Anesthesiology 2002; 96:1019–20

Postdural Puncture Upper Back Pain as an Atypical Presentation of Postdural Puncture Symptoms

Carlos L. Errando, M.D., Ph.D., Celsa M. Peiró, M.D., Ph.D.†*

ACCIDENTAL dural puncture is the most frequent complication after performing an epidural technique. Its incidence ranges between 0.16–1.3% in experienced hands. Postdural puncture headache (PDPH) develops in 16–86%[1,2] of these cases, depending on the studied population. It is generally accepted that the continuous loss of cerebrospinal fluid (CSF) through the dural hole produced by the needle causes a decrease in the CSF pressure. For patients in the upright position this pressure decrease would traction the meningeal structures, nerves, and vessels, producing the painful symptoms.[3,4]

Typically the PDPH manifests as postural frontal, frontotemporal, or occipital headache, worsened by ambulation, and improved by decubitus. The accompanying symptoms are usually nausea, vomiting, and neck stiffness.[2,4] Atypical symptoms after accidental dural puncture have been sparsely described. The current authors present a case of severe upper back pain without headache after an accidental dural puncture, which required an epidural blood patch.

Case Report

A 39-yr-old, 92 kg, 170 cm man presented to our pain clinic with severe lumbar pain accompanied by radicular symptoms. His medical history revealed previous opioid addiction, chronic hepatitis B and C, knee arthritis, dislipemia, and heavy smoking. His physical examination revealed an obese and anxious patient with acute lumbalgia (acute lumbar pain). Magnetic resonance imaging showed vertebral disk herniation at the L2–L3, L3–L4, and L4–L5 levels and sacralization of L5. Two epidural steroid injections were proposed and accepted as initial treatment. They were performed in an ambulatory setting. The epidural procedure was performed with an 18-gauge Tuohy needle, with loss of resistance to air technique, in the L3–L4 interspace. The drugs used were paramethasone 40 mg diluted in 4 ml bupivacaine, 0.25%. During the first epidural injection the patient had a vasovagal syncope that was treated with 1 mg intravenous atropine. In the second block an accidental dural puncture at L3–4 occurred. The steroid injection was eventually performed one space above. The patient was asked to remain supine for 2 h. Intravenous paracetamol 2,000 mg and 1,500 ml lactated Ringer's solution were given. The asymptomatic patient was discharged home with written instructions to contact the clinic in case of headache or other symptoms. Paracetamol 500 mg plus codeine 30 mg taken orally twice a day, and copious liquid intake was recommended.

Twenty-four hours later the patient complained of moderate upper back pain that was attributed to anxiety and muscle spasm. Forty-eight hours after the procedure light neck pain with stiffness developed, along with severe incapacitating upper back pain. The pain was described as severe, continuous, interscapular pressure without radiation. The patient reported no headache. Neurologic evaluation was normal. A PDPH syndrome was suspected because the symptoms increased when the patient was in the upright position. After orally taking 300 mg caffeine the patient developed great anxiety and insomnia, with a slight improvement in the intensity of the pain. The dorsal pain recurred, and 72 h after the procedure an epidural blood patch was proposed to the patient (additional caffeine was not accepted). Under sterile conditions an epidural blood patch was performed at L2–L3 with 20 ml blood injected through an 18-gauge Tuohy needle. After 15 ml of blood was injected the dorsal pain disappeared, and after 20 ml the neck pain had almost completely gone. The patient was totally asymptomatic 24 h later. The neck pain recurred throughout the next 2 months but paracetamol 500 mg taken orally was enough to control it. In a follow-up examination 4 months after the steroid injection, the patient had significant improvement of the lumbar radicular pain, and the upper back pain had disappeared.

Discussion

Although somewhat controversial, the initial treatment of acute lumbalgia and radiculopathy with epidural steroids could be effective.[5]

After an unintended dural puncture, PDPH should be expected and treated as such.[2] Prevention with hydration, prophylactic epidural blood patch, caffeine infusions, or other therapies are preferred by some.[6] The diagnosis is fairly easy when the headache presents typically. The decision to perform an epidural patch depends on the patient and the severity and duration of the headache. The effectiveness of the blood patch is about 91–100%. Conversely, the blood patch could have undesirable effects such as lumbar pain, neck pain, nerve root irritation, infection, and fever.[3,4] Moreover, despite an uneventful epidural blood patch, PDPH could recur.

In the patient discussed herein, the atypical presentation of postdural puncture symptoms in the form of dural puncture-related dorsal thoracic pain delayed the correct diagnosis and treatment. The neck pain, the clinical features of the upper back pain, the slight improvement with caffeine, and the severity of the pain led us to recommend an epidural blood patch. The absence of headache and other related symptoms (dizziness, nausea, vomiting, nystagmus, tinnitus) contributed to the delay in diagnosis and treatment.

Differential diagnosis must be carried out before mak-

*† Staff Anesthesiologist, Hospital General Universitario de Valencia.

Received from the Hospital General Universitario de Valencia, Valencia, Spain. Submitted for publication April 26, 2001. Accepted for publication September 26, 2001. Support was provided solely from institutional and departmental sources.

Address reprint requests to Dr. Errando: Servicio de Anestesiología, Reanimación y Tratamiento del Dolor, Hospital General Universitario de Valencia, Av/Tres Cruces s/n, 46014, Valencia, Spain. Address electronic mail to: errando@ctv.es.

ing the diagnosis of atypical postdural puncture event. Spinal abscess, septic or aseptic meningitis, spinal hematoma, arachnoiditis caused by intrathecal steroids, myofascial syndrome, transient neurologic syndrome or related symptoms, unspecific postdural puncture lumbalgia, neural toxicity of the drugs, and anterior spinal artery syndrome should be ruled out.[5,7,8] The absence of fever, meningeal rigidity, or other meningeal features helped us with the diagnosis in this case. The relative short time it took for symptoms to develop meant that infection was unlikely. In addition, radicular symptoms improved in this patient despite the appearance of dorsal pain. However, additional tests such as magnetic resonance imaging could be performed in cases with atypical postdural puncture symptoms, to exclude the possibility of developing serious complications.

Few cases of atypical postdural puncture symptoms have been reported in the literature. Lybecker *et al.*[4] classified the PDPH based on the intensity and characteristics of the cephalalgia, and cited the interscapular pain as "related musculoskeletal symptom," however, no instances of upper back pain are cited among the 75 cases of PDPH reported by the authors. Neck stiffness is frequently reported (43%), always together with headache. McGrady and Freshwater[9] reported a case of posterior neck pain (C2–4) without headache after spinal anesthesia. Very recently, Schabel *et al.*[10] reported a case of arm pain with dysesthesia after an unintended dural puncture, and explained it as irritation of the C5 and C6 nerve roots caused by central traction. Two cases of postdural puncture thoracic pain were reported by Dunbar,[11] one after an inadvertent lumbar puncture, another after a cervical puncture, both, as in the current scenario, for therapeutic steroid injection. All cases reported received a lumbar epidural blood patch that was always curative.

The pain sensation is probably transmitted *via* the V cranial nerve (n. trigeminus, pars frontalis) to the frontal and periorbital regions; through the IX and X cranial nerves (n. glossopharyngeal and n. vagus) to the occipital, and through the cervical nerve roots C2 and C3 to the neck and shoulders. Sometimes the III, IV, VI (diplopia), and VIII (tinnitus, hypacusia) cranial nerves are involved.[2,5]

This case report and others suggest that the thoracic nerve root and meningeal traction could be involved in atypical cases of pain related to dural puncture, despite the fact that high thoracic nerve roots would be less anchored to the vertebral foramen,[10] and theoretically less tractioned than the upper roots. An atypical thoracic, dorsal, or arm pain, appearing after an accidental or intended dural puncture, should be considered as a possible PDPH (provided other causes are excluded), and should be treated as such, including treatment with an epidural blood patch.

The authors thank Carlo D. Franco, M.D. (Department of Anesthesiology, Cook County Hospital, Chicago, IL) for critically reviewing the manuscript.

References

1. Liu S, Carpenter RL, Neal JM: Epidural anesthesia and analgesia. ANESTHESIOLOGY 1995; 82:1474–1506
2. Reynolds F: Dural puncture and headache: Avoid the first but treat the second. BMJ 1993; 306:874–6
3. McSwiney M, Phillips J: Post dural puncture headache. Acta Anaesthesiol Scand 1995; 39:990–5
4. Lybecker H, Dyernes M, Schmidt JF: Postdural puncture headache (PDPH): Onset, duration, severity and associated symptoms: An analysis of 75 consecutive patients with PDPH. Acta Anaesthesiol Scand 1995; 39:605–12
5. Abram SE: Treatment of lumbosacral radiculopathy with epidural steroids. ANESTHESIOLOGY 1999; 91:1937–41
6. Berger CW, Crosby ET, Grodacki W: North American survey of the management of dural puncture occurring during labour epidural analgesia. Can J Anaesth 1998; 45:110–4
7. Horlocker TT, Wedel DJ: Neurologic complications of spinal and epidural anesthesia. Reg Anesth Pain Med 2000; 25:83–98
8. Errando CL: Transient neurologic syndrome (TNS), transient radicular irritation (TRI) or postspinal musculoskeletal symptoms (MSS), are we describing the same 'syndrome' in all patients? Reg Anesth Pain Med 2001; 26(letter):128–9
9. McGrady EM, Freshwater JV: Spinal headache with no headache. Anaesthesia 1991; 46(letter):794
10. Schabel JE, Wang ED, Glass PSA: Arm pain as an unusual presentation of postdural puncture intracranial hypotension. Anesth Analg 2000; 91:910–2
11. Dunbar SA, Katz NP: Post-dural puncture thoracic pain without headache: Relief with epidural blood patch. Can J Anaesth 1995; 42:221–3[

Anesthesiology 2002; 96:1021–2

Altered Level of Consciousness after Combined Spinal-Epidural Labor Analgesia with Intrathecal Fentanyl and Bupivacaine

Barbara M. Scavone, M.D.

COMBINED spinal-epidural labor analgesia has become increasingly popular because of the rapid onset of profound analgesia accompanied by minimal motor blockade.[1] The technique usually includes an intrathecal injection of opioid, often fentanyl or sufentanil, either alone or in combination with a local anesthetic. Reported side effects include pruritus, hypotension, nausea and vomiting, urinary retention, fetal bradycardia, and respiratory depression or, more rarely, respiratory arrest.[2] Several authors have reported the occurrence of high sensory blockade[3,4] associated with facial tingling, dysphagia, and dyspnea. Fragneto and Fisher[5] recently reported a case of "mental status change and aphasia" after the intrathecal injection of 10 μg sufentanil and 2.5 mg isobaric bupivacaine. The author reports a case of mental status changes associated with automatisms and an inability to speak after intrathecal injection of 25 μg fentanyl in combination with 2.5 mg bupivacaine.

Case Report

A 27-yr-old woman, gravida 3, para 2, with full-term, singleton vertex gestation was admitted to the labor and delivery unit with painful uterine contractions. The patient's medical history and antenatal course were unremarkable. She had not received neuraxial analgesia with her previous deliveries. She denied use of alcohol or any illicit drugs. The obstetrician's examination revealed 4-cm cervical dilation, 80% effacement, +1 station and ruptured membranes. The patient requested epidural labor analgesia. She had not received any medications.

The patient was placed in the sitting position, and combined spinal-epidural analgesia was initiated at the L3–L4 interspace *via* a needle through needle technique, using a 17-gauge epidural needle and a 27-gauge Whitacre spinal needle (Becton Dickinson, Franklin Lakes, NJ). The intrathecal injection consisted of 25 μg fentanyl (fentanyl; Elkins-Sinn, Inc., Cherry Hill, NJ, USA; 50 μg/ml, 0.5-ml) in combination with 2.5 mg bupivacaine (Sensorcaine-MPF; Astra USA, Inc., Westborough, MA, USA; 0.5%, 0.5-ml). A single open end-hole epidural catheter was threaded approximately 4-cm into the epidural space and an epidural test dose (1.5% lidocaine with epinephrine 1:200,000 [3-ml]) was administered. The test dose was considered negative on the basis of no change in heart rate, or development of dense spinal blockade. A continuous epidural infusion was initiated with a solution containing 0.06% bupivacaine and fentanyl, 2 μg/ml, at 15 ml/h. The patient's vital signs were monitored for approximately 15 min, during which time her blood pressure ranged from 145/85 to 105/55 mmHg. Minimal motor weakness of the lower extremities was present.

Approximately 25 min after the patient received the intrathecal medications, the anesthesiologist was called. Upon arrival in the labor room, the anesthesiologist noted that the patient was not responsive to verbal stimuli, and was generally combative, swinging her arms wildly. Respiratory rate was 6 breaths/min and pulse oximetry revealed a hemoglobin oxygen saturation of 94% while breathing room air. Heart rate was 100 beats/min, blood pressure was 105/55 mmHg and the patient was moving her upper and lower extremities well. She was given oxygen, positive pressure ventilatory assistance *via* bag and mask, and 160 μg intravenous naloxone (naloxone HCl; Abbott Laboratories, N. Chicago, IL; 0.4 mg/ml) in divided doses. The epidural infusion was discontinued.

Within 1–2 min, the patient's respiratory rate was 20 breaths/min, and oxygen saturation was 100%. She was no longer combative, but she was not fully alert: She looked absently around the room, and did not speak, or attempt to mouth words, when questioned. She exhibited behaviors best described as automatisms, such as looking intently at her intravenous tubing and picking it up. Several minutes later, she communicated by nodding her head in response to yes/no questions, or squeezing the examiner's hand, but still did not speak. She had a sensory level to cold in the distribution of the maxillary division of the trigeminal nerve. Over the next 15 min, the patient gradually recovered the ability to speak, although she was still not quite fully alert. It was noted that the patient scratched occasionally.

Forty minutes after treatment with naloxone (65 min after the intrathecal medications had been given), while the anesthesiologist was still in the room, the patient suddenly began scratching her face and upper body quite severely and over the next minute she once again became less responsive and more combative. She was given an additional 80 μg intravenous naloxone and she once again became more alert, though not fully so. Again, she looked around the room, displayed automatisms, and did not speak. After several minutes she communicated through nonverbal methods and then gradually regained the ability to speak.

Approximately 30 min after the second dose of naloxone (95 min after the intrathecal medications had been given), the patient was speaking fluently and complaining of labor pain. Obstetrical examination revealed complete cervical dilation and effacement and +2 station. She was delivered of a liveborn female infant shortly thereafter. One and 5 min APGAR (appearance, pulse, grimace, activity, and respiration) scores were 9 and 9.

One hour after delivery, the patient was awake, fully alert, and oriented to person, place, and time and was released from the labor and delivery unit by the anesthesiologist. She had incomplete recall of the events, including a vague recollection of being unable to speak.

Discussion

As combined spinal-epidural labor analgesia is used more commonly, several uncommon adverse reactions

Assistant Professor of Anesthesiology, Department of Anesthesiology, Northwestern University Medical School.

Received from the Department of Anesthesiology, Northwestern University Medical School, Chicago, Illinois. Submitted for publication June 11, 2001. Accepted for publication October 29, 2001. Support was provided solely from institutional and/or departmental sources.

Address reprint requests to Dr. Scavone: Department of Anesthesiology, 251 East Huron, Wesley 101, Chicago, Illinois 60611. Address electronic mail to: bscavone@nmff.org. Individual article reprints may be purchased through the Journal Web site, www.anesthesiology.org.

have been reported, including excessive sedation and severe respiratory depression.[2] Sensory blockade that extends to the high thoracic dermatomes, or even the trigeminal dermatomes can occur because the opioid or local anesthetic intrathecal solutions commonly injected are hypobaric, and analgesia is often initiated with the patient in the sitting position.[3,4] An English language literature search revealed no other reports of this type of reaction occurring after intrathecal fentanyl and bupivacaine.

The time of onset of the event makes it likely that it was a reaction to the intrathecal medications. The sedation, respiratory depression, and pruritus are consistent with cephalad spread of fentanyl, and naloxone quickly reversed these symptoms. The patient required a second dose of naloxone for these symptoms after 40 min, which is consistent with its duration of action. The patient's other behaviors (decreased levels of alertness and attentiveness and automatisms accompanied by muteness) did not respond to treatment with naloxone. Perhaps a higher dose of naloxone would have reversed these symptoms also. It is possible that cephalad spread of bupivacaine played an undetermined role in this patient's presentation.

Although the patient's test dose was negative, it is still possible that the epidural catheter was placed intravascularly. If this were the case the patient would have received approximately 12.5 μg fentanyl and 3.75 mg bupivacaine over approximately 25 min. While this dose is too small to entirely explain these symptoms, intravenous fentanyl-bupivacaine could have worsened the clinical situation. Opioid induced hypoventilation could also have worsened the patient's clinical course.

The combination of decreased alertness and attentiveness, automatisms, and inability to speak are reminiscent of temporal lobe seizure activity, and it is possible that this patient's behaviors represented some sort of seizure, the mechanism of which is unclear. Unfortunately, there was no electroencephalogram documentation during or after the event.

Fragneto and Fisher[5] reported a case of combined spinal-epidural labor analgesia with 10 μg intrathecal sufentanil and 2.5 mg bupivacaine followed by mild respiratory acidosis and mental status changes including "aphasia" and "an apparent disassociated state," symptoms very similar to those of our patient. They hypothesized that the reaction was caused by cephalad spread of either the opioid or the bupivacaine. They did not attempt to treat the patient with naloxone. A similar mechanism of action may have been present in both the case reported by Fragneto and Fisher and the case presented here.

Although high sensory blockade is not uncommon after intrathecal fentanyl and bupivacaine are administered for labor analgesia, it is unlikely that sensory blockade of the larynx (recurrent and superior laryngeal branches of the tenth cranial nerve) could account for difficulty with speech. In cases where such sensory deficits are known to exist (for instance, during sensory blockade in preparation for conscious intubation), patients are able to speak. Thus, normal sensation is not necessary for speech production.

It is not likely that the lidocaine and epinephrine epidural test dose was injected into the intrathecal or subdural space because the patient did not exhibit appreciable motor weakness and/or hypotension. In addition, it is unlikely that the patient had isolated motor weakness of the laryngeal nerves. She did not appear to mouth words, as if attempting to speak.

In summary, the author presents a case of an altered level of consciousness and inability to speak after intrathecal fentanyl and bupivacaine administered for labor analgesia. Clinicians should be aware of this possible complication when this analgesic technique is used.

The author thanks M-Marsel Mesulam, M.D., (Department of Neurology, Northwestern University Medical School, Chicago, Illinois) for his help with preparing this manuscript.

References

1. Eisenach JC: Combined spinal-epidural analgesia in obstetrics. ANESTHESIOLOGY 1999; 91:299–302
2. Ferouz F, Norris MC, Leighton BL: Risk of respiratory arrest after intrathecal sufentanil. Anesth Analg 1997; 85:1088–90
3. Hamilton CL, Cohen SE: High sensory block after intrathecal sufentanil for labor analgesia. ANESTHESIOLOGY 1995; 83:1118–21
4. Currier DS, Levin KR, Campbell C: Dysphagia with intrathecal fentanyl. ANESTHESIOLOGY 1997; 87:1570–1
5. Fragneto RY, Fisher A: Mental status change and aphasia after labor analgesia with intrathecal sufentanil/bupivacaine. Anesth Analg 2000; 90:1175–6

Anesthesiology 2002; 96:1023–5

Iliopsoas Abscess and Persistent Radiculopathy: A Rare Complication of Continuous Infusion Techniques of Epidural Anesthesia

Yohichi Aota, M.D., Katsuhiro Onari, M.D.,* Yuichi Suga, M.D.†*

THE authors report a case of psoas and foraminal abscess as a complication of epidural anesthesia, with secondary foraminal encroachment of the nerve root due to scar.

Case Report

A 67-yr-old woman was admitted to our hospital for anterior knee pain, which developed after a motorcycle accident. Two months after the injury, the patient's pain became persistent and unbearable. After obtaining informed consent, an epidural catheter was inserted under sterile conditions in the L3–L4 interspace, using a loss of resistance technique, without difficulty. Sterile gloves and syringes were used, and the tubing connection was swabbed with povidone-iodine. The catheter was advanced 3 cm into the epidural space and secured with a sterile transparent dressing. After an initial bolus dose of 0.25% bupivacaine hydrochloride, subsequent administration was maintained by continuous infusion. Disposable equipment and a micropore filter were used. The patient did not receive prophylactic antibiotics. A 70% reduction of pain was observed. The catheter site was examined daily for any sign of inflammation or contamination and was removed after 13 days.

Two days after removal of the catheter, the knee pain recurred. A second epidural catheter was inserted into the L2–L3 interspace without difficulty, using the same technique as before. There was no evidence of infection at the site before catheter insertion, and no pain or paresthesia occurred. The patient's pain partially improved; however, 2 days after the catheter insertion she reported that another low back pain of stronger intensity had appeared, radiating to the left thigh. Four days after the insertion she noted a sudden onset of high fever (39.0°C) and purulent material leaking from the new insertion site. At that time, physical examination showed tenderness of the left paravertebral muscle. The catheter was removed. Her low back and left thigh pain increased. She assumed a hip flexed position, but nuchal rigidity was absent. Cerebrospinal fluid cultures for bacteria were negative and her white blood count was 19.6×10^3 after removal of the second catheter. Computed tomography of the lumbar spine was compatible with psoas abscess (fig. 1). Bacterial cultures from the catheter tip were positive for Staphylococcus aureus, therefore, intravenous antibiotics were used for 2 weeks and her temperature gradually returned to normal in the course of 8 days, not exceeding 37.0°C.

Two months after the epidural anesthesia she was afebrile, but refractory thigh pain remained. Magnetic resonance imaging (MRI) showed residual swelling of the left iliopsoas muscle and narrowing of the left L2–L3 foramen (fig. 2). An L2 nerve root block was performed with 2 ml bupivacaine hydrochloride, 0.25%, for left L2–L3 foraminal stenosis. The patient had 70% improvement in thigh pain, but the relief lasted only 3 days. Infiltration of the L1 or L3 nerve root produced no relief of leg pain. In the following 5 months, L2 nerve root block was repeated 5 times.

Seven months after the epidural anesthesia MRI showed complete resolution of the psoas abscess but foraminal narrowing remained (fig. 3). To decompress this foraminal stenosis, surgery under general anesthesia was performed. In a prone position, a posterior midline skin incision was made and after partial facetectomy of the left L2–L3 facet joint, the left L2–L3 foramen was explored. The left L2 dorsal root ganglion was surrounded by a scar without bony impingement. This scar tissue surrounding the dorsal root ganglion was completely removed. The postsurgical course was excellent. The patient reported that the thigh pain disappeared the day after the surgery.

One and a half years after the epidural anesthesia, the patient had a follow-up examination. Although she still had the same knee pain, which had continued to be present through the entire period of treatment and was under treatment in a pain clinic in another hospital, the thigh pain had never recurred.

Discussion

Pyogenic psoas abscess is often associated with epidural abscess,[1] which has been reported as a rare complication of epidural anesthesia.[2–5] Until now, however,

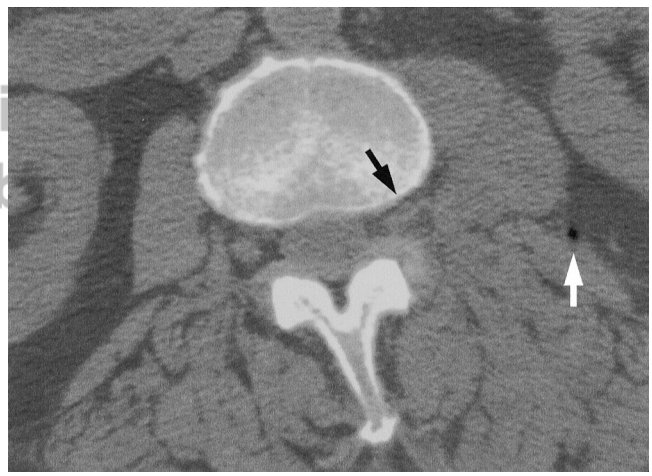

Fig. 1. Lumbar spine axial computed tomography scans at L2–L3 foramen level at the onset of high fever. The left iliopsoas muscle was swollen with an inappropriate collection of gas (white arrow). The left L2 dorsal root ganglion was swollen and a margin between the ganglion and epidural fat was blurred (black arrow).

* Department of Orthopedic Surgery, Yokohama Minami Kyosai Hospital, Yokohama City, Kanagawa Prefecture. † Department of Orthopedic Surgery, Miura Municipal Hospital, Miura City, Kanagawa Prefecture, Japan.

Received from the Department of Orthopedic Surgery, Yokohama Minami Kyosai Hospital, Yokohama City, Kanagawa Prefecture, Japan. Submitted for publication March 9, 2001. Accepted for publication October 30, 2001. Support was provided solely from institutional and/or departmental sources. Presented at the annual meeting of Kanto Society of Orthopedics and Traumatology, Tokyo, Japan, November 21, 1998.

Address reprint requests to Dr. Aota: Yokohama Minami Kyosai Hospital, Mutsuura-cho 500, Yokohama City, Kanagawa Prefecture, Japan. Address electronic mail to: yaota33@hotmail.com.

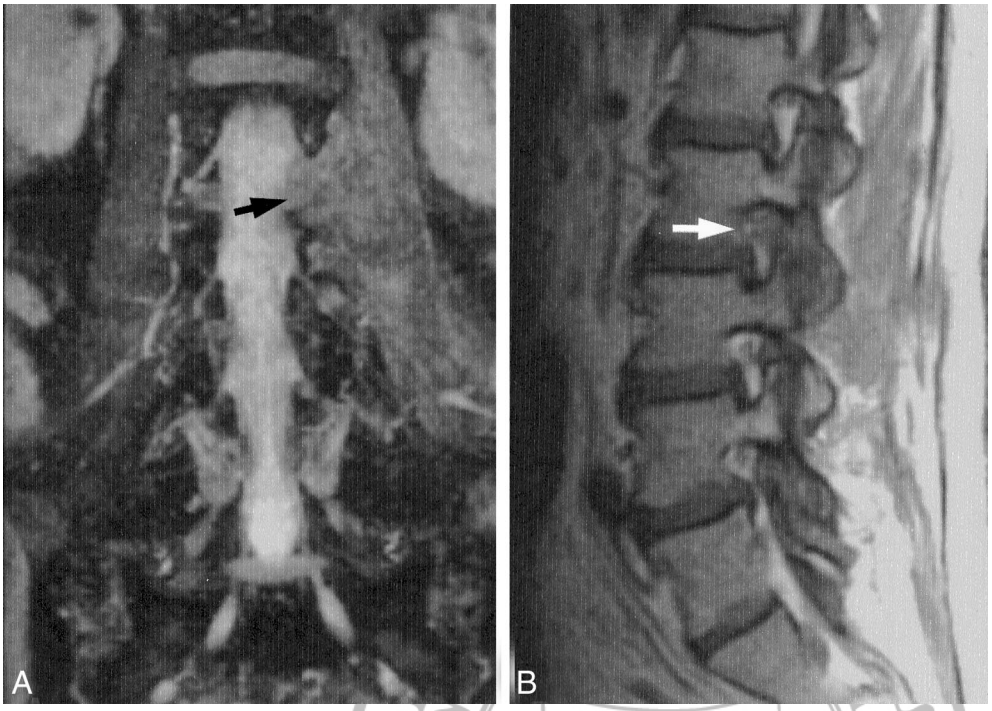

Fig. 2. Magnetic resonance images (MRI) 2 months after epidural anesthesia. (*A*) T2* weighted lumbar MRI in coronal section showed that the left iliopsoas muscle was still swollen. The abscess has spread through the L2–L3 foramen (arrow). (*B*) T1-weighted lumbar MRI in parasagittal section showed disappearance of fat at the left L2–L3 foramen (arrow).

there has been no report of psoas abscess as a complication of epidural anesthesia.

The patient in our study developed a psoas abscess after epidural catheter infusion and subsequent radiculopathy caused by the foraminal infection. Although her symptoms suggested the possibility of an accompanying epidural abscess, such a diagnosis could not be made because the radiologic findings did not demonstrate evident signs of epidural involvement. The lack of epidural infection might be possible since the catheter could have passed out the intervertebral foramen or bacteria could have been washed out the foramen during injection. Indeed, in his computed tomography studies of epidural catheter tip position, Hogan[6] showed that tips were most often found lateral to the dura, in the foramen and sometimes in the paravertebral tissue lateral to the foramen.

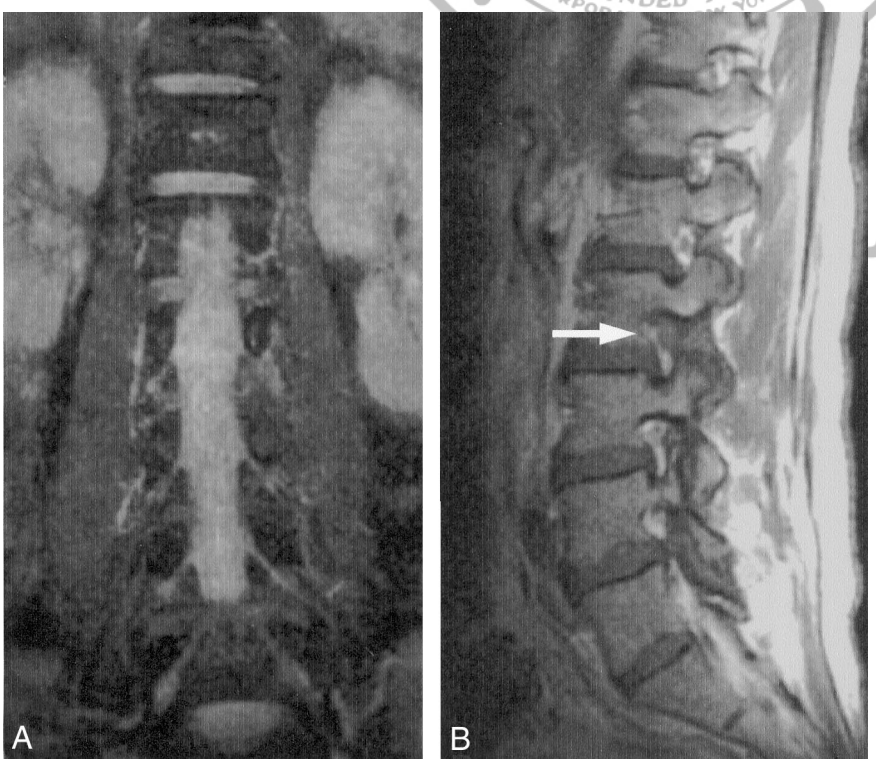

Fig. 3. Magnetic resonance images (MRI) 7 months after epidural anesthesia. (*A*) T2* weighted lumbar MRI in coronal section showed disappearance of the left iliopsoas muscle swelling. (*B*) Note constant disappearance of fat at the left L2–L3 foramen at T1-weighted image in parasagittal section (arrow).

Fibrous foraminal stenosis is not a rare etiology of lumbar radicular symptoms. Kunogi and Hasue[7] reported that out of their 28 patients with surgically confirmed foraminal nerve root involvement, four had no apparent nerve root compression, but narrowing and adhesion of the nerve root. However, to our knowledge there has been no report of iatrogenic foraminal stenosis.

Several similarities in symptoms of two different clinical entities, *i.e.*, L2 nerve root irritation and psoas abscess, could be observed. Low back pain with possible thigh or hip radiation is the most common symptoms for both diseases. Hip extension provokes thigh pain in L2, L3, and L4 nerve roots irritation, however, hip flexion position is a classic sign of the psoas abscess.[8,9] These similarities have made authors hesitate to perform immediate surgery. Although foraminotomy was performed 7 months after the onset of radicular pain, the pain completely disappeared even when surgery was performed late.

In conclusion, we present the first reported case of foraminal and psoas abscess as a complication of epidural anesthesia, which developed secondary foraminal stenosis. The decompressive surgery was effective for persistent radiculopathy because of secondary foraminal stenosis.

The authors thank Professor Katsuyuki Fujii, M.D., Ph.D., (Chairman, Department of Orthopaedic Surgery, The Jikei University, School of Medicine, Tokyo, Japan) for his kind advice and supervision.

References

1. Lin MF, Lau YJ, Hu BS, Shi ZY, Lin YH: Pyogenic psoas abscess: Analysis of 27 cases. J Microbiol Immunol Infect 1999; 32:261–8
2. Baker AS, Ojemann RG, Swartz MN, Richardson EP: Spinal epidural abscess. N Engl J Med 1975; 293:463–8
3. Danner RL, Hartman BJ: Update of spinal epidural abscess: 35 cases and review of the literature. Rev Infect Dis 1987; 9:265–74
4. Fine PG, Hare BD, Zahniser JC: Epidural abscess following epidural catheterization in a chronic pain patient: A diagnostic dilemma. Anesthesiology1988; 69:422–24
5. Du Pen SL, Peterson DG, Williams A, Bogosian AJ: Infection during chronic epidural catheterization: Diagnosis and treatment. ANESTHESIOLOGY 1990; 73:905–9
6. Hogan Q: Epidural catheter tip position and distribution of injection evaluation by computed tomography. ANESTHESIOLOGY 1999; 90:964–70
7. Kunogi J, Hasue M: Diagnosis and operative treatment of intraforaminal and extraforaminal nerve root compression. Spine 1991; 16:1312–20
8. Ricci MA, Rose FB, Meyers KK: Pyogenic psoas abscess: Worldwide variations in etiology. World J Surg 1986; 10:834–843
9. Fairbank JC, Hall H: History taking and physical examination: Identification of syndromes of back pain, The Lumbar Spine, 2nd edition. Edited by Wiesel SW, Weinstein JN, Herkowitz H, Dvorak J, Bell G. Philadelphia, WB Saunders, 1996, pp 85–104

Anesthesiology 2002; 96:1025–7

Delayed Emergence and St. John's Wort

Suzanne Crowe, F.F.A.R.C.S.I., Kevin McKeating, F.F.A.R.C.S.I.†*

INTERACTIONS between prescribed medications and anesthetic drugs are often encountered during the induction and maintenance of general and regional anesthesia. We have become accustomed to the majority of these interactions and routinely take steps to avoid their consequences.

Increasing numbers of surgical patients are taking herbal medicines, according to a recent study in the United States suggesting that 22% of patients are using herbal remedies in the preoperative period.[1] These may be unlicensed preparations, purchased over the counter.

Information on active drug concentrations in such preparations may not be available. Or the patient may not be familiar with the dose or potential side effects of the herbal medicine. Many clinicians have little experience with herbal medicines and their potential to interact with sedative medications, and therefore fail to ask about herbal medicines when taking the patients' history. This is the first report of a clinically significant interaction between a herbal medicine and drugs used in anesthesia. It provides a detailed account of delayed emergence from general anesthesia with coincident self-administration of large doses of St. John's wort.

Case Report

A 21-yr-old woman was admitted for incision, drainage, and marsupialization of a Bartholin abscess. Preanesthetic examination revealed nothing of significance. Of note, she was taking the herbal preparation St. John's wort for depression. At 12 yr of age she underwent a tonsillectomy with uneventful anaesthesia and recovery.

Before induction of anesthesia for the incision and drainage, intravenous access was established and an infusion of compound sodium lactate solution commenced. Fentanyl citrate, 1 μg/kg, was administered, followed by propofol, 3 mg/kg, intravenously. Anesthesia was maintained with sevoflurane in oxygen and nitrous oxide, F_{IO_2} 0.5, *via* a facemask. Observations of vital signs during the procedure remained normal, with a mean blood pressure of 105/45 mmHg, heart rate 90 beats/min, and oxygen saturation and end-tidal carbon dioxide within the normal range. At the end of the procedure, 100 mg rectal diclofenac was administered.

Total anesthesia time was approximately 10 min. The patient was then transferred to the recovery room, with the institution of oxygen 40% by facemask, and blood pressure and oxygen saturation monitoring.

Thirty minutes later, the patient could not be roused, even when subjected to painful stimulation. Observations of vital signs were nor-

* Specialist Registrar, † Consultant Anaesthetist, Department of Anaesthesia, National Maternity Hospital, Dublin, Ireland.

Received from the Department of Anaesthesia, National Maternity Hospital, Holles Street, Dublin, Ireland. Submitted for publication June 25, 2001. Accepted for publication October 30, 2001. Support was provided solely from institutional and/or departmental sources.

Address reprint requests to Dr. Crowe: 2 Chelmsford Avenue, Ranelagh, Dublin 6, Ireland. Address electronic mail to suzbar@gofree.indigo.ie. Individual article reprints may be purchased through the Journal Web site, www.anesthesiology.org.

mal, and her pupils were equal, constricted, and reactive to light. Her blood glucose was 4.1 mM.

Forty-five minutes after anesthesia was administered, the woman now flexed and issued incoherent sounds to painful stimulation. A full blood count, electrolyte count, arterial blood gas, and toxicology screen were sent to the laboratory. Her white cell count was marginally elevated, 12. 1×10^9. Electrolyte assay revealed a sodium concentration of 138 mM, and a potassium concentration of 4.4 mM. The arterial blood gas showed an elevated P_{CO_2} of 46.5 mmHg. The toxicology screen was positive only for opiates.

At 90 min postanesthesia, the patient was easily rousable, with spontaneous eye opening. She was orientated in person and place, and was discharged from the recovery room to the ward.

Eight hours later the patient was interviewed on the ward, where she had a Glasgow coma score of 14. She had no recollection of the procedure or the ensuing events. She denied taking any benzodiazepine, barbiturate, narcotic, or cannabinoid drugs preoperatively. She had been taking St. John's wort for the preceding 3 months for depression on the advice of a herbalist. She had increased the recommended dose after several weeks however, because of perceived lack of effect. At the time of her procedure she was self-administering St. John's wort in tablet form, 1,000 mg three times daily. The patient was advised to discontinue this medication and was referred to her general practitioner.

Discussion

Delayed emergence is a relatively frequent occurrence in the recovery room. It is usually related to drugs administered in the course of the procedure, and their timing of administration. Less commonly, it is caused by metabolic or electrolyte disturbance, hypotension, hypoxia, or intracerebral pathology.[2] All except intracerebral pathology were excluded in this case. The patient's premorbid condition, duration of anesthesia, and complete recovery make an intracerebral event an unlikely possible diagnosis. Under normal circumstances, the sedative effects of fentanyl citrate, propofol, and sevoflurane would not hamper a rapid emergence from general anesthesia at the end of the procedure.

St. John's wort comes from the flowers of the perennial plant *Hypericum perforatum L.*, native to Europe and Asia. The flower's red-staining oil accounts for the herb's name, with legend suggesting that St. John's wort arose from the blood of John the Baptist after his beheading. It is advocated in the treatment of anxiety, insomnia, and depression. There have been several clinical trials comparing it with conventional antidepressants, the most recent concluding that St. John's wort is not effective in the treatment of major depression.[3]

It is available as a cream or liquid tincture, and in tablet and capsule form. The active ingredient is hypericin, and most preparations are standardized according to their hypericin content.

However, there are many constituents in the flowering plant with biologic activity including other naphthoquinone derivatives, flavanoids, and hyperphorin. Therefore, standardization of hypericin extracts on hypericin content alone may not guarantee pharmacological bioequivalence.[4]

As herbal preparations are not subject to the stringent licensing regulations enforced in the preparation of medical drugs, the stated content may vary considerably from the actual concentration of active drug. Some preparations may contain contaminants such as heavy metals or potentially toxic botanicals.[5] The product that this patient was taking was a 500 mg tablet, standardized to 0.3% hypericin.

Of the seven compounds contained within St. John's wort, most information available to date relates to hypericin and its active metabolite, hyperphorin. *In vitro* studies using hypericin have demonstrated affinity for adenosine, benzodiazepine, γ-aminobutyric acid receptor type A ($GABA_A$), and γ-aminobutyric acid receptor type B ($GABA_B$).[6]

The GABA receptor-chloride channel is generally considered to be the most likely potential anesthetic target site. This receptor-channel complex contains modulatory sites for benzodiazepines, propofol, etomidate, barbiturates, and volatile anesthetics.[7] This receptor may also be a potential site of interaction with hypericin.

Hyperphorin, an active metabolite, is also a centrally acting compound. It has been shown to be an uptake inhibitor of 5-Hydroxytryptamine, dopamine, norepinephrine, GABA, and L-glutamate. Hyperphorin causes irreversible inhibition of monoamine oxidase a and b enzymes. Hyperphorin is also a potent inducer of the cytochrome p4503A4 and p1A2 enzymes. These are high-capacity, low-specificity inducible hepatic enzymes. Interaction at this site with other medications clearly has the potential for important side effects.[8,9] Cytochrome p4503A4 substrates frequently used as part of a balanced general anesthetic include alfentanil, midazolam, lignocaine, calcium channel antagonists, and serotonin receptor antagonists.[10] It is possible that St. John's wort may have caused profound sedation by interacting with anesthetic agents centrally, at neurotransmitter receptor sites, and at hepatocellular enzyme sites.

Given that the elimination half-lives of hypericin and hyperphorin are 25 and 9 h, respectively, it would seem wise to counsel patients to discontinue use of St. John's wort 5 days before surgery.[6,10]

Because of concerns about drug safety, in the year 2000 the Irish Medicine Board recommended that St. John's wort be made subject to prescription control.[11] Because plants and parts of plants are not eligible forpatent, the Food and Drug Administration in the United States classifies St. John's wort as a dietary supplement.

Side effects attributable to St. John's wort include gastrointestinal symptoms, photosensitivity, dizziness, confusion, fatigue, and sedation.[4] Herbal medicines are perceived by the public as being harmless, and for that reason may be taken on an empirical basis, as in this case where the patient continued to increase the dose to provide greater effect. Because of the assumption that

these remedies are complementary to traditional medicines, their use often remains unreported.

The onus is on the anesthetist to ask the patient directly about alternative therapies in the preoperative assessment. Familiarity with herbal remedies and their potential side effects has also become necessary, to avert complications in the perioperative period.

References

1. Tsen LC, Segal S, Pothier M, Bader AM: Alternative medicine use in the presurgical patients. ANESTHESIOLOGY 2000; 93(1):148–51
2. Aitkenhead AR: Postoperative care, Textbook of Anesthesia, 3rd edition. Edited by Aittkenhead AR, Smith G. Edinburgh, Churchill Livingstone, 1996, pp 409–10
3. Shelton RC, Keller MB, Gelenburg A, Dunner DL, Hirschfeld R, Thase ME, Russell J, Lydiard RB, Crus-Cristoph P, Gallop R, Todd L, Hellerstein D, Goodnick P, Keitner G, Stahl SM, Halbreichu: Effectiveness of St. John's wort in major depression. JAMA 2001; 285:1978–86
4. Ernst E, Rand JI, Barnes J, Stevinson C: Adverse effects profile of the herbal antidepressant St. John's wort (Hypericum perforatum L.). Eur J Clin Pharmacol 1998; 54(8):589–94
5. De Smet PAGM: Should herbal medicine-like products be licensed as medicines. BMJ 1995; 310:1023–4
6. Barnes J, Anderson LA, Phillipson D: St. John's wort (Hypericum perforatum L.): A review of its chemistry, pharmacology and clinical properties. J Pharm Pharmacol 2001; 53(5):583–600
7. Bovill JG: Mechanisms of anaesthesia: Time to say farewell to the Meyer-Overton rule. Curr Opin Anaesth 2000; 13(editorial):433–6.
8. Piscitelli SC, Burstein AH, Chaitt D, Alfaro RM, Falloon J: Indinavir concentrations and St. Johns' wort. Lancet 2000; 355:547–8
9. Ruschitzka F, Meier PJ, Turina M, Luscer TF, Noll G: Acute heart transplant rejection due to Saint Johns' wort. Lancet 2000; 355:548–9
10. Ang-Lee MK, Moss J, Yuan CS: Herbal medicines and perioperative care. JAMA 2001; 286(2):208–16
11. Herbalmedicines, Drug Safety Newsletter, Ninth edition. Irish Medicines Board, Dublin, February 2000

Anesthesiology 2002; 96:1027–9

Acute Brain Fat Embolization Occurring after Total Hip Arthroplasty in the Absence of a Patent Foramen Ovale

David M. Colonna, M.D., Douglas Kilgus, Ph.D.,† William Brown, Ph.D.,‡ Venkata Challa, M.D.,§ David A. Stump, Ph.D.,‖ Dixon M. Moody, M.D.#*

DURING total joint arthroplasty, showers of bony spicules, marrow fat, and clot are carried by venous blood to the lungs[1]; conditions not unlike those present in patients who have suffered traumatic long bone fractures. Like the fat embolism syndrome, which often has a component of neurologic dysfunction, there is recent evidence that total joint arthroplasty and femoral nailing are associated with intraoperative brain embolization as determined by transcranial Doppler ultrasonography[2–4] and magnetic resonance brain imaging.[5] While there are good data demonstrating that intraoperative brain embolization occurs during total joint arthroplasties, the makeup, and even more importantly, the clinical significance of these emboli remain speculative. The authors describe a case of acute brain embolization that occurred in an adult woman undergoing a total hip arthroplasty.

Case Report

A 77-yr-old, 68-kg woman with chronic lymphocytic anemia, emphysema, hypothyroidism, and gastroesophageal reflux disease fell in her home and suffered a left periprosthetic femur fracture 2 days before she was admitted to the hospital. A transthoracic echocardiogram performed 4 yr before this admission did not demonstrate a patent foramen ovale, although no specific maneuvers were done to diagnose septal defects (*e.g.*, a bubble test). Because of chest pain complaints 3 yr before this current admission, a cardiac catheterization was performed that revealed mild, nonobstructive atherosclerotic coronary artery disease, normal left ventricular wall motion with a 59% ejection fraction, and normal valvular function.

On the morning of surgery, noninvasive monitors were applied, intravenous access was obtained, and a radial artery catheter was inserted. A spinal anesthetic was performed with intrathecal bupivacaine plus epinephrine and fentanyl. After the block was placed, the patient's blood pressure gradually fell from 142/75 mmHg to 108/69 mmHg during 30 min. Thirty minutes after the incision (and approximately 1 h after injection of bupivacaine), methyl methacrylate cement was injected into the femoral canal, immediately followed by the insertion of a stemmed femoral prosthesis. Six minutes later, the patient abruptly developed severe bradycardia to a heart rate of 35 beats/min. She rapidly lost consciousness and was pulseless. She was immediately intubated, and chest compressions were begun. After 35 min of chest compressions and epinephrine administration, she was successfully defibrillated, but she required a continuous epinephrine infusion to support her blood pressure. Her hip wound was rapidly sutured at that point.

An intraoperative, transesophageal echocardiogram was then performed, demonstrating marked right-ventricular dilation, and an underfilled left ventricle with poor contractility. Echogenic material was observed in both ventricles and in the aortic arch. The intracardiac echogenic material did not have the highly reflective appearance that is usually typical of air. No septal defects were noted. The patient remained intubated and was sent to the intensive care unit, where she became progressively hypotensive. Her pupils remained fixed and dilated, and she died approximately 3 h 45 min after her initial cardiac arrest in the operating room.

An autopsy revealed multiple fat emboli to the lungs with giant cell reaction and fat embolization to the brain, kidney, and heart, when the tissues were treated with a neutral fat stain for microscopic examination. Furthermore, fat globules were noted in postcapillary pulmonary

* Assistant Professor, ‖ Associate Professor, Department of Anesthesiology, † Associate Professor, Department of Orthopedic Surgery, ‡ Research Associate Professor, # Professor, Department of Radiology, and § Professor, Department of Pathology, Wake Forest University School of Medicine.

Received from the Wake Forest University School of Medicine, Winston-Salem, North Carolina. Submitted for publication April 6, 2001. Accepted for publication August 8, 2001. Supported by grant No. NS 20618 from the National Institutes of Health, Bethesda Maryland (to Dr. Moody).

Address reprint requests to Dr. Colonna: Department of Anesthesiology, Wake Forest University School of Medicine, Medical Center Boulevard, Winston-Salem, North Carolina 27157-1009. Address electronic mail to: dcolonna@wfubmc.edu.

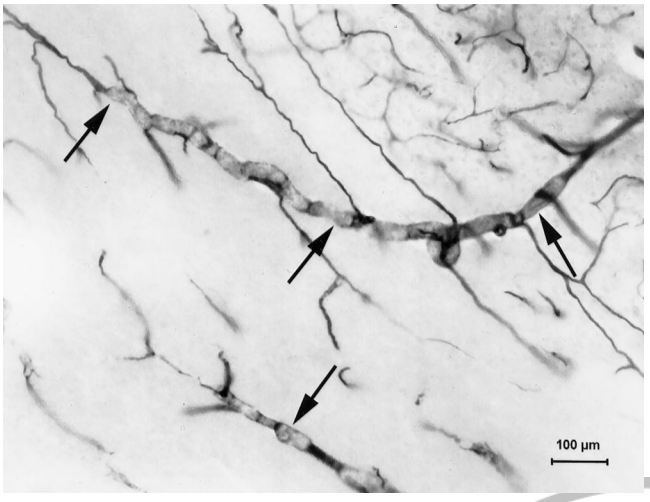

Fig. 1. Autopsy specimen of the brain. Alkaline phosphatase enzyme histochemistry was employed. Black arrows point to abnormal capillary dilatations caused by brain microembolization.

venules, suggesting that fat traversed the pulmonary circulation during the 3 to 4 h elapsed from the time of femoral cement introduction to the time of her death. Acute coronary artery occlusions were not observed, nor was a patent foramen ovale present. On gross examination, the brain was swollen and the gyri somewhat flattened. Portions of the brain were embedded in celloidin, sectioned 100 μm-thick, and alkaline phosphatase enzyme histochemistry was employed for microscopic examination of the cerebral vasculature.[6] Examinations revealed elongated, sausage-shaped emboli, presumably triglycerides or neutral fat, in the small capillaries and arterioles of this woman's brain (Fig. 1). After hand-counting the emboli in multiple, representative, microscopic frames, this brain section was extrapolated to contain approximately 5,000 emboli/cm^3.

In summary, this patient had acute cardiac arrest during a cemented repair of a periprosthetic hip fracture. After 35 min of cardiopulmonary resuscitation, a cardiac rhythm was successfully reinstated. Unfortunately, the patient died a little over 3 h later. Her autopsy revealed systemic fat embolization with an extraordinary degree of emboli counted within the brain, despite the absence of a patent foramen ovale.

Discussion

This case is instructive for two reasons. First, recent data suggest that brain embolization occurs in 40–60% of patients during total joint arthroplasty,[2–4] though the structural nature of the emboli and the degree to which the brain is embolized are unknown. This report is unique in its presentation of human brain specimens, demonstrating extensive brain fat embolization acutely after cemented total joint arthroplasty. There was no evidence of cement or blood clot microembolization in this patient. Second, though several case reports have clearly shown that paradoxical brain fat embolism can occur in the setting of long bone fractures and joint arthroplasties in patients who have patent foramen ovales,[7–9] it is unclear whether clinically significant brain fat embolism occurs in patients who do not have patent foramen ovales. This report suggests that large numbers of fat emboli are able to rapidly traverse the pulmonary circulation (in less than 4 h) in the setting of total hip arthroplasty, even in the absence of a patent foramen ovale. This is supported experimentally in a study using a dog model of femoral pressurization,[10] mimicking femoral nailing in humans, which revealed that systemic fat embolization occurred within 3 h after femoral fat release. This suggests that, at least in dogs, fat emboli in large numbers are able to traverse the lungs rapidly after release from femoral marrow. A recent clinical case report by Byrick *et al.*[5] supports this laboratory finding. This case report told of a woman who had prolonged coma and magnetic resonance imaging findings compatible with brain embolization after undergoing nailing of a femoral shaft fracture, despite the absence of a patent foramen ovale.

Except in the aforementioned dog study, little is known about the histopathologic characteristics of the brain emboli found in a patient after femoral prosthesis insertion. This case report is unique in demonstrating the lipid nature of such brain emboli. Of interest, the brain emboli found in the patient described in this case report appear to be identical to those observed in brain specimens from nonsurvivors of cardiopulmonary bypass. These emboli have been named small capillary arteriolar dilatations (SCADs).[11] The large number of SCADs counted in this patient's brain (approximately 5000/cm^3) is greater than the number of cerebral fat emboli found in each of the brains of 54 cardiopulmonary bypass nonsurvivors.[11]

We believe that brain embolism during total joint arthroplasties has clinical importance, because of our suspicion that it may underlie postoperative delirium (also referred to as confusional states or cognitive dysfunction). This condition is common in the elderly, occurring in 10–15% of general surgery patients, and in as many as 44–55% in particular subgroups of orthopaedic surgery patients.[12–13] Elderly patients with femoral neck fractures comprise the patient group at greatest risk for postoperative delirium, possibly because of their advanced age and their higher incidence of preoperative cognitive dysfunction.[13] Postoperative confusion is associated with a four-fold increase in the duration of hospital stay after hip fracture surgery.[14] It remains unproven why orthopaedic surgery patients may be at greater risk for postoperative cognitive dysfunction. One testable hypothesis is that some orthopaedic surgeries routinely produce brain embolism (*e.g.*, femoral nailing, hip arthroplasties), causing postoperative cognitive dysfunction. Consistent with this thesis, a recent series of 5 patients described in the journal *Stroke* revealed that neurologic dysfunction occurred after long bone fractures and was associated with brain microembolism, as detected by transcranial Doppler.[15]

In summary, our patient illustrates that brain lipid embolization can occur acutely after insertion of a

cemented femoral stem, as shown by the intraoperative transesophageal echocardiography (TEE), even in the absence of cardiac septal defects. In addition, the lipid emboli appear microscopically identical to SCADs, the pathologic brain lesions found in nonsurvivors of cardiopulmonary bypass.[11] The identification of fat emboli within this patient's brain raises many important questions, such as, what is the true incidence of systemic (brain) fat embolization in orthopaedic surgery patients? What is the prognostic importance of lipid brain embolization? What patient subgroups are most susceptible to cognitive dysfunction after brain embolization during orthopaedic surgery? Specifically, are patients with cardiac septal defects at greater risk for brain embolization during orthopaedic surgery?[7–9] Are there differences in brain embolization rates between patients who have cemented *versus* uncemented prostheses? Further study is warranted.

References

1. Capan LM, Miller SM, Patel KP: Fat embolism. Anesthesiol Clin North Am 1993; 11:25–54
2. Sulek CA, Davies LK, Enneking FK, Gearen PA, Lobato EB: Cerebral microembolism diagnosed by transcranial Doppler during total knee arthroplasty: Correlation with transesophageal echocardiography. ANESTHESIOLOGY 1999; 91: 672–6
3. Edmonds CR, Barbut D, Hager D, Sharrock NE: Intraoperative cerebral arterial embolization during total hip arthroplasty. ANESTHESIOLOGY 2000; 93:315–8
4. Colonna DM, Stump DA, Kilgus DJ, Manuel JC, Hilbawi HR: Total hip arthroplasty produces intraoperative brain embolization and neuropsychologic dysfunction up to 6 weeks postoperatively. ANESTHESIOLOGY 1999; 91:A79
5. Byrick RJ, Korley RE, McKee MD, Schemitsch EH: Prolonged coma after unreamed, locked nailing of femoral shaft fracture. ANESTHESIOLOGY 2001; 94: 163–5
6. Bell MA, Scarrow WG: Staining for microvascular alkaline phosphatase in thick celloidin sections of nervous tissue: Morphometric and pathological applications. Microvasc Res 1984; 27:189–203
7. Della Valle CJ, Jazrawi LM, Di Cesare PE, Steiger DJ: Paradoxical cerebral embolism complicating a major orthopaedic operation: A report of two cases. J Bone Joint Surg Am Vol 1999; 81:108–10
8. Weiss SJ, Cheung AT, Stecker MM, Garino JP, Hughes JE, Murphy FL: Fatal paradoxical cerebral embolization during bilateral knee arthroplasty. ANESTHESIOLOGY 1996; 84:721–3
9. Pell AC, Hughes D, Keating J, Christie J, Busuttil A, Sutherland GR: Brief report: fulminating fat embolism syndrome caused by paradoxical embolism through a patent foramen ovale. N Engl J Med 1993; 329:926–9
10. Byrick RJ, Mullen JB, Mazer CD, Guest CB: Transpulmonary systemic fat embolism. Studies in mongrel dogs after cemented arthroplasty. Am J Respir Crit Care Med 1994; 150:1416–22
11. Brown WR, Moody DM, Challa VR: Cerebral fat embolism from cardiopulmonary bypass. J Neuropathol Exp Neurol 1999; 58:109–19
12. Fisher BW, Flowerdew G: A simple model for predicting postoperative delirium in older patients undergoing elective orthopedic surgery. J Am Geriatr Soc 1995; 43:175–8
13. Lipowski ZJ: Delirium in the elderly patient. N Engl J Med 1998; 578–82
14. Berggren D, Gustafson Y, Eriksson B, Bucht G, Hansson LI, Reiz S, Winblad B: Postoperative confusion after anesthesia in elderly patients with femoral neck fractures. Anesth Analg 1987; 66:497–504
15. Forteza AM, Koch S, Romano JG, Zych G, Bustillo IC, Duncan RC, Babikian VL: Transcranial doppler detection of fat emboli. Stroke 1999; 30:2687–2691

Anesthesiology 2002; 96:1029–31

Paradoxical Cerebral Fat Embolism: An Unusual Cause of Persistent Unconsciousness after Orthopedic Surgery

Alain M. Dive, M.D., Ph.D., Philippe E. Dubois, M.D.,† Christophe Ide, M.D.,‡ Pierre A. Bulpa, M.D.,§ Serge M. Broka, M.D.,# Etienne Installé, M.D.‖*

FAT embolism syndrome (FES) is a known complication of long bone trauma and orthopedic surgery with in tramedullary manipulation. The syndrome typically occurs 8 to 72 h after trauma or surgery and is characterized by respiratory failure, neurologic dysfunction, and thrombocytopenia with petechial rash.[1] The clinical presentation of FES varies greatly, however, so that diagnosis may be difficult, particularly in the postoperative period. The authors describe a patient with atypical manifestations of FES in the perioperative period, in relation to fat embolism through a patent foramen ovale.

Case Report

A 16-yr-old boy (height: 150 cm; weight: 50 kg) underwent bilateral femoral lengthening surgery for constitutional short stature. After premedication (prazepam and glycopyrrolate), anesthesia was induced with propofol, sufentanil, clonidine, and cisatracurium. The lungs were ventilated with oxygen and nitrous oxide (2l/2l). Anesthesia was maintained with propofol (total dose: 2320 mg) and small boluses of sufentanil (total dose: 36 μg). During the 9-h operation, heart rate, mean arterial blood pressure, oxygen saturation, end tidal carbon dioxide and core temperature remained within physiologic ranges. Hemoglobin decreased from 10.1 to 9.1 g/dl. Before the end of surgery, the patient received proparacetamol 2 g, tramadol 100 mg, and ketorolac 20 mg.

Ten minutes after withdrawal of anesthetic agents, the patient opened his eyes but did not follow commands consistently. Since cough and swallow reflexes were present, the patient was extubated and transferred to the recovery room where he was noted to have a roving gaze, and mumbled vague sounds after auditory stimuli. His pupils were equal and reactive and he moved both arms spontaneously. His respiratory rate was 16/min, blood pressure 170/68 mmHg,

* Chef de Clinique, ‖ Chef de Service, Département de Soins Intensifs, † Résident, Département d' Anesthésiologie, ‡ Chef de Clinique adjoint, Département de Radiologie, § Chef de Clinique adjoint, Département de Soins Intensifs, # Chef de Clinique adjoint, Département d' Anesthésiologie, Université Catholique de Louvain.

Received from the Departments of Intensive Care, Anesthesia, and Radiology, Mont-Godinne University Hospital, Université Catholique de Louvain, B-5530 Yvoir, Belgium. Submitted for publication April 4, 2001. Accepted for publication November 1, 2001. Support was provided solely from institutional and/or departmental sources.

Address reprint requests to Dr Dive: Department of Intensive Care, Mont-Godinne University Hospital, B-5530 Yvoir, Belgium. Address electronic mail to: dive@rean.ucl.ac.be. Individual article reprints may be purchased through the Journal Web site, www.anesthesiology.org

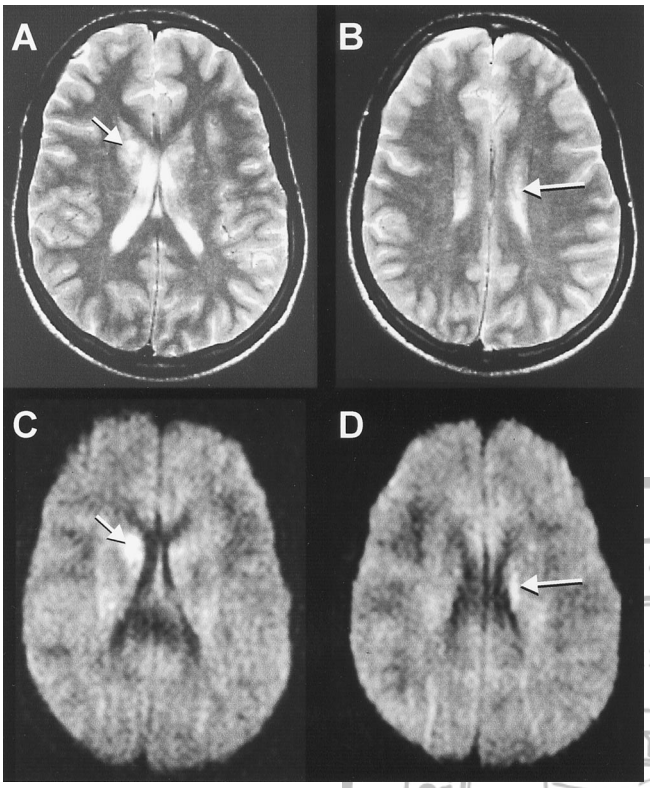

Fig. 1. Cerebral fat embolism in a 16-yr-old male following orthopedic surgery. Initial magnetic resonance imaging (transverse scans) 10 h after surgery. Spotty areas of high signal intensity were detected in both thalami, in the head of the right caudate nucleus (arrows). (*A*) T2-weighted scan; (*C*) diffusion-weighted scan; and in the body of the left caudate nucleus (long arrows), (*B*) T2-weighted scan; (*D*) Diffusion-weighted scan.

heart rate 68/min, and oxygen saturation 97% under 2 l/min oxygen by face mask.

Over the next few hours, the patient sank progressively into a deeper coma. No analgesics or sedatives were administered after surgery. Cardiorespiratory parameters were stable. On neurologic examination 8 h postoperatively, the Glasgow coma score was 6 (eyes opening only to painful stimuli; absence of verbal response to any stimulus; motor response characterized by a withdrawal of upper extremities to pain). A positive Babinski reflex was noted bilaterally. Brain contrast computed tomography scan was normal.

The patient was transferred to the intensive care unit. Laboratory data (electrolytes, glucose, ammonium, arterial blood gases, toxicological screening), chest x-ray, electroencephalogram, funduscopic examination, and contrast transthoracic echocardiography were unremarkable.

In view of the neurologic deterioration, the patient was reintubated to protect his airway and magnetic resonance imaging (MRI) was performed. Small hyperintense foci were demonstrated on conventional sequences (proton density and T2-weighted turbo spin-echo sequences and FLAIR sequence) in the basal nuclei (Fig. 1). The high signal intensity of the lesions appeared more conspicuous on the diffusion sequences (Fig. 1). These findings suggested the existence of focal acute ischemic lesions of embolic origin.

On the basis of these findings, a repeat echocardiographic examination was performed (contrast transesophageal echocardiography [TEE], under pressure support ventilatory mode), demonstrating the presence of a patent foramen ovale with right to left shunt. There were no signs of pulmonary hypertension and the right ventricle was not dilated.

The next day, a petechial rash was noticed on the trunk, and the platelet count decreased to 149,000 mm^{-3}, from 265,000 mm^{-3} preoperatively.

By the third postoperative day, the patient showed some neurologic improvement, opening his eyes to verbal stimuli, and performing handgrip on command. The patient exhibited no clinical or radiologic signs of lung involvement throughout his postoperative course. He was extubated on day 4, and transferred to the orthopedic ward on day 7, recovering cognitive functions completely within the next 10 days. Limb elongation (ratcheting of the prosthetic devices for gradual lengthening) was achieved by physiotherapy, and the patient was discharged 4 weeks after surgery. Magnetic resonance imaging at 2 months showed complete regression of the hyperintensities in the basal nuclei.

Discussion

The patient failed to wake after surgery. No hypotension or hypoxia had been observed during surgery and searches for a metabolic or toxic origin were negative. Fat embolism was finally diagnosed although respiratory manifestations were totally absent.

Although neurologic manifestations of FES were originally thought to be a consequence of arterial hypoxemia, recent observations suggest that they are related to cerebral fat embolism. Cerebral fat emboli have indeed been found at autopsy in patients who died from FES,[2] and MR findings in patients with acute FES are characteristic of ischemic lesions of embolic origin.[3–6] Cerebral fat embolization is thought to result from the passage of fat emboli to the systemic circulation either directly through the pulmonary vasculature, or *via* intracardiac shunts.[7]

A diagnosis of FES in this patient was made on the basis of the close temporal association between medullary manipulation and the occurrence of symptoms, the development of cerebral symptoms with the exclusion of other causes of coma, the presence of hyperintense lesions located bilaterally in the basal nuclei on MRI, and the late occurrence of petechiae over the chest wall. Moreover, the demonstration of a patent foramen ovale with right-to-left shunting on contrast TEE provides an explanation of the mechanism of cerebral embolization of fat particles in the patient.

This case is remarkable because of its unusual presentation; lung involvement was absent, and interestingly, the patient had a prolonged period of unconsciousness after elective surgery.

Rare incidents of isolated cerebral fat embolism without pulmonary involvement have been reported.[5,8–9] The reason for the absence of pulmonary manifestations in these cases is unclear. In contrast to our patient, in whom persistent unconsciousness after surgery misled diagnosis, these individuals presented more typically with a sudden deterioration several hours after trauma or surgery. In FES, the delay that is normally present before the appearance of neurologic signs has been suggested to be related to the time

required for transpulmonary passage of emboli.[10] In our patient, this delay may have been masked because of the long duration of surgery and because of the intracardiac (rather than transpulmonary) passage of the fat emboli.

References

1. Levy D: The fat embolism syndrome: A review. Clin Orthop 1990; 261:281–6
2. Kamenar E, Burger PC: Cerebral fat embolism: A neuropathological study of a microembolic state. Stroke 1980; 11:477–84
3. Erdem E, Namer IJ, Saribas O, Aras T, Tan E, Bekdik C, Zileli T: Cerebral fat embolism studied with MRI and SPECT. Neuroradiology 1993; 35:199–201
4. Finlay ME, Benson MD: Case report: Magnetic resonance imaging in cerebral fat embolism. Clin Radiol 1996; 51:445–6
5. Bardana D, Rudan J, Cervenko F, Smith R: Fat embolism syndrome in a patient demonstrating only neurologic symptoms. Can J Surg 1998; 41:398–402
6. Takahashi M, Suzuki R, Osakabe Y, Asai JI, Miyo T, Nagashima G, Fujimoto T, Takahashi Y: Magnetic resonance imaging findings in cerebral fat embolism: correlation with clinical manifestations. J Trauma 1999; 46:324–7
7. Sevitt S: The significance and pathology of fat embolism. Ann Clin Res 1977; 9:173–80
8. Font MO, Nadal P, Bertran A: Fat embolism syndrome with no evidence of pulmonary involvement. Crit Care Med 1989; 17:108–9
9. Jacobs S, al Thagafi MY, Biary N, Hasan HA, Sofi MA, Zuleika M: Neurological failure in a patient with fat embolism demonstrating no lung dysfunction. Intensive Care Med 1996; 22(letter):1461
10. Byrick RJ: Fat embolism and neurological dysfunction. Anesth Analg 1999; 88(letter):1427