Journal of
NEUROLOGY
NEUROSURGERY
& PSYCHIATRY

Editorial

Spontaneous intracerebral haemorrhage

The increased use of the CT scanner in the investigation of patients with cerebrovascular disease has led to more frequent recognition of strokes caused by intracerebral haemorrhage (ICH). The diagnosis is being made at both extremes of the clinical spectrum. At one end are patients in coma with an extremely poor prognosis who, in the past, would have been considered on clinical grounds to have an intracerebral haemorrhage. At the other are patients with only minor focal neurological deficits, who were previously regarded as having suffered an ischaemic episode and therefore were not investigated by CT scanning.

The inaccuracy of diagnosis in the past is one reason that the choice of treatment remains very controversial. The debate should be advanced by the changing use of CT and the greater awareness of the smaller lesion. Previous trials of surgical treatment, even when randomised and controlled, have failed to match patient groups for the size of the clot and have resulted in further confusion. Any form of treatment is likely to be more successful with smaller haemorrhages. Unnecessary surgical evacuation of small clots may be followed by a good result, while the outcome of surgery for very large lesions in deeply comatose patients will be poor.[1]

Intracerebral haemorrhage is relatively common (20 per 100 000 per year) and, with subarachnoid haemorrhage (10 per 100 000 per year), accounts for 15% of all strokes. While there are now more than 137 CT scanners in the United Kingdom, their distribution is very uneven,[2] so that confirmation of the diagnosis on CT scan is likely to vary according to local practice. Intracerebral haemorrhages are now being diagnosed with magnetic resonance imaging.[3]

Two kinds of decision are required in a patient with an intracerebral haemorrhage: first, how to manage the haematoma, and second, how to prevent rebleeding. The need for measures to prevent rebleeding depends upon aetiology, which is usually clarified by angiography. The prevention of rebleeding is not considered here, but is obviously of great importance, and often influences the management of the acute haematoma.

Aetiology

Hypertension is the most common cause of intracerebral haemorrhage, and its control is probably the main factor responsible for the decreasing incidence of stroke.[4] Anticoagulation, platelet and coagulation disorders are still common causes of haemorrhage in patients presenting in neurosurgical units. Other causes of spontaneous haemorrhage include the abuse of drugs, particularly those which induce hypertension,[5] and acute hypertension in pregnancy and childhood.[6] It should never be forgotten that an intracerebral haemorrhage may be the result of a ruptured berry aneurysm. The differentiation of a subarachnoid haemorrhage from an intracerebral haemorrhage is not always possible on clinical grounds alone, and indeed the lesions often coexist on CT scanning. Pasqualin described 309 cases of ICH and showed that the site of the haematoma may help in pointing to the likelihood of an aneurysm,[7] although this is less reliable with a large haematoma.[8] Arteriovenous malformations are more likely to present with an intracerebral haemorrhage than with a subarachnoid haemorrhage, and should always be considered as a cause, particularly in younger people. Of the tumours that cause intracerebral haemorrhage, metastatic melanoma is one of the commonest.

Pathophysiology

The great majority of haematomas result from rupture of an artery or arteriole and therefore the pressure within the haematoma is initially identical to arterial blood pressure. This increase in pressure causes compression of the surrounding brain parenchyma with resulting ischaemia. Around any haematoma there is an area of complete ischaemia surrounded by an area of oligaemia which is analogous to the penumbra of occlusive stroke. Experimental studies have indicated that the area of ischaemia may be much larger than the haematoma itself.[9,10] The ischaemia is partly the result of mechanical compression of the surrounding microcirculation, although the vasospastic properties of blood probably also play a role.[11,12] The release of "toxins" from bloods within the haematoma may further aggravate the ischaemia.[13] It has also become clear that rebleeding is associated with a worse prognosis.[14] The damage which may occur around the haematoma may therefore be focal, largely as a result of ischaemia, or global, as a result of reduction in the cerebral perfusion pressure (CPP) which occurs mainly because of rising intracranial pressure. Cerebral perfusion pressure may also fall from the ill-advised treatment of reactive hypertension, particularly if it is due to a Cushing response.

After the initial ischaemic episode, the marginal zone around the haematoma may become oedematous and this in turn may further elevate the intracranial pressure. The initial factors responsible for oedema include the release of arachidonic acid and free radicals. A large number of other agents may be mediators of the brain oedema which surrounds these lesions, and different agents may exert their effects at different times. Recent experimental evidence has shown that there is an immune component to the pathogenesis of this oedema.[15] It is now recognised that there is a rapid rise in excitatory amino acids including glutamate.[16,17] Kinins and other proteins including

putresine, and leukotrienes may cause further extension of the oedema. Ultimately, neuronal death will be the result of an influx of calcium. It is treatment of this cascade of events in the marginal zone which is most likely to result in clinical benefit, and a large number of agents have been tried experimentally. Agents with therapeutic potential include the use of calcium antagonists, NMDA receptor blockers (competitive and non-competitive), superoxide dismutase, steroids and possibly immunosuppressive agents. At present clinical trials with these agents have not been undertaken in patients with ICH. Their value in the treatment of patients must therefore remain speculative.

Clinical features

The clinical features of spontaneous intracranial haemorrhage are well known. They can be divided into two syndromes: the sudden onset of elevated intracranial pressure, and the development of focal neurological signs, which are appropriate to the site of clot.

Epilepsy may be an early or late complication of intracerebral haemorrhage. It is more common with lobar haemorrhage than with deep seated or basal ganglia haemorrhage. The percentage of patients that develop epilepsy with lobar haemorrhage has been reported to be as high as 62% compared with the average of 2·5% for a series of 1402 cases.[18]

Treatment

Treatment of the haematoma itself has not been well evaluated in formally controlled trials; this is the consequence of the difficulty of finding comparative groups of well-matched but untreated patients. Opinions are therefore divided about the need for surgical treatment; some being enthusiastic[19 20] but others less so.[21] Kanno[22] has reviewed the results of surgical and medical treatment in a large number of patients from Japan and agrees that the treatment remains controversial.

The features of patients with an ICH vary widely and it is not possible to generalise about treatment except at each end of the spectrum. Few neurosurgeons would doubt that delayed deterioration in a young patient with a subcortical haematoma is a clear indication for surgical evacuation whereas most neurosurgeons would not contemplate the evacuation of a large dominant hemisphere haematoma in an elderly patient who has been in coma with fixed dilated pupils from the outset. The real dilemma, which involves the greatest number of patients, applies to the group between these two extremes. Sakan[23] has suggested that surgical evacuation should be reserved for those patients with coma scores of between six and eight, once again without proper comparison with a control group. McKissock's original study[24] indicated that there was no overall benefit from surgery, with the results of the surgically treated group being slightly worse than in the medically treated group. Volpin *et al* [25] related the outcome to size, and indicated that lesions larger than 85 mls were almost always fatal, while survival was more likely with surgical evacuation in haematomas of about 50 ml volume on CT scan. Kanno[22] reported 459 patients and felt that overall, there was no difference between surgically and medically treated patients. Results tended to be better with more laterally situated lesions and if surgical treatment was undertaken within six hours of the ictus. If one looked at the ultimate effect on activities of daily living, however, there was no advantage in surgical treatment. Juvela *et al* [26] reported the results of a prospective randomised controlled study, and showed no benefit from surgical treatment.

Special types of haematoma

a) Pontine haemorrhage

Pontine haemorrhage is seldom associated with elevated ICP unless there is accompanying hydrocephalus. The outcome is related to the extent of the haemorrhage, with bilateral pontine haematomas being almost universally fatal.[27] The subject was reviewed by Ochiai *et al* [28] and there are some enthusiasts for surgical treatment.[29]

b) Cerebellar haemorrhage

As with pontine haemorrhage, the prognosis is related to the severity of the haemorrhage, with patients in coma being less likely to survive.[30] The prognosis may be related to size and to obliteration of basal cisterns. Patients with complete obliteration of the basal cisterns are unlikely to survive, while those with open cisterns have a better prognosis whatever the form of treatment.[31] Stereotaxic aspiration of cerebellar haematomas has been described[32] and the subject has been reviewed by a number of authors.[33 34] It was thought that the surgical treatment of cerebellar haemorrhage was often successful but this has not been the subject of rigorous controlled investigation.[35–37]

c) Chronic encapsulated haematomas

Attention has recently been drawn to the presence of chronic encapsulated intracerebral haematomas.[38 39] Although these lesions are presumably the late result of a healing process, some may undergo delayed expansion. Surgical aspiration is likely to be successful in those cases undergoing late deterioration.

Current and future developments

Alternatives to conventional medical and surgical methods of management of ICH are being proposed. There are an increasing number of reports of surgical treatment by stereotaxic aspiration[40–46] instead of "open" evacuation. The use of urokinase to promote liquifacation of the clot before aspiration has also been proposed.[47]

The first prospective randomised controlled study to provide evidence that surgical treatment was superior to medical treatment came from Auer *et al* [48] who reported a mortality of 46% after endoscopic aspiration compared with a mortality of 70% after medical treatment. The high mortality in the medically treated group emphasises the importance of careful matching of patients. Whether these results will be replicated remains to be determined; endoscopy is not in routine use in most neurosurgical units.

Ultimately, progress in management of ICH will depend upon better understanding of the pathophysiological mechanisms leading to damage. ICP measurement in patients with a traumatic intracerebral haematoma predicts the likelihood of subsequent deterioration[49] but it is done much less often in spontaneous haematomas. The studies reported to date are largely anecdotal and do not permit a definite statement on the value of ICP monitoring.[50 51] There are differences between traumatic and spontaneous haematomas, for example, there is more oedema around a traumatic haematoma[52]; but also there are many similarities. Lessons learnt about the management of traumatic intracerebral haematomas may be applicable to spontaneous ICH. An understanding of the pathophysiology of spontaneous intracerebral haemorrhage may result in more widespread use of "brain protective agents" which will also have to be subjected to randomised controlled studies.

Conclusion

The increasing availability of CT in district general

hospitals and its use in patients with a stroke will highlight the need to establish the best way to manage spontaneous ICH. This information is needed both by specialists in neurosurgery/neurology and by general physicians who, more and more, will need to decide if referral to a neurosurgeon is appropriate.

Unfortunately, at present a definite statement cannot be made about the treatment of many patients with intracerebral haemorrhage. Some clearly warrant surgical evacuation; for others surgical treatment is definitely not indicated (either those with very small haematomas who remain well or those with very large haematomas who are moribund). The uncertainty relates to the patients in the middle of the spectrum and probably the only way to resolve the uncertainties about the treatment of these patients is to undertake randomised controlled trials of the different forms of therapy. This will hopefully lead to less uncertainties than currently surround the management of spontaneous intracerebral haemorrhage.

A DAVID MENDELOW

Regional Neurosciences Centre,
Newcastle General Hospital,
Newcastle upon Tyne.

1 Nath FP, Nicholls D, Fraser RJ. Prognosis in intracerebral haemorrhage. *Acta Neurochir* 1983;67:29–35.
2 Hewer RL, Wood VA. Availability of computed tomography of the brain in the United Kingdom. *BMJ* 1989;298:1219–20.
3 Bydder GM, Pennock JM, Porteous R, Dubowitz LM, Gadian DG, Young IR. MRI of intracerebral haematoma at low field (0·15T) using T2 dependent partial saturation sequences. *Neuroradiology* 1988;30:367–71.
4 Garraway WM, Whisnant JP, Furlan AJ, Phillips LH II, Kurland LT, O'Fallon WH. The declining incidence of stroke. *New Engl J Med* 1979;300:449–52.
5 Wajak JC, Flamm ES. Intracranial haemorrhage and cocaine use. *Stroke* 1987;18:712–15.
6 Freitas PE, Aquini MG. Spontaneous intracerebral haematoma during childhood. *Neurosurgery* 1987;21:103–5.
7 Pasqualin A, Bazzan A, Cavazzani P, Scienza R, Licata C, Da Pian R. Intracranial haematomas following aneurysm rupture: Experience with 309 cases. *Surg Neurol* 1986;25:6–17.
8 Hayward RD, O'Reilly GVA. Intracerebral haemorrhage: accuracy of computerised transverse axial scanning in predicting the underlying aetiology. *Lancet* 1976;i:1–4.
9 Bullock R, Brock-Utne J, van Dellen J, Blake G. Intracerebral haemorrhage in a primate model. Effect on regional cerebral blood flow. *Surg Neurol* 1988;29:101–7.
10 Mendelow AD, Bullock MRR, Teasdale GM, Graham DI, McCullock J. Intracranial haemorrhage induced at arterial pressure in the rat. Part II. Short-term changes in local cerebral blood flow measured by autoradiography. *Neurol Res* 1984;6:189–93.
11 Jenkins A, Mendelow AD, Graham DI, Nath FP, Teasdale GM. Experimental intracranial haematoma: The role of blood constituents in early ischaemia. *Br J Neurosurg* 1990;4:45–51.
12 Sinar EJ, Mendelow AD, Graham DI, Teasdale GM. Experimental intracranial haemorrhage: effect of a temporary mass lesion. *J Neurosurg* 1987;66:568–76.
13 Inoue T, Kanno T. Marginal zone of a haematoma: its choline metabolism in surgically and non-surgically treated dogs. *J Neurosurg* 1990 (in press).
14 Chen ST, Chen SD, Hsu CV, Hogan EL. Progression of hypertensive intracerebral haemorrhage. *Neurology* 1989;39:1509–14.
15 Kane P, Modha PG, Mendelow AD, Proctor S, Fox C. Reduction of brain oedema in rats by immunosuppression with whole body radiation. In: Reulen H-J, Baethmann A, Marmarou A, eds. *Proc 8th International Symposium on Brain Oedema*. Bern: 1991 (in press).
16 Bullock R, Butcher SP, McCullock J. Regional cerebral blood flow and extracellular glutamate release after acute subdural haematoma in the rat. In: Reulen H-J, Baethmann A, Marmarou A, eds. *Proc 8th International Symposium on Brain Oedema*. Bern: 1991 (in press).
17 Katayama Y, Becker DB. Early cellular swelling in experimental traumatic brain injury: a phenomenon mediated by excitatory amino acids. In: Reulen H-J, Baethmann A, Marmarou A, eds. *Proc 8th International Symposium on Brain Oedema*. Bern: 1991 (in press).
18 Sung CV, Chu NS. Epileptic seizures in intracerebral haemorrhage. *J Neurol Neurosurg Psychiatry* 1989;52:1273–6.
19 Kanaya H, Yukawa H, Kanno T, *et al.* A neurological grading for patients with hypertensive intracerebral haemorrhage and a classification for haematoma location on computed tomography. *Proc 7th Conference on Surgical Treatment of Stroke*. Tokyo: Neuron, 1978:265–70.
20 Kaneko M, Tanaka K, Shimada T, *et al.* Long-term evaluation of ultra-early operation for hypertensive intracerebral haemorrhage in 100 cases. *J Neurosurg* 1983;58:838–42.
21 Dei-Anang K, Kramer G, Besser R, Muller-Forell W. Treatment of spontaneous intracerebral haemorrhage—operative or conservative? *Radiologe* 1989;29:423–6.
22 Kanno T, Sanno H, Shinomiya Y, *et al.* Role of surgery in hypertensive intracerebral haematoma. *J Neurosurg* 1984;61:1091–9.
23 Sakas DE, Singounas EG, Karvounis PC. Spontaneous intracerebral haematomas: surgical versus conservative treatment based on Glasgow Coma Scale score and computer tomography data. *J Neurosurg Sci* 1989;33:165–72.
24 McKissock W, Richardson A, Taylor J. Primary intracerebral haemorrhage. A controlled trial of surgical and conservative treatments in 180 unselected cases. *Lancet* 1961;ii:221–6.
25 Volpin L, Cervellini P, Colombo F, Zanusso M, Benedetti A. Spontaneous intracerebral haematomas: a new proposal about the usefulness and limits of surgical treatment. *Neurosurgery* 1984;15:663–6.
26 Juvela S, Heiskanen O, Poranen A, *et al.* The treatment of spontaneous intracerebral haemorrhage. A prospective randomized trial of surgical and conservative treatment. *J Neurosurg* 1989;70:755–8.
27 Kushner MJ, Bressman SB. The clinical manifestations of pontine haemorrhage. *Neurology* 1985;35:637–43.
28 Ochiai C, Sano K, Kobayashi S, Sasaki T, Mayanagi Y. Clinical study of pontine haemorrhage with special reference to CT classification and surgical indication. *No To Shinkei* 1979;31:803–11.
29 Mattos-Pimenta LH, Mattos-Pimenta A, Zuckerman E. Pontine haematoma: successful removal of two cases with review of 22 cases previously described in accessible literature. *Neurosurg Rev* 1981;4:139–42.
30 Dunne JW, Chalzera T, Kermode S. Cerebellar haemorrhage—diagnosis and treatment: a study of 75 consecutive cases. *Q J Med* 1987;245:739–54.
31 Taneda M, Hayalzawa T, Mogami H. Primary intracerebral haemorrhage: quadrigeminal cistern obliteration on CT scans as a predictor of outcome. *J Neurosurg* 1987;67:545–52.
32 Niizumi H, Suzuki J. Computed tomography-guided stereotactic aspiration of posterior fossa haematomas: a supine lateral retromastoid approach. *Neurosurgery* 1987;21:422–7.
33 Van der Hoop RC, Vermeulen M, van Gijn J. Cerebellar haemorrhage: diagnosis and treatment. *Surg Neurol* 1988;29:6–10.
34 Lui TN, Fairholm DJ, Shu TF, Chang CH, Lee ST, Chen H-R. Surgical treatment of spontaneous cerebellar haemorrhage. *Surg Neurol* 1985;23:555–8.
35 Philippon J, Rivierex M, Nachanakian A, Horn YE, Grob R. Cerebellar haemorrhage. Clinico-topographic correlations and therapeutic indications. *Neurochirurgie* 1983;29:381–6.
36 Chin D, Carney P. Acute cerebellar haemorrhage with brainstem compression in contrast with benign cerebellar haemorrhage. *Surg Neurol* 1983;19:406–9.
37 Weisberg LA. Cerebellar haemorrhage in adults. Clinical and computerized tomographic findings. *Comput Radiol* 1982;6:75–81.
38 Fiumara E, Gambacorta M, D'Angelo V, Ferrara M, Corona C. Chronic encapsulated intracerebral haematoma: pathogenetic and diagnostic considerations. *J Neurol Neurosurg Psychiatry* 1989;52:1296–9.
39 Lainez-Andres JM, Rieger SJ, Torrella EJ, Nicolas CM, Gonzales MR, Marino BC. Chronic intracerebral haematoma. *Br J Neurosurg* 1989;3:513–6.
40 Hayashi M, Hasegawa T, Kobayashi H, Munemoto S, Yamamoto S. Aspiration of hypertensive intracerebral haematoma by stereotactic technique (author's transl). *No Shinkei Geka* 1981;9:1365–71.
41 Hondo H. CT-guided stereotactic evacuation of hypertensive intracerebral haematomas. A new operative approach. *Tokushima J Exp Med* 1983;30:25–39.
42 Lunsford LD, Martinez AJ, Latchaw RE. Stereotaxic surgery with a magnetic resonance and computerized tomography-compatible system. *J Neurosurg* 1986;64:872–8.
43 Tanizaki Y, Sugita K, Toriyama T, Hokama M. New CT-guided stereotactic apparatus and clinical experience with intracerebral haematomas. *Appl Neurophysiol* 1985;48:11–7.
44 Tanikawa T, Amano K, Kawamura H, *et al.* CT-guided stereotactic surgery for evacuation of hypertensive intracerebral haematoma. *Appl Neurophysiol* 1985;48:431–9.
45 Shiwaku T, Tanikawa T, Amano K, *et al.* A new treatment of hypertensive intracerebral haematoma—a follow-up study on 46 patients with haematoma treated by CT guided stereotactic method. *No Shinkei Geka* 1986;14:751–8.
46 Honda E, Hayashi T, Shimamoto H, *et al.* A comparison between stereotaxic operation and conservative therapy for thalamic haemorrhage. *No Shinkei Geka* 1988;16(suppl 5):665–70.
47 Niizuma H, Otsuki T, Johkura H, Nakazato N, Suzuki J. Guided stereotactic aspiration of intracerebral haematoma—result of a haematoma-lysis method using urokinase. *Appl Neurophysiol* 1985;48:427–30.
48 Auer LM, Deinsberger W, Niderkjorn K, *et al.* Endoscopic surgery versus medical treatment for spontaneous intracerebral haematoma: a randomized study. *J Neurosurg* 1989;70:530–5.
49 Galbraith S, Teasdale G. Predicting the need for operation in the patient with an occult traumatic intracranial haematoma. *J Neurosurg* 1981;55:75–81.
50 Papo I, Janny P, Caruselli G, Colnet G, Luongo A. Intracranial pressure time course in primary intracerebral haemorrhage. *Neurosurgery* 1989;4:504–11.
51 Duff TA, Ayeni S, Levin AB, Javid M. Neurosurgical management of spontaneous intracerebral haematoma. *Neurosurgery* 1981;9:387–93.
52 Statham PFX, Todd NV. Intracerebral haematoma: aetiology and haematoma volume determine the amount and progression of brain oedema. In: Reulen H-J, Baethmann A, Marmarou A, eds. *Proc 8th International Symposium on Brain Oedema*. Bern: 1991 (in press).