INTRAVENTRICULAR MORPHINE FOR INTRACTABLE CRANIOFACIAL PAIN

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ABSTRACT

This case management report on a patient with advanced craniofacial neoplasm discusses the successful treatment of chronic pain by the cortical intraventricular narcotic administration.

A previously treated patient with surgery and radiotherapy for carcinoma of the palate developed severe intractable pain despite high dose oral morphine therapy. Investigations revealed that neoplasm had reoccurred with extensive infiltration.

Intraventricular morphine therapy was discussed and accepted by the patient and family. A ventricular shunt with an Ommaya reservoir was inserted under local anaesthesia. Preservative-free morphine sulphate in increasing doses of 0.25 to 1 mg was administered, once daily, which kept the patient in a pain-free state. The treatment was initiated in the hospital and continued at home till the demise of the patient on the 9th week. The home care was provided by the nurses of Home Nursing Foundation and Singapore Cancer Society under physician supervision. There were no complications which had been reported in the literature, observed in the management of this patient.

Keywords: Intraventricular morphine, craniofacial pain

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INTRODUCTION

Despite the widespread use of opioids as analgesia for many centuries, specific mammalian central nervous system opioid receptors were only discovered in 1971 (1) and subsequently, identified in the brain and spinal cord of rats, monkeys and human (2, 3). The analgesic action of morphine was demonstrated after direct administration in the subarachnoid space of experimental animals (4) and human (5). Epidural and intrathecal spinal opiates have been used for the treatment of pain of multiple origins (6-11). Cancer pain in particular, has been treated successfully with intrathecal, epidural and intraventricular administration of morphine (5, 12-16). The advantages of administering the morphine directly into the central nervous system are that a much smaller dose is used as compared to oral or parenteral routes of administration, effect of pain relief is long lasting, intermittent or continuous infusion are possible with different types of drug delivery systems available (e.g Ommaya device, Port-A-Cath).

We report a patient with advanced malignancy of the palate associated with intractable craniofacial pain who was treated successfully with intraventricular injection of preservative free morphine sulphate (David Bull Laboratories).

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CASE REPORT

A 54 year old Indian male consulted a dentist in January 1987 for toothache and was found to have squamous cell carcinoma of the palate. He underwent a right maxillectomy in February 1987 followed by a six week course of radiotherapy.

Three weeks after the radiotherapy, he developed diffuse pain involving the right side of his head and face. This was followed by ptosis, proptosis and ophthalmoplegia of his right eye. His right craniofacial pain became more severe over the next few months. This severely handicapped his mobility. The patient had insomnia and difficulty in swallowing because of the pain which was only partially relieved by 400 mg oral morphine sulphate per day. He also experienced side effects of morphine such as nausea, vomiting and constipation.

A CT scan done in January 1988 showed extensive bony destruction of the right side of the base of the skull, involving the right maxillary antrum, the right pterygoid plate, the right turbinates, the floor of the middle cranial fossa as well as right side of the sella (Fig. 1). Tumour mass was also seen occupying the posterior nasal space, the right infratemporal fossa and extending into the right retrobulbar cavity causing proptosis of the right eye (Fig 2).

As the pain was more severe over the right side of his forehead, a right supra-orbital diagnostic nerve block using local anaesthetic provided some relief. Hence, he consented to right supra-orbital neurectomy under local anaesthesia in January 1988. However, the operation only offered a very short term partial relief of the pain involving his right forehead. Further surgery was not considered justifiable because of the extensive tumour infiltration. Informed consent was obtained from the patient to start intraventricular morphine therapy.

Fig 1
CT scan of the head showing destruction of the right pterygoid plate and the base of the skull; tumour tissue can be seen invading into the right middle cranial fossa (arrow).

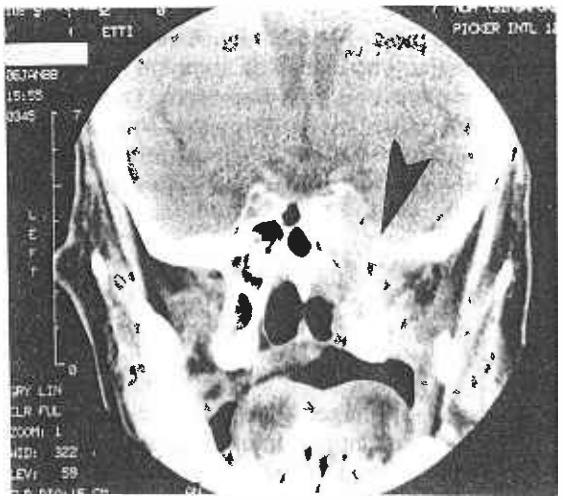
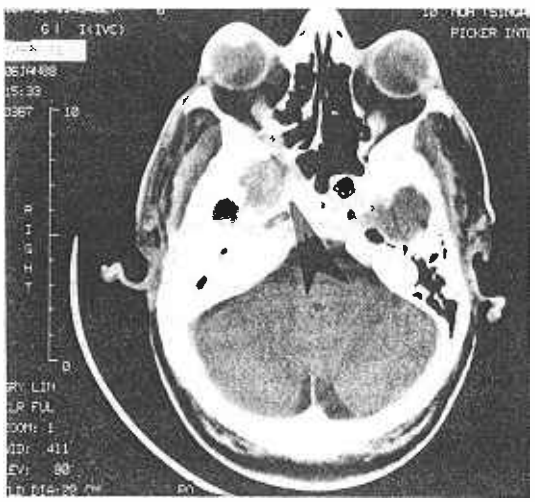


Fig 2
CT scan of the head showing tumour tissue occupying the right retrobulbar cavity (arrow), causing proptosis of the right eye.



An Ommaya device (ACCU-FLO shunt system, Codman and Shurtleff, INC. Randolph, MA 02368, USA) was inserted into his right lateral cerebral ventricle under local anaesthesia in April 1988 (Fig 3). The device consisted of a transparent reservoir (24 mm in diameter, capacity about 1.5 ml) connected to a 15 cm silicone rubber catheter with a straight connector (Fig 4). The catheter was inserted into the right cerebral ventricle through a right paramedial precoronal burrhole. The reservoir was placed subcutaneously in the epicranium.

The patient was monitored for three days in the Intensive Care Unit after the intraventricular morphine sulphate therapy was started. The patient's heart rate and respiration were continuously monitored and displayed on a bedsided monitor (Hewlett Packard 78353B). A pulse oximeter (Nellcor N-100E) was used to monitor his oxygen saturation continuously. His blood pressure was monitored hourly with a sphygmomanometer. His conscious state was also monitored and charted by the staff nurses. The injection technique consisted of Betadine skin preparation, followed by injection of 0.25 mg of preservative free morphine sulphate into the Ommaya resevoir percutaneously once a day. The 0.25 mg of morphine sulphate was administered in 1 ml of normal saline using a 25 gauge needle.

Fig 3
Lateral skull x-ray of the patient showing the Ommaya device, the translucent area indicated by the arrow is the reservoir.

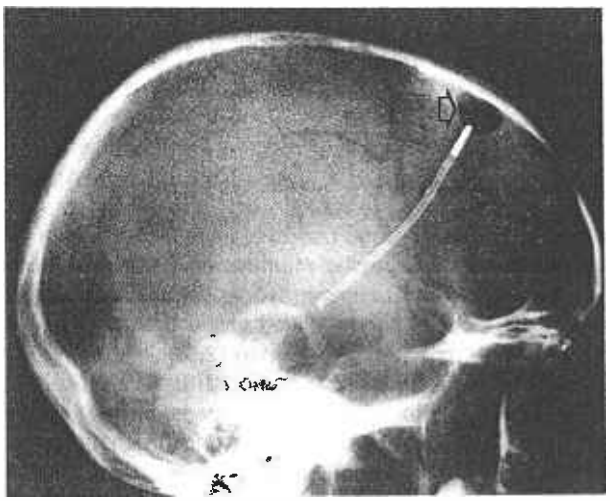
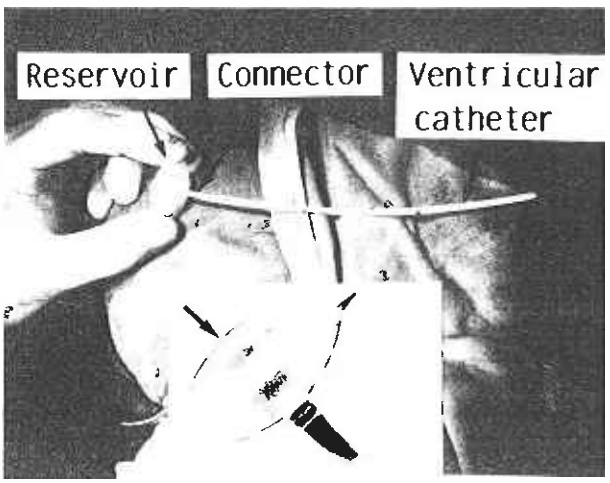


Fig 4
Photograph of the Ommaya device used in this patient. Inset shows the lateral profile of the reservoir, the arrow indicates the site of injection through the upper surface of the reservoir which is buried beneath the scalp.



The site of the injection into the reservoir was moved slightly each day. The correct minimal depth of the 25 gauge needle insertion was confirmed by withdrawal of clear cerebrospinal fluid (CSF) before the narcotic was injected. The needle should not hit the base of the reservoir which will cause the bent 25 gauge needle to tear the reservoir surface on withdrawal. This will result in CSF leak into the subcutaneous tissue. Dispersal of the narcotic from the reservoir was achieved by multiple gentle compression of the skin over the Ommaya device. The daily dose of morphine sulphate given and duration of analgesia obtained are shown in Table I.

Analgesia was obtained in 20 to 30 minutes after each injection. After the first intraventricular morphine injection, the intensity of his pain was reduced to a point where it was bearable and he was able to smile and sleep comfortably at night. There were no evidence of respiratory depression, itching or urinary retention. He was noted to be somnolent during the first three days of the treatment. However, he was more alert from the fourth day onwards, the pain relief was 90-100%. He was able to increase his mobility and improve his appetite. 2 ml of CSF sample was aspirated from the reservoir for morphine assay on the sixth day, before the next morphine injection. The morphine level as measured by enzyme immunoassay (EMIT) was reported to be less than 1 µg/ml.

Table I
Daily dose of intraventicular morphine sulphate

Day	1 - 3	4 - 9	10 - 19	20 - 62
Total dose (mg) in 1 ml normal saline	0.25	0.5	0.75	1
Duration of analgesia (hours)	14-16	16-18	20-22	18-23

The patient was discharged from the hospital two weeks after the Ommaya device was inserted. Outpatient staff nurses from the Home Nursing Foundation and the Singapore Cancer Society continued the home treatment after supervised training on the aseptic technique of injection. The progress of the patient was updated by feedback from the staff nurses and by home visits conducted by one of the authors. The patient's family was happy to accept him as he was able to look after himself in a painfree state. The dose of morphine was eventually increased to 1 mg/injection daily, two and half weeks after the intraventricular morphine therapy was started. Nine weeks after the intiation of intraventicular morphine therapy, the patient passed away during sleep at home.

DISCUSSION

Efforts to develop effective, safe and predictable methods for alleviating chronic severe pain produced by malignancy and other pain producing diseases have met with varying degree of success. Drug therapy, nerve blocks and electrical stimulation are examples of these methods, most of which are either poorly effective or associated with undesirable side effects.

Our patient was suffering from severe right craniofacial pain due to recurrence of squamous cell carcinoma of the palate. Further palliative surgery was not considered because of the extensive tumour infiltration (Fig 1 & 2). High dose of oral morphine sulphate was ineffective and not well tolerated because of difficulties with swallowing due to pain and narcotic side effects such as nausea, vomiting and constipation. He experienced only partial relief of his pain while on an oral morphine sulphate 400 mg a day. Trigeminal nerve block was excluded due to the extensive local tumour infiltration. Supra-orbital neurectomy was unsuccessful. As the patient's pain is localized in the craniofacial regions, intrathecal spinal morphine has been reported to be ineffective (12). Injection of a small dose of narcotic into the right lateral cerebral ventricle brings the drug into direct contact with the high affinity specific opioid receptors located in the subcortical and periventricular structures. The injection can be done percutaneously with an Ommaya device. This device can be inserted by the neurosurgeon under local anaesthesia with low complication rate.

Our criteria of selecting this patient is similar to those previously reported (16). 0.25 to 1 mg of intraventricular morphine a day gave complete pain relief to our patient for 18 to 23 hours. He was ambulatory and his family could look after him at home. The mechanism and site of action of intraventricular morphine are not well known. It is possible that repeated administration of morphine creates a reservoir of drug in the cranial compartment of the cerebrospinal fluid (CSF) which diffuses via passive circulation of the CSF, and may lead to activation of different pain-modulating structures throughout the neuraxis, including the spinal cord. In this manner, very low concentration of morphine at multiple levels may act synergically resulting in intense and long lasting analgesia (17-19). Intraventricular morphine has been used successfully to treat cancer pain involving all parts of the body (13, 14).

Our patient was started on 0.25 mg/day morphine which was increased to 1 mg/day after two and a half weeks of therapy. Lobato et al (16) reviewed a series of 197 patients from different centres treated by intraventricular morphine. This review indicated that the initial morphine sulphate doses ranged from 0.1 to 4 mg, the usual maintenance doses ranged from 0.5 to 2 mg per day, the quality of analgesia was judged to be excellent in 75 to 100% of the reported cases and duration of pain relief ranged from 12 to 58 hours. Majority of the reported patients developed tachyphylaxis after 1 to 2 weeks of therapy with decrease in the duration of analgesia. This was compensated by either increasing the frequency or the dose of morphine sulphate.

We measured the CSF morphine level obtained from the reservoir and showed that the morphine level was less than 1µg/ml after 0.5 mg morphine injected into the reservoir 24 hours earlier. Lobato et al (16) measured CSF morphine level in 9 patients following intraventricular administration of 0.25 mg of morphine, the mean CSF level reported at 24 hours was also less than 1 µg/ml. The clearance of morphine after intraventricular administration (20) will depend on:-

1) local uptake into the brain tissues
2) movement in the rostral-caudal CSF axis, and
3) transdural penetration with vascular redistribution

Some reported side-effects of this technique (16) included: nausea and vomiting, somnolence, disorientation, mental clouding, visual hallucinations,

dizziness, itching and urinary retention. These symptoms usually occurred soon after the start of the treatment and subsided spontaneously within hours or few days without discontinuation of the treatment. Our patient was noted to be somnolent for the first three days after the initiation of intraventicular morphine. Subsequently he became alert despite increases in morphine doses. Some patients were reported to be euphoric without knowledge of imminent death (12). A minority of patients presented with somnolence, mental clouding or behavioural changes during the late phase of treatment(17). Whether these changes were related to the progression of the underlying disease or the treatment is uncertain. Acute and chronic administration of opioids in animals and man do not appear to cause spinal cord or meningeal toxicity (21, 22).

Two serious complications reported (17) were respiratory depression and infection which did not occur in our patient. Naloxone was used successfully by titration to reverse the respiratory depression but not the analgesia. Subsequent intraventircular morphine injections did not cause respiratory depression despite increasing doses. The incidence of reservoir bacterial contamination was reported to be 2%. Although serial CSF samples can be withdrawn from the reservoir for bacteriological analysis, however, we concluded that the additional puncture of the reservoir can increase the chance of bacterial contamination of the reservoir. It has been suggested that multiple reservoir puncture can be circumvented by using a refillable continuous infusion device (17).

In view of the encouraging results reported by this case and cases from other centres, we feel that intraventricular administration of morphine is a useful adjunct to treat a selected group of patients with intractable pain and short life expectancy.

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