Facial Nerve Palsy After Intracisternal Papaverine Application During Aneurysm Surgery
—Case Report—

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Abstract

A 61-year-old woman suffered transient mydriasis and prolonged facial nerve palsy after intracisternal papaverine application subsequent to elective clipping of an unruptured middle cerebral artery aneurysm. The mydriasis resolved within 90 minutes, but the facial nerve dysfunction persisted for 2 months before complete recovery. Prolonged irrigation of the cisterns may have washed the papaverine into contact with the facial nerve. This case supports previously reported evidence of a possible effect of topical intracisternal papaverine hydrochloride application on the facial nerve.

Key words: papaverine, vasospasm, oculomotor nerve palsy, facial nerve palsy

Introduction

The muscle-relaxant properties of papaverine hydrochloride were first used for treating “cerebral vascular spasm” in 46 patients with “cerebral episodes with or without hypertension” in 1948. Intravenous papaverine administration was also used in a patient who underwent carotid ligation for an apparently unruptured, large, left supraclinoid, fusiform aneurysm in 1950. Intraarterial papaverine administration during arteriography has been used to prevent and reverse cerebral vasospasm after aneurysmal subarachnoid hemorrhage or resection of arteriovenous malformations. Intrathecal, i.e., intracisternal papaverine application has been used to prevent vasospasm which can be caused by both intraoperative arterial manipulation and subarachnoid hemorrhage. Topical papaverine is also used in non-neurosurgical operations in which vessel manipulation may induce vascular spasm, such as infant renal surgery. Transient ipsilateral pupillary dilation (mydriasis) with pupillary areflexia after intracisternal and intraarterial papaverine application is a common benign side effect. Papaverine is commonly used today and this mydriatic effect is well known so this is no longer reported. High-dose papaverine (240 mg) is used in our center to prevent mechanical vasospasm and the occasional case of delayed spasm after clipping of unruptured aneurysms.

We treated a patient who was operated for a cerebral artery aneurysm with topical intracisternal administration of papaverine, resulting in transient pupillary dilation and prolonged facial nerve palsy.

Case Report

A 61-year-old woman presented with a one-year history of vertigo. An aneurysm was found at the bifurcation of the right middle cerebral artery during an investigation for labyrinthitis. We clipped the aneurysm during an elective operation via a right pterional approach. Intraoperatively there was no evidence of previous hemorrhage. After clip placement, 240 mg of papaverine hydrochloride (David Bull Laboratories, Mulgrave, Vic., Australia) in 20 ml of normal saline was instilled in the cerebrospinal fluid (CSF) spaces around the aneurysm clip to prevent manipulation-related vasospasm. During closure, about 3–4 minutes after papaverine instillation, we irrigated the cisterns more than usual, using about 100 ml of normal saline solution, because of bleeding from the dural edges. When the drapes were removed we noted pupillary dilation (mydriasis) and pupillary areflexia on the right,
which resolved within 90 minutes. The first neurological examination in the recovery room shortly after extubation found clear evidence of facial nerve dysfunction, which developed within 30 minutes into House and Brackmann grade 4 right lower motor neuron facial nerve palsy. Improvement was noted a few hours later but the weakness did not resolve spontaneously.

A facial nerve blink study on the 1st postoperative day showed a normal direct response on the right but abnormally prolonged ipsilateral R1 latencies. Ipsilateral R2 latencies were also prolonged to bilateral stimulation. This suggested right proximal facial nerve dysfunction. At 5 weeks follow up, she had subjectively improved by about 50% clinically (House and Brackmann grade 2). Further neurophysiological tests including nerve conduction studies showed a reduction in the amplitude of the right facial compound motor action potential which was marginally prolonged in latency compared with the opposite side on direct testing. Needle electromyography (EMG) revealed mild to moderate changes of active denervation with some polyphasia. This was consistent with recovering lower motor neuron facial nerve palsy. Two months later her palsy had fully recovered with normal findings on facial nerve EMG and motor nerve conduction studies.

Discussion

The present case provides further evidence of a possible effect of topical intracisternal papaverine hydrochloride application on the facial nerve. Previously, a patient with an acoustic neuroma was operated through a translabyrinthine approach with intraoperative facial nerve monitoring, and papaverine was applied after dissection-related anteroinferior cerebellar artery vasospasm, resulting in immediate loss of all spontaneous and stimulated activity from the facial nerve. The exact dose of papaverine hydrochloride 30 mg/ml was not reported. At the end of the operation, the nerve could be partially stimulated with conduction block at the cerebellopontine angle and more peripherally. The patient had postoperative facial nerve palsy, which resolved within 12 hours. Based on this experience, the effects of varying concentrations of papaverine on the facial nerve in the cerebellopontine angle in an animal model were studied, but could not reproduce this effect.

Our patient’s course differs in some ways from the previous case, but the effect of papaverine on the facial nerve was immediate in both cases. Although we did not apply papaverine directly to the facial nerve, we assume that the prolonged irrigation washed the papaverine further down into the basal cisterns. The delay between application and the full clinical picture in our case can be attributed to the time required for CSF passage from the point of application in the sylvian fissure to the cerebellopontine angle after the patient’s head was placed 30 degrees up following extubation.

One might speculate that the cisternal blood could have caused the facial nerve deficit. However, this interpretation seems unlikely because hemorrhage-related vasospasm occurs with a much greater delay than that observed. There was no mechanical trauma to the facial nerve. We cannot explain why only the facial nerve of the more caudal cranial nerves was affected. However, the facial nerve may be more susceptible than others to the effects of papaverine, the mechanisms of which are unknown. Such a papaverine-based cause-and-effect relationship is supported by the typical transient mydriasis and pupillary areflexia which also occurred in our patient. This is the most common single neurological finding after intracisternal papaverine application of 3 ml of 2% solution.

We suggest that there are various ways of applying papaverine which may influence the dose used. A small dose can be used if a papaverine-soaked piece of Surgicel or gelfoam is left directly in the operative field. A larger dose is used if papaverine is injected into the basal cisterns after hemostasis and no further irrigation follows. We use 240 mg papaverine because we continue with irrigation after papaverine instillation. This protocol has been safely used in more than 1000 aneurysm cases operated over more than 20 years by the senior author.

Although most reports due to intracisternal papaverine administration involve unilateral mydriasis and pupillary areflexia, which usually resolves within 2–4 hours, one case of bilateral mydriasis and pupillary areflexia persisted for 4 days before the pupillary light reaction returned. This report supports a dose-related response which may influence both the extent of neurological deficit and the time course of recovery, which was prolonged in our case.

The findings and complications associated with intraarterial papaverine administration include respiratory arrest, hypotension, thrombocytopenia, and raised intracranial pressure. As with intracisternal application, all side effects were transient and reversible within 24 hours.

Papaverine (6,7-dimethoxy-1-vero-trylisoquinoline) is an alkaloid extracted from the unripe seed capsules of the poppy plant, Papaver somniferum. Papaverine is present in about 1% of crude opium.
but is unrelated chemically and pharmacologically to the opioid alkaloids. Papaverine acts as a non-specific smooth muscle relaxant, but the mechanism of action is yet to be fully determined. The inhibitory effect of papaverine in enteric neurons involves at least in part the release of noradrenaline in sympathetic nerves acting on alpha adrenoceptors. Papaverine also acts as a muscle relaxant independent of depolarization but its potency is influenced by the influx of calcium ions. Therefore, the degree of depolarization of the vessel is an important consideration.13)

Isoquinolines have been shown to act on mu receptors.20 Activated mu-receptors can delay neurotransmission and produce an analgesic effect. In sufficient doses, papaverine may interact with opioid receptors to delay neurotransmission, which may yield an explanation for the effects which we have observed.8,18) High-dose papaverine can form a crystalline precipitate with components of human serum and may cause microembolic-related ischemic events, but this consideration appears to be only relevant to intraarterial papaverine administration.15)

Although we cannot clearly establish a cause-and-effect relationship, we suggest that the clinical and electrophysiological course of this case is striking enough to support the previous report that topical papaverine application can lead to transient facial nerve dysfunction.

References


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