory failure is often due to critical illness polyneuropathy. Needle studies of the diaphragm confirm denervation.[13]

The encephalopathy recovers first, then the ventilatory failure; the neuropathy eventually recovers, but often not completely.

Respiratory Muscle Fatigue in the ICU

Fatigue, indicating anaerobic metabolism or energy failure, is not applicable to respiratory failure in the ICU. Failure to wean from the ventilator in general ICUs is related to weak, not fatigued, muscles from muscle disease, neuromuscular transmission failure or peripheral nerve dysfunction. There is rarely a problem with central drive.[14]

Cerebrovascular Autoregulation

Autoregulation allows a constant regional blood flow (rCBF) within a range of mean arterial pressures. Angiotensin converting enzyme (ACE) inhibitors cause a shift to the left of the autoregulation curve, allowing maintenance of rCBF at mean arterial pressures that ordinarily would not be tolerated.[15] This may have therapeutic implications.

There is little evidence for direct neurogenic or myogenic control over rCBF in the pial circulation, and metabolic regulation seems more likely. An arginine metabolite has been found which regulates tissue perfusion in other organs. Efforts are underway to determine if it plays a role in the CNS.[15]

Using confocal microscopy it was shown that capillary circulation was variable; leukocytes alter perfusion in the microcirculation. In the no-reflow phenomenon, leukocyte activation plays a major role in capillary perfusion. This may relate to an endothelial product which in turn is released in response to cytokines.[15]

Subarachnoid Hemorrhage

The hyponatremia after subarachnoid hemorrhage is not always due to SIADH, but is often due to salt wasting by the kidney.[16] Intravascular volume is then decreased (as measured using the radiolabelled albumin technique). In this situation, it is counterproductive to withhold fluids and/or saline. A more rational therapy is to give extra saline to produce a mildly hypertensive, hypervolemic state to ensure better brain perfusion (e.g. in the presence of vasospasm). This is instituted after the aneurysm is clipped.

Vasospasm from Subarachnoid Hemorrhage

Boker et al.[17] showed the effectiveness of selective catheterization and injection of intra-arterial nimodipine in treating angiospasm. Initially they did not clip the aneurysm first and found the aneurysm enlarged after nimodipine. They now recommend that the aneurysm be clipped before using this therapy.

Spontaneous Parenchymal Hemorrhage

Ropper[18] found a relationship between lateral pineal shift and level of consciousness (3-5 mm = drowsy; 5-7 mm = stupor; > 8 mm = coma). Systemic administration of vasodilators, such as calcium antagonists, should be avoided as they cause further increases in intracranial pressure (ICP). Medical measures to lower ICP should be used first, using standard therapy. In his experience corticosteroids may be of some help. Surgical removal of the clot should be considered in patients who are refractory to medical therapy. With cerebellar hemorrhage, surgical removal is indicated if the hematoma is > 3 cm in diameter or if there is hydrocephalus and obliteration of basal cisterns.

Drainage of ventricular clot can be beneficial. Some preliminary success has been reported with the stereotaxic drainage of parenchymal clot, along with injection of urokinase to break up the clot.[19]

Management of Mass-producing Cerebellar Infarction

Surgical therapy can be life saving in some cases of cerebellar infarction. With just ventricular drainage, there is a risk of upward transtentorial herniation or severe rostral brainstem compression. Patients who require operation do better with a combination of ventricular drainage and resection of infarcted or edematous cerebellar tissue.[20]

Thrombolytic Therapy

Ferbert[21] and Mori[22] each gave their experience with thrombolytic therapy for ischemic stroke. If patients are caught early in the course of stroke, reperfusion without deficit is sometimes possible. This seems best for the M1 segment of middle cerebral artery or basilar artery occlusions. Hacke[23] reported more success with basilar occlusions than with thrombi in the anterior circulation. Hemorrhages have not been a major problem. Definitive trials are underway in Japan and Germany.

Sawada cautioned that thrombolytic therapy may be occasionally associated with multiple cholesterol (atheromatous) emboli, but it was difficult to know whether arterial catheterization played an important role.[24] Ropper had several cases of Guillain-Barre syndrome after the introduction of thrombolytic therapy (personal communication).

Neurological Involvement in Early Ischemic Stroke

Hacke[25] recommended that neurologists play a central role in the early treatment of ischemic stroke. Results are best when intervention occurs within the first 6 hours. Antihypertensive medication should not be given unless the diastolic pressure is > 120 mm Hg. Even mild hyperglycemia should be corrected.

Superior Sagittal Sinus Thrombosis

The presentation is variable.[26] Only 20 per cent present acutely, like a subarachnoid hemorrhage. Some patients took days or weeks to evolve full symptomatology. Mortality was 30% by 1 week. The causes and presenting symptoms were classical. The CT often shows parenchymal hemorrhages in the parasagittal region. The appearance is characteristic and should differentiate this condition from herpes simplex encephalitis, subarachnoid hemorrhage or hypertensive hemorrhages.

Venous back pressure increases and collateral venous channels open up, particularly the basal veins, so that the intracranial drainage is altered.

Early heparinization was beneficial: none of those who were treated early died, compared to 30% in the nontreated group. With anticoagulation the morbidity was also significantly less than for those who were not anticoagulated. The rationale is that heparinization prevents progression of the obstruction to the superior sagittal sinus or draining veins. Further hemorrhages do not occur because the latter are due to back pressure on capillary beds which results from venous occlusion. Heparinization, if anything, should ultimately lead to a reduction or failure of progression of this process.

Surgical Intervention for ICP Elevation and Mass Effect

Preliminary success was reported from a trial of decompressive craniectomy for cerebral infarction for persons < 40 years of age with stroke, trauma or temporal lobe swelling in herpes simplex encephalitis.[27] The decompressions were extensive and always included the middle fossa. Indications included failure to control ICP, tendency for herniation syndromes or marked mass effect on neuroimaging.

Measurement of Intracranial Pressure

In general, intraventricular pressure monitoring is favored for subarachnoid hemorrhage and meningitis, while epidural monitoring is favored for stroke, hematoma and head trauma. It is used as a guide for care and for prognosis.[28]

A discussion followed in which it was pointed out that one published study showed that ICP monitoring did not influence outcome. Most felt ICP monitoring was helpful in patient management, but that a controlled trial probably needs to be done to establish its applications and effectiveness.

New Concepts in Brain Herniation

Ropper[29] reported a series of cases with clinical features of "uncal herniation syndrome" in which special MT, MRI or post mortem studies showed that there was little if any downward transtentorial herniation. In a number of cases the movement of the rostral brainstem was in an upward direction. Furthermore, the perimesencephalic cisterns were not obliterated. The shift or displacement was mainly lateral in the supratentorial compartment. Third nerve palsy ipsilateral to the mass was due to stretching of the nerve against the edge of the clivus, just as it entered the cavernous sinus. The involvement of the "other pupil", which occurs later, is usually a midbrain sign.

Much discussion and debate followed, but credit had to be given Dr. Ropper for his original observations which run counter to traditional concepts. His conclusions, which were well supported by his data, apply mainly to the early phase of the herniation syndrome.[29]

The Electrophysiology of Trauma

With severe brain injury, EEG patterns are simpler and show less variety and variability than with minor injuries.[30] Evoked responses may sometimes be prognostically misleading in brain trauma, as later cortical responses may be absent with reversible brainstem injuries. Thus it is important to repeat the tests. Clinical neurophysiology has a role in trauma, but great care should be taken that the tests are used properly.

Ethics in the ICU and Brain Death

In North America and Europe it is generally agreed that death of the brain is equivalent to death of the individual. Brain death is regarded as a legal definition of death. Ventilation and other life support measures can be discontinued without the consent of relatives. In general, however, full consultation with the next of kin should be conducted.[31]

In Germany ancillary tests which show absence of brain circulation (cerebral angiography, nuclear medicine scans and transcranial doppler) are used to speed the diagnosis of brain death when the usual interval between clinical assessments is to be more than several hours.[32] Such tests are also used when the clinical criteria cannot be applied. In general, however, the clinical criteria form the basis for the diagnosis of brain death.

Status Epilepticus and Other Seizure Phenomena

Bleck found that anesthetic barbiturates may contribute to mortality.[33] He has switched to Midazolam, which is an effective anti-status drug with fewer side effects and shorter wash-out time.

Complex partial status epilepticus should be treated urgently as patients may be left with permanent memory impairment.[34]

Focal seizures may present in infancy with life-threatening apnea as the principal or sole feature.[35] The limbic system, especially the temporal lobe, is consistently involved. Treatment is difficult. Primidone seemed to be more effective than other drugs in a series of 3 cases.

Guillain-Barre Syndrome

Ropper[36] reviewed the recent trial which used gamma globulin in Guillain-Barre syndrome (to be published shortly). The results were superior to plasma exchange. The benefit, although statistically significant, appears to be minimal — 9 days less on the ventilator and a shorter time to walking.

Ropper pointed out that the main determinant of good recovery and low morbidity and mortality rests with basic care. This includes: 1) nasotracheal as opposed to orotracheal intubation, which is done in a non-emergency situation, based on an assessment of ability to clear secretions and to maintain airway, before decompensation of vital capacity or blood gases. 2) Surveillance for and prompt treatment of infections, especially pneumonia and urinary tract infections. 3) Care of nutrition, management of hyponatremia and hyperkalcemia. 4) Early physiotherapy, particularly passive movements of limbs. 5) Management of autonomic problems, including increased or decreased vagal tone which is mainly manifested by changes or lack of change in heart rate. 6) Awareness of and prompt treatment of hypotension, which often results from increases in vasodepressor tone. 7) Watching for ileus. 8) Anticoagulation to prevent pulmonary thromboembolism.

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