Short report

Spinal cord necrosis after intrathecal injection of methylene blue

M. M. SHARR, R. O. WELLS, 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 rhinorrhea. 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 Lorhthoir (1957), Arieff and Pyzik (1960), Evans and Keeghan (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 rhinorrhea 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 rhinorrhea. 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 rhinorrhea.

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-
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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


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