

*Short report*

# Spinal cord necrosis after intrathecal injection of methylene blue

M. M. SHARR, R. O. WELLER, AND J. G. BRICE

*From the Wessex Neurological Centre, Southampton University Hospitals, Southampton, England*

**SUMMARY** A 59 year old man had 6 ml of unbuffered methylene blue injected into the lumbar theca in an attempt to localise the source of cerebrospinal fluid rhinorrhoea. After injection of the dye he became shocked, and within the next few days he developed a mild paraparesis which subsequently progressed to a total paraplegia. The distribution of the spinal cord damage found at necropsy, eight and a half years after injection of the dye, is described and its relationship to the clinical picture discussed.

Walker (1949) was the first to report the adverse clinical effects of methylene blue upon the central nervous system. This was followed by accounts of the toxic effects of intrathecal injection of the dye by Brihaye and Lorthoir (1957), Arieff and Pyzik (1960), Evans and Keegan (1960), Jensen *et al.* (1962), Schultz and Schwarz (1970), and Gross (1974). The pathological changes in the spinal cord were described by Wolman (1966) in a patient who died 34 hours after methylene blue injection into the lumbar theca, but there are no pathological descriptions of the long-term effects of methylene blue nor of the relationship between the pathology and the clinical picture. The present paper is a report of the clinical and pathological findings in a patient who died eight and a half years after developing a severe neurological deficit as a result of intrathecal injection of methylene blue.

## Case report

### CLINICAL HISTORY

A 59 year old lorry driver was investigated for unilateral cerebrospinal fluid rhinorrhoea of six months' duration; investigations were negative except for some loss of the cortical margin of the left orbital plate on skull radiography. Because the symptoms persisted, 6 ml of 1% methylene blue were injected into the lumbar subarachnoid space in an attempt to identify the source of the CSF

rhinorrhoea. Two hours later the patient became shocked, vomited, and within the next 24 hours developed a paraparesis, with urinary retention but without sensory loss. Some improvement occurred in the power of the lower limbs after two months, but the paraparesis then progressed, and the urinary retention persisted. Sensory loss appeared four months after the injection. Clinical assessment 18 months after the injection revealed complete loss of power in the right lower limb, and by three and a half years after the injection there was a total paraplegia with a level at T9 dermatome, which persisted until the patient's death five years later.

### PATHOLOGY

At postmortem examination a 60 mm long polyp was found attached to the orbital aspect of the frontal lobe and passed through the hole in the cribriform plate into the nose, and this was presumed to be the source of the cerebrospinal fluid rhinorrhoea.

Examination of the spinal cord showed fibrous thickening of the dura and arachnoid membranes around the lower thoracic and lumbar spinal cord. Nerve roots in the cauda equina were bound together in a fibrous mass. Gross shrinkage and softening of the cord was seen with cystic change particularly in the lumbar segments.

Histological examination revealed the pattern of damage depicted in the Figure. Tissue destruction was most severe in the lumbar region. At L5 segment, the dorsal region of the cord was destroyed although some anterior horn neurones were still present in the grey matter and the short inter-

Address for reprint requests: Dr M. M. Sharr, Wessex Neurological Centre, Southampton General Hospital, Southampton SO9 4XY, England.

Accepted 31 October 1977

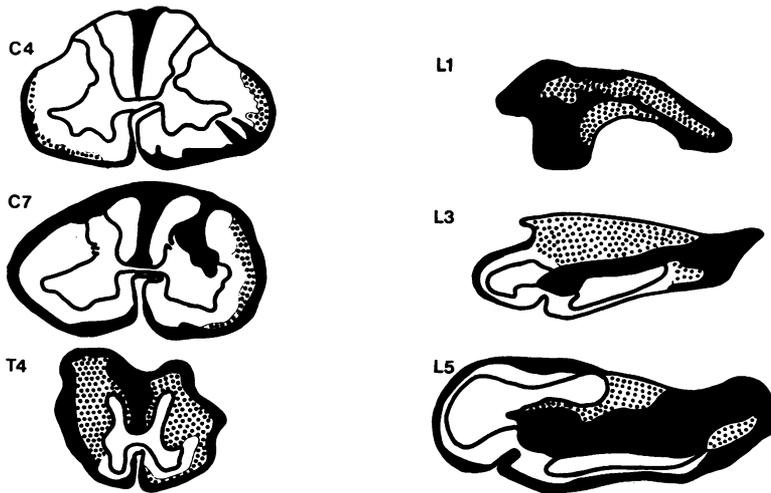


Figure Camera lucida drawings of the spinal cord at various levels to show the distribution of complete tissue destruction (solid black areas) and partial loss of axons and myelin (stippled areas). Plain white areas are histologically preserved grey and white matter.

segmental tracts of white matter were preserved; extensive fibrosis and thickening of the meninges were seen at this level. The first lumbar segment was the most severely affected with shrinkage of the cord and almost complete destruction of myelinated tracts and grey matter. At this level the anterior spinal artery had lost its elastic lamina and smooth muscle coat, and the media had been replaced by dense fibrous tissue. Firm evidence of thrombotic occlusion was seen in a posterior spinal artery at L1 segment where the vessel showed some recanalisation. In the upper thoracic and cervical cord, there was destruction of white matter on the surface of the cord and degeneration of the ascending pathways, particularly the gracile tracts. An area of cystic infarction was seen in the right posterior horn of grey matter at C7 segment extending into the medial part of the right lateral corticospinal tract. Extensive loss of myelinated fibres was seen in the cauda equina and in the nerve roots below the midthoracic region. The most severely damaged nerve roots were at L1 segment where organised thrombi were seen occluding radicular vessels. No inflammatory changes were seen in the cord, nerve roots, or meninges.

### Discussion

The exact mode of action of methylene blue upon neural tissue is unclear but it may be a combination of the toxic effect of the dye itself and the effect of the low pH (pH 3.6–3.7) of the solution. A similar toxic reaction has been described after intrathecal alcohol (Wolman, 1966). Jensen *et al.* (1962) claimed that mixing cerebrospinal fluid with methylene blue before injection would neutralise

the action of the dye but Schultz and Schwarz (1970) found that damage still occurred with this mixture.

In the present case it appears that there were three phases of spinal cord and nerve root damage. The initial phase, shortly after the intrathecal injection of the dye, may have been due to the direct damage to the surface of the cord and to its surface blood vessels; this was probably accentuated by poor perfusion during the period of hypotension which ensued. Wolman (1966) observed damage to the surface of the spinal cord as an acute reaction to intrathecal methylene blue, and similar changes have been described in dogs (Evans and Keegan, 1960). The second stage in the present patient was the temporary recovery that may have been related to a regression of oedema around areas of infarction in the cord, as has been described after phenol injection (Hughes, 1970). Similar recovery of neurological function, after acute cord damage from intrathecal injection of methylene blue, has been described by Evans and Keegan (1960). The third phase was progression to total paraplegia which may have been a result of progressive ischaemia of the cord accompanying fibrosis and scarring of the meninges. Histopathological evidence of blood vessel damage was found at necropsy, and this probably also contributed to infarction of the cord and nerve roots.

Although this paper is the first account of ischaemic damage to the spinal cord after intrathecal methylene blue, similar changes, including vessel wall fibrosis, meningeal thickening, acute arteritis, and spinal cord necrosis have been described after spinal anaesthesia or intrathecal alcohol injection (Brain and Russell, 1937; Green-

field *et al.*, 1955; Wolman, 1966). No pathological accounts are available of spinal cord damage in patients surviving for long periods after intrathecal injection of methylene blue, but previous clinical accounts have shown that the recovery of neurological function is variable (Evans and Keegan, 1960). Wolman (1966) suggested that complications were related to the volume of dye injected but other reports suggest that even small amounts of the dye are dangerous (Arieff and Pyzik, 1960; Schultz and Schwarz, 1970). It is clear from this study and from previous accounts that the risk of intrathecal injection of even small amounts of the dye is too great and that its use should be abandoned.

### References

- Arieff, A. J., and Pyzik, S. W. (1960). Quadriplegia after intrathecal injection of methylene blue. *Journal of the American Medical Association*, **173**, 794–796.
- Brain, W. R., and Russell, D. S. (1937). Myelomalacia following spinal anaesthesia. *Proceedings of the Royal Society of Medicine*, **30**, 1024–1030.
- Brihaye, J., and Lorthoir, J. (1957). Observation clinique d'un syndrome de la queue de cheval après injection de bleu de méthylène dans le cul-de-sac arachnoïdien lombo-sacré. *Acta Chirurgica Belgica*, **56**, 312–316.
- Evans, J. P., and Keegan, H. R. (1960). Danger in the use of intrathecal methylene blue. *Journal of the American Medical Association*, **174**, 856–859.
- Greenfield, J. P., Rickards, A. G., and Manning, G. B. (1955). The pathology of paraplegia occurring as a delayed sequela of spinal anaesthesia with special reference to the vascular changes. *Journal of Pathology and Bacteriology*, **69**, 95–107.
- Gross, S. W. (1974). Letter to Editor. *Neuroradiology (Berlin)*, **7**, 117.
- Hughes, J. T. (1970). Thrombosis of the posterior spinal arteries: a complication of an intrathecal injection of phenol. *Neurology (Minneapolis)*, **20**, 659–664.
- Jensen von H. P., Gerlach, J., and Spuler, H. (1962). Nil nocere! Gefahren der farbstoffinjektion in den liquorarum. *Münchener Medizinische Wochenschrift*, **104**, 1081–1084.
- Schultz, P., and Schwarz, G. A. (1970). Radiculomyelopathy following intrathecal installation of methylene blue. *Archives of Neurology (Chicago)*, **22**, 240–244.
- Walker, A. E. (1949). Spontaneous ventricular rhinorrhoea and otorrhoea. *Journal of Neuro-pathology and Experimental Neurology*, **8**, 171–183.
- Wolman, L. (1966). The neuropathological effects resulting from the intrathecal injection of chemical substances. *Paraplegia*, **4**, 97–115.