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REVIEW ARTICLES

Obstetric epidurals and chronic adhesive arachnoiditis

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It has been suggested that obstetric epidurals lead to chronic adhesive arachnoiditis (CAA). CAA is a nebulous disease entity with much confusion over its symptomatology. This review outlines the pathological, clinical, and radiological features of the disease. The proposed diagnostic criteria for CAA are: back pain that increases on exertion, with or without leg pain; neurological abnormality on examination; and characteristic MRI findings. Using these criteria, there is evidence to show that epidural or subarachnoid placement of some contrast media, preservatives and possibly vasoconstrictors, may lead to CAA. No evidence was found that the preservative-free, low concentration bupivacaine with opioid mixtures or plain bupivacaine currently used in labour lead to CAA.

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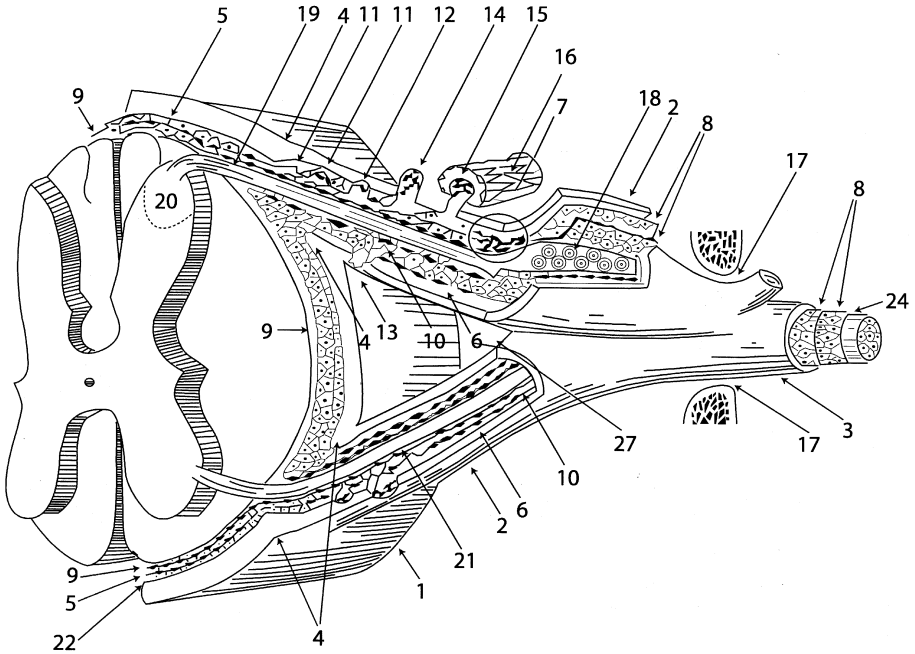
Chronic adhesive arachnoiditis (CAA) is an extremely rare but debilitating condition, that has recently received increased media attention. Less than 1000 cases have been reported in the last 50 yr.[69] On April 15, 2001, the *Sunday Express* newspaper ran a double page article entitled 'Birth Jabs Cripple Women', outlining what they described as 'the scandal of epidurals that have wrecked lives'. They claimed that epidurals for labour have left thousands of women disabled or paralysed; and that this 'fact' was one of the NHS's most closely guarded secrets. A week later, they ran two articles: one entitled 'Time to acknowledge this danger' implied a reluctance of the medical profession to acknowledge the iatrogenic causes of arachnoiditis; and the other including an alleged quote, about epidurals in labour, from a former director of women and children's health at WHO: 'They are being told they are safe. This is a lie'. This article was supported by The Arachnoiditis Trust whose patron had written an article easily accessible on the internet (www.backtalk.nildram.co.uk/arach.htm), in which she claimed that epidural anaesthesia is implicated in the aetiology of arachnoiditis. In these days of increasing accountability and public interest in medical malpractice, issues such as these are difficult to ignore.

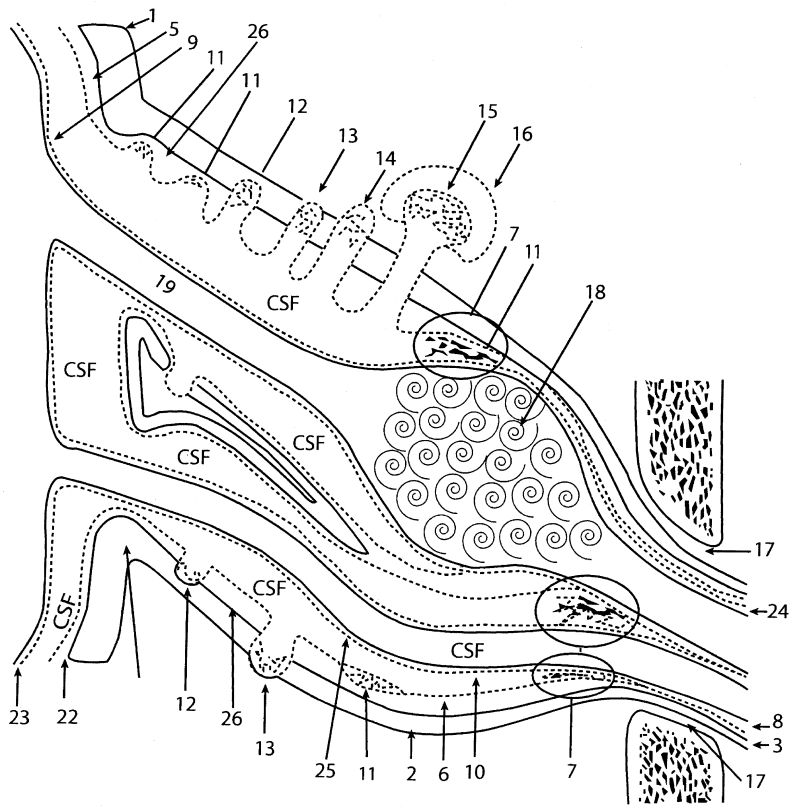
Although the incidence of irreversible neurological complications after epidural anaesthesia is very low,[28] the Woolley and Roe case[27] in 1954 serves to illustrate the catastrophic effect neural damage caused by central nerve block can have. After this report, public confidence in spinal anaesthesia disappeared for two decades. Increasingly, pregnant women are asking about the risks of arachnoiditis after an epidural. This information is not readily available. We therefore conducted a review of the current literature for any evidence of obstetric epidurals causing CAA.

Nature of arachnoiditis

Arachnoiditis was first recognized as a separate disease entity in 1909 by Victor Horsley. Since this time, it has been described by several authors using varied terminology. Titles used include: chronic spinal arachnoiditis, adhesive spinal arachnoiditis, meningitis serosa circumscripta spinalis, chronic spinal meningitis, spinal meningitides with radiculomyelopathy, lumbar adhesive arachnoiditis, spinal arachnoiditis, spinal fibrosis, and lumbosacral adhesive arachnoiditis. Arachnoiditis can be described as arachnoiditis ossificans, calcific arachnoiditis, or pachymeningitis, depending upon the extent of the radiographic or pathological findings. Indeed, there is debate as to whether this constitutes a single disease entity. It should also be noted that the radiological and pathological findings do not

invariably correlate with the clinical features. Thus, there is much confusion over this disease process. More recently, CAA has been used to describe clinically significant non-specific inflammation of the arachnoid and intrathecal neural elements. We shall use this terminology throughout this review.





Anatomy

The arachnoid consists of many layers of flat squamous cells lying one on top of another with potential space between the layers. A network containing collagen, elastic fibres, and blood vessels holds these layers together.[101] Drugs pass from the epidural space, through the dura, arachnoid and pia mater to produce their effect.[108] It is the arachnoid rather than the dura that is the principle barrier to drugs in the epidural space reaching the spinal nerves.[11 100]

Intercellular pores have been demonstrated in animal and human arachnoid.[101] In rabbits, these are large enough to allow the passage of erythrocytes.[103] Arachnoid mater covering the ventral and dorsal roots of spinal nerves has proliferations of cells, which form villi.[101] These have been classified depending upon their degree of protrusion through the dura. Types IV and V breech the dura, with Type V also protruding into the epidural space (see the two parts of Fig. 1).

Thus, the arachnoid is a dynamic structure through which substances placed in the epidural space must pass in order to have their effect. As the epidural and subarachnoid spaces are not entirely separate, substances placed in either space may have effects on this delicate structure.

Pathology

The progressive inflammation of the arachnoid that occurs with CAA was described in the 1970s by Burton.[22] He described an initial stage, 'radiculitis', involving inflammation of the pia-arachnoid with nerve root swelling and hyperaemia. Strands of collagen begin to form between the nerve roots and the pia-arachnoid. 'Arachnoiditis' follows, characterized by collagen deposition, a decrease in nerve root swelling, and adherence of the nerve roots to each other. 'Adhesive arachnoiditis' is the resolution of the inflammatory process, with dense collagen deposition. This causes complete encapsulation of the nerve roots, which undergo progressive atrophy, as a result of interference with their blood supply. Microscopic studies have shown characteristic arteritis in the blood vessels of the chronically inflamed arachnoid.[111] It is not yet known whether this is as a result of the arachnoiditis or the cause.

It would appear that although in the past CAA has been described mainly in the thoracic or cervical region, since the 1950s there has been a trend towards a higher incidence in the lumbar spine. In 1978, Shaw reported that 71% of cases involved the lumbosacral spine alone.[102] This may reflect a change in aetiological factors.

The arachnoiditis adhesions generally occur on the dorsal segments;[68] the reason for this is not fully understood. With the exception of rare cystic forms, the adhesions are arranged peripherally and have been described as looking 'like the bark of a tree', when viewed by myelography.[68]

Clinical features

CAA presents a complex clinical picture. Because of the varied symptomatology, clinical diagnosis is difficult. The precise relationship between the pathological findings and symptomatology has not been defined.

Back pain with or without leg symptoms (e.g. pain, paraesthesia, or weakness) is typical, but a wide range of neurological abnormalities have been associated with CAA.[52] Physical signs are not specific, although there is generally some abnormality to be found. As yet, a typical clinical syndrome has not been identified. Reported case series show a variety of symptoms and signs (Table 1).

The following clinical features occur most frequently: back pain increased by activity; leg pain, often bilateral; hyporeflexia; decreased range of movement of the trunk; sensory abnormality; decreased straight leg raising; and urinary sphincter dysfunction. These clinical features can lead to CAA being erroneously diagnosed as spinal stenosis, spinal tumour, a lumbar disc lesion, or any other compressive lesion of the spinal cord.

Earlier case series described CAA as a progressive disease.[39] Most of these patients had cervical or thoracic CAA.[102] With fewer cases being secondary to infection, most CAA now occurs in the lumbar region.[102] Although the course of CAA is typically irregular, more recent case series report the disease as progressive in 1.8–33% of patients and static in 50–59%.[46 69 102]

Laboratory studies are not helpful in the diagnosis of CAA. Some have reported an increase in CSF proteins with CAA,[81] but this is not thought to be a reliable indicator of the disease.[8 19 46 60 102] Clinical neurophysiological testing (e.g. electromyelography) is also not useful in the diagnosis of CAA.[19 46 69]

Fig 1 Drawings of the spinal cord, dorsal and ventral roots, dorsal root ganglion, and common nerve trunk. The different types of arachnoid villi are illustrated (refs [11 12 13 14 15]). Reproduced with permission from Lippincott Williams & Wilkins. See reference [101] for more details. Key: 1, spinal-cord dura mater; 2, spinal-root dura mater; 3, perineurium and epineurium of peripheral nerve; 4, dural collar; 5, spinal-cord arachnoid mater; 6, spinal-root arachnoid mater; 7, spinal-root pia and arachnoid coming together, with obliteration of the subarachnoid space; note the arachnoid proliferation at this point (circled); 8, perineural epithelium, a continuation of pia arachnoid membrane on to the peripheral nerve; 9, spinal-cord pia mater; 10, spinal-root pia mater; 11, arachnoid proliferations (Type I) protruding into spinal-root subdural space; 12, arachnoid villi (Type II) partially penetrating the spinal-root dura; 13, arachnoid villi (Type III) completely penetrating the spinal-root dura and then exposing itself to the epidural space; 14, arachnoid villi (Type IV) protruding out of the spinal-root dura into the epidural space; 15, arachnoid villi (Type V) protruding into a vein in the epidural space after emerging out of the spinal-root dura; 16, epidural vein; 17, intervertebral foramina; 18, dorsal root ganglion; 19, dorsal spinal root; 20, substantia gelatinosa; 21, ventral spinal root; 22, spinal-cord subdural space; 23, spinal-cord subpial space; 24, peripheral nerve subperineural space (a continuation of the root subpial space (25)); 25, spinal-root subpial space; 26, spinal-root subdural space; 27, inter-root or lateral epidural space (between dorsal and ventral spinal roots), CSF, Cerebrospinal fluid in the spinal cord and spinal-root subarachnoid spaces

Table 1 Summary of clinical findings in CAA. SLR=straight leg raise

Author	Date published	Number of patients	Symptoms	Frequency (%)	Basis of diagnosis
Lombardi[68]	1961	41	Pain and parasthesiae	63	Myelography
			Sphincter abnormality	63	
			Hypoaesthesia	95	
			Motor abnormality	98	
De La Porte[30]	1973	38	Back pain	50	Myelography
			Leg pain	74	
			Sphincter disturbance	29	
			Abnormal reflexes	66	
Jorgensen[60]	1975	72	Back pain	93	Myelography
			Leg pain	43	
			Sphincter disturbance	3	
Benner[8]	1978	68	Back pain	84	Myelography
			Leg pain	91	
			Motor deficits	72	
			Sensory deficits	82	
			Abnormal reflexes	88	
			Urinary incontinence	25	
			Bowel incontinence	16	
Burton[22]	1978	100	Back pain +/– leg pain	100	Myelography
			Decreased SLR	Frequent	Direct surgical observation
			Decreased trunk movement	Often	
Quiles[81]	1978	38	Back pain	76	Myelography
			Leg symptoms	63	
			Decreased SLR	42	
			Decreased trunk movement	24	
			Abnormal reflexes	79	
			Motor weakness	37	
			Sensory abnormality	21	
			Sphincter abnormality	26	
Shaw[102]	1978	80	Back pain +/– leg pain	95	
			Bilateral sciatica	97	
			Decreased SLR	49	
			Motor weakness	23	
			Progressive symptoms	25	
			Static symptoms	50	
Guyer[46]	1989	50	Back pain	96	Myelography
			Leg pain	98	Direct surgical observation
			Decreased trunk movement	87	
			Motor weakness	66	
			Sensory abnormality	74	
			Decreased SLR	53	
			Abnormal reflexes	70	
			Sphincter abnormality	23	
			Progressive symptoms	33	
			Static symptoms	59	
			Able to walk unaided	72	
Long[69]	1992	321	Back p ain	94	Myelography
			Leg pain	81	
			Neurogenic claudication	92	
			Decreased trunk movement	91	
			Motor weakness	74	
			Sensory abnormality	81	
			Abnormal reflexes	96	
			Decreased SLR	61	
			Sphincter abnormality	14	
			Progressive symptoms	18	
			Able to walk unaided	84	

Radiological features

The myelographic appearance of CAA is variable and includes: a homogeneous contrast pattern without root shadows; prominent nerve roots; and subarachnoid filling defects (partial or complete block, loculation or pseudocyst formation), with narrowing and shortening of the thecal sac.[29 57 106] MRI changes of CAA are: conglomerations of roots residing centrally in the dural sac, or adhesions tethering the nerve roots peripherally, giving rise to an 'empty sac' appearance, and soft tissue replacing the

subarachnoid space.[88] It has been reported that these changes seen on MRI have a sensitivity of 92%, a specificity of 100%, and an accuracy of 99% in the diagnosis of CAA.[88]

Proposed definition of CAA

From our study of the literature, we have attempted to define the common features that characterize CAA:

- Back pain, increasing with activity.
- Leg pain, which may be bilateral.
- Some neurological abnormality on examination, most commonly hyporeflexia.
- MRI changes consistent with CAA (myelography changes were accepted for earlier studies).

Suspected aetiologies

Since it was first described in 1909, various factors have been implicated in the aetiology of lumbosacral adhesive arachnoiditis. In the 19th century, infections such as syphilis, gonorrhoea, and tuberculosis were the most prevalent causes, whereas in the 1940s blood in the CSF (after subarachnoid haemorrhage (SAH) or surgery) became the most important cause. More recently, the following have been implicated in the aetiology of CAA: contrast media, epidural steroids, trauma, blood, preservatives, contaminants, vasoconstrictors, and local anaesthetics. Unfortunately, because of the rarity of this disease, there are no randomized controlled trials available. Case reports of CAA and studies involving these suspected aetiologies were reviewed. The proposed definition of CAA was applied to each study to assess its relevance based on our criteria. In older studies, where MRI was unavailable, a diagnosis of CAA on myelography findings as outlined was allowed.

Contrast media

Since the 1970s, contrast myelography has been a common cause of arachnoiditis. Ethyliophendylate ('Myodil' in UK, 'Pantopaque' in USA) is an ionized fatty acid compound that is extremely radio-opaque. The incidence of adhesive arachnoiditis after its use is dose-dependant and has been quoted as 1%.[102] It has a prolonged excretion time, sometimes up to 1 yr. It has therefore been suggested that the contrast media should be removed from the CSF immediately after imaging.[61] However, there is no evidence that this reduces the incidence of arachnoiditis. A study in dogs has shown an increased inflammatory reaction with ethyliodophendylate plus blood and it is now advised to abandon the procedure if a bloody tap occurs.[57] The use of oil-based iodine agents has largely been abandoned,[56] but water-based agents are also capable of producing arachnoiditis, thought to be related to their tonicity.[105] Metrizamide is thought to be the safest; its clearance from the CSF has a half-life of 4 h, and there have been no reported cases of arachnoiditis after its use in humans (although arachnoiditis can be induced in monkeys using very high concentrations).[61]

Epidural steroids

Injection of corticosteroid preparations into the epidural space in an attempt to relieve back pain is a common procedure. Corticosteroids used include: hydrocortisone acetate, methylprednisolone acetate (MPA), methylprednisolone succinate, and triamcinolone. MPA (e.g. Depomedrone) is the most commonly used. There have been reports of CAA after intrathecal injection of MPA,[12 13 75 91] leading to calls to abandon its use.[10 13] Some doubt the validity of these claims.[112]

MPA is suspended in polyethylene glycol (a non-ionic detergent), and myristyl gamma chloride (a long chain fatty acid) to reduce its aqueous solubility. It is thought that polyethylene glycol is the trigger for CAA.[10 12 75] Other steroid agents do not contain polyethylene glycol but do contain bacteriostatic agents, for example benzyl alcohol or phenol, which are considered more noxious.[13]

Some authors feel that MPA should not be used in the epidural space, because of the potential for transfer to the intrathecal space, possibly leading to CAA.[75] However, animal experiments have not shown significant inflammatory changes in the meninges after epidural MPA or triamcinolone.[4 25 31] Dilution of steroid with saline or local anaesthetic before injection into the epidural space lowers the concentration of polyethylene glycol.[10] This may be why there are no reports of CAA after uncomplicated injection of epidural corticosteroids. Indeed, Abram and O'Connor found no cases of CAA after administration of epidural corticosteroids in their large review.[3]

Blood

It has been suggested that blood in the CSF can lead to an inflammatory reaction. Cases of CAA have been reported after SAH, the so called 'aseptic haemogenic meningitis' occurring several days post-SAH.[48 107] Nelson reported a case in which post-mortem studies showed an increase in inflammation of the pia-arachnoid leading to fibrosis after SAH.[76] It has been suggested that the breakdown products of haemoglobin form free radicals, which can cause damage to nerves.[58 82] Indeed, placement of the breakdown products of blood into the CSF of dogs causes more meningeal inflammation than does fresh blood.[58] Other researchers have found that the deliberate placement of autologous blood in the epidural space produced no more tissue reaction than a normal lumbar puncture and so does not result in chemical meningitis.[33] Obviously, this is relevant to those patients requiring an epidural blood patch for treatment of postdural puncture headache. Furthermore, bleeding into the epidural space can occur on insertion of an epidural needle

or catheter, a 'bloody tap'. Incidences for this have been quoted up to 18%.[72] Evidence that minor bleeding is not uncommon with the insertion of epidural catheters has been found at epiduroscopy.[15]

A case has been reported in which an epidural blood patch was alleged to have caused CAA.[5] Several attempts were made to locate the epidural space in a 34-yr-old woman in labour. After an epidural catheter had been inserted, the injection of 10 ml of bupivacaine 0.25% resulted in sensory analgesia to T2, suggestive of subdural placement of the catheter. After delivery, 19 ml of autologous blood were injected down the catheter as prophylaxis against postdural puncture headache. Five days later, the patient complained of backache, a burning sensation in both feet, and photophobia. An MRI scan showed a subdural haematoma, atypical clumping of the nerve roots, and also an extradural collection of blood. The patient was treated with anti-inflammatory drugs and phenytoin, but did not improve significantly. Although the patient had good clinical and MRI evidence of arachnoiditis, it was probably a result of the subdural, rather than epidural, blood patch. The use of the catheter to place the blood patch must be questioned, as it was already doubtful that the tip of the catheter was in the epidural space.

Abouliesh[2] followed up 118 epidural blood patches over a 2-yr period. He found 19 cases of residual backache, three cases of limited back movement, and two cases with occasional radicular pain down both legs, but no cases of CAA. However, the study contains little detail of how the patients were followed up. Although it would appear that some were examined, there is no mention of further investigations including myelography or MRI.

Trauma

It is well known that CAA occurs after spinal surgery, particularly if it is either extradural,[17 81]or repeated. It has been implicated for many years as a factor in Failed Back Surgery Syndrome.

It has been suggested that the epidural catheter may cause an inflammatory reaction in the epidural space, particularly if left in the epidural space long-term.[62 65] In rats, a fibrous sheath has been shown to form around an epidural catheter after it had been left *in situ* for several days.[36] Moderate inflammatory changes can be seen at post-mortem in some patients who have had continuous epidural catheters *in situ*, with thickening along the indentations of the dura where there had been contact with the catheter.[114] It should be noted that epidural catheters are not commonly left *in situ* for long periods of time in obstetric practice.

It was recognized in the 1960s that traumatic lumbar puncture led to an increase in CSF proteins, which did not occur in uncomplicated cases.[9 71] This was postulated to be evidence of meningeal irritation; an inflamed meningeal barrier would allow more protein to cross into the CSF. Transient paraesthesiae occur during 24–44% of epidural catheter placements indicating possible trauma.[87] There is no evidence, however, to suggest that this meningeal irritation progresses to CAA. It has been suggested that the incidence of prolonged neurological abnormalities may be increased if paraesthesiae are elicited during insertion of an epidural needle or catheter.[114]

Reynolds documented seven cases, six obstetric and one surgical, in which neurological damage followed spinal or combined spinal epidural (CSE) anaesthesia.[83] All patients experienced pain during the insertion of the spinal needle, which was believed by the operator to be at the L2/L3 interspace. MRI showed irrefutable evidence of spinal cord damage. However, there was no CAA demonstrable on MRI.

Haisa[47] reported a case in Tokyo of CAA after obstetric epidural anaesthesia. At the time of epidural insertion, the patient felt a sudden sharp pain radiating down the left leg, and continued to complain of pain in her left leg and buttock. After a presumed diagnosis of disc herniation, the symptoms were treated by repeated epidurals each containing local anaesthetic and steroid. She also underwent myelography before an MRI, which was diagnostic of CAA. Unfortunately, this case report did not reveal details as to which drug was placed in the epidural and subarachnoid spaces during the many injections the patient received. It is therefore difficult to determine the exact aetiology of the CAA, but it should be noted that there were contributing factors including the traumatic epidural insertion, use of repeated epidural steroids, and myelography.

Detergents and contaminants

The Woolley and Roe case of 1954 famously advanced contamination with detergents as a cause of neurological abnormalities after spinal anaesthesia.[27] Indeed, at laminectomy, Cecil Roe had thickening and cyst formation of his arachnoid mater, suggestive of CAA. Several cases have been described of neurological abnormalities,[113] aseptic meningitis,[43 96] and CAA,[79] after subarachnoid blocks. The authors all postulated that these were because of contamination with detergents used to clean instruments. However, none put forward good evidence to support their claims.

Aseptic meningitis has been reported after CSE for analgesia during labour, thought to be a result of contamination by the chlorhexidine spirit used to clean the patient's back.[49] Experimentally, intrathecal detergents can cause a pronounced cellular proliferation of the arachnoid in monkeys, dependant upon the detergent used and its concentration.[32 111] However, concentrations used were far in excess of those that could contaminate spinal anaesthetic equipment under normal clinical conditions.

The needle-through-needle technique is probably the commonest method of establishing CSE.[26] Some are concerned that friction between the needles produces metallic fragments that are then introduced into the subarachnoid space, causing an inflammatory reaction.[37]

This has been postulated as a cause of aseptic meningitis.[38] However, it is debatable whether metallic fragments are indeed produced.[23 50 51] Medical grade stainless steel needles do not cause inflammation in nickel-sensitive patients.[40]

Vasoconstrictors

Boiardi and colleagues reported four cases of CAA occurring after non-obstetric epidural anaesthesia, using epidural bupivacaine with epinephrine.[16] The authors suggested that a subarachnoid hyperaemic reaction had occurred secondary to drug placement in the epidural space. No detergents were used, but it is not clear whether preservatives were present in the solutions used. Chliapparini and colleagues reported 16 cases of serious neurological deficit after lumbar epidural anaesthesia over a 7-yr period, including nine cases of CAA developing 1 month to 8 yr later.[24] Only one case involved an obstetric epidural. All used bupivacaine, with six also using epidural epinephrine (concentration unstated). CAA was diagnosed using MRI in seven cases and myelography in the remaining two. The obstetric case had epidural bupivacaine with epinephrine for analgesia during labour. Ten months later, she developed spastic paraparesis and decreased sensation. There was a delay of 10 yr before MRI findings diagnosed CAA. The authors allude to the fact that preservatives in the epidural solution may have been the causative factor, although which preservatives were used was not stated.

Preservatives

Sghirlanzoni and colleagues[99] reported six patients from Italy, diagnosed with CAA using myelography, up to 3 yr after receiving non-obstetric epidural anaesthesia between 1983 and 1988. All their cases had received epidural local anaesthetics from multiple dose vials containing the preservatives, methyl and propyl paraben. Sklar and colleagues[106] reported seven cases of CAA diagnosed using MRI, which were referred to their Miami hospital after epidural analgesia in labour, 2 months to 12 yr previously. All these women originated from South America and it is thought that they may all have received lidocaine 2% with the preservatives metabisulfite and methylparaben. Both these preservatives were banned in the USA at the time of this study, as they were known to have toxic effects. Indeed, Gissen's study in rabbits demonstrated the neurotoxicity of sulfite-containing preservatives, although there was no comment on the reaction of the meninges.[42]

Local anaesthetics

Gemma and colleagues[41] reported a case of CAA diagnosed by MRI after a non-obstetric epidural of bupivacaine 0.5% without epinephrine. An epidural catheter was not used. Little information was given on this case. No information was reported concerning the use of detergents or preservatives. The patient suffered from lumbar pain with paraesthesiae in his big toes, more prominent on the left side.

Arachnoid reactions to local anaesthetics are thought to be a function of their histotoxic properties.[44] Topically applied local anaesthetics cause altered perineural permeability and oedema of nerve fibres.[74] Myers[74] suggested that ester local anaesthetics (e.g. chloroprocaine and tetracaine) are more neurotoxic, producing significant oedema of perineural tissues at clinically relevant concentrations. Topical application of increasing concentrations of bupivacaine to rabbit sciatic nerves *in vitro* showed increased adherence of nerves to each other, suggestive of a dose-dependant inflammation of perineural tissues.[98] Although hyperglycaemia worsens neurological recovery after an ischaemic event, the addition of glucose 7.5% does not appear to increase neurotoxicity.[92] There is no proof that 'allergic sensitivity' of the meninges to local anaesthetic occurs.[44] Cases of CAA who were tested for allergy to local anaesthetics have proved negative.[63 64]

CAA and cauda equina syndrome have been widely reported after spinal anaesthesia using a continuous microcatheter technique.[63 66 86 93] Drasner reported a case of cauda equina syndrome after continuous epidural analgesia in a 52-yr-old man.[34] However, there was doubt as to whether the tip of the epidural catheter was extradural throughout the case. It has been shown by the use of glass spine models that injection of lidocaine 5% with glucose 7.5% has a non-uniform distribution in the CSF, because of the slow flow rate as it leaves the tip of the microcatheter.[66 85] It is thought that this maldistribution unmasks the neurotoxic potential of local anaesthetics, by facilitating areas of high concentration within the CSF.[86] This is potentiated by the use of hyperbaric solutions.[86] Animal studies have shown that neurotoxicity can occur at clinically used concentrations of lidocaine and bupivacaine with a continuous infusion down a spinal microcatheter.[35 67]

Opioids

Opioids are widely used in the epidural and intrathecal space for pain relief in the perioperative, obstetric, and chronic pain settings. Fentanyl, alfentanil, diamorphine, and morphine are those most commonly used in the UK. Unfortunately there are no data from controlled trials investigating the long-term side effects of neuraxial opioids. Histopathological studies after long-term administration of intrathecal morphine in monkeys,[1] and epidural administration of morphine and bupivacaine in humans,[104 109] showed no evidence of arachnoiditis. A review of the literature by a panel of experts in chronic pain relief noted that the intrathecal administration of morphine and fentanyl at clinically effective concentrations appeared to be safe.[9]

Table 2 CAA cases reported after epidural anaesthesia

Author	Date published	Number of cases	Suspected aetiology	Diagnostic criteria	Confounding factors	Obstetric?
Aldrete[5]	1997	1	Blood	MRI	Subdural injection myelography	Yes
Haisa[47]	1995	1	Trauma	MRI	Nil	Yes
Paddison[79]	1954	1	Detergents	PM	Pneumoencephalogram	No
Boiardi[16]	1983	4	Epinephrine	MRI	Nil	No
Chiapparinni[24]	2000	9	Epinephrine	Myelography	Nil	Yes
Sghirlanzoni[99]	1989	6	Preservatives	MRI	Nil	No
Sklar[106]	1988	7	Preservatives	MRI	Laminectomy(1 patient)	Yes
Gemma[41]	1994	1	Bupivacaine	MRI	Nil	No

Epidural solutions commonly used in UK

In 1992, Holdcroft[53] found that 69% of respondents at the annual meeting of the Obstetric Anaesthetists Association used epinephrine in epidurals, either as a test dose or to establish block. Twenty per cent of those using epinephrine whilst establishing analgesia, and 76% of those using epinephrine as part of their test dose, chose a premixed solution of bupivacaine with epinephrine (which contains the preservatives sodium metabisulfite and hydrochloric acid). In total, 17 (19.5%) respondents used a premixed solution of local anaesthetic containing preservatives.

Burnstein's 1996–7 survey of epidural analgesia in the UK revealed that the most commonly used epidural test dose was 3 ml bupivacaine 0.25%, with only 9.5% regularly using lidocaine 2% as a test dose.[21] Only five (3%) regularly added epinephrine to the test dose in this survey, in contrast to Holdcroft's findings. No comment was made as to whether premixed solutions containing epinephrine were used. Ten millilitre bupivacaine 0.25% was most often used to initiate analgesia. A trend towards the increasing use of low concentrations of bupivacaine was shown with 89.1% using bupivacaine 0.125% plain or less for maintenance of analgesia. Opioids were added to the epidural solutions in 88.1% of units, with fentanyl being the most common, but alfentanil and diamorphine were also used. A CSE for labour analgesia was regularly used in 24% of units, the Queen Charlottes' regime being the most common (1 ml bupivacaine 0.25% plain with 15–25 μg fentanyl intrathecally, and bupivacaine 0.1% with fentanyl 2 μg ml^{-1} as an infusion or bolus doses).

Evidence for back pain after epidural analgesic

There have been many studies performed to discover the association between low back pain and epidurals for labour.[10 18 56 89 90 94] As back pain is a common symptom of CAA, these studies might be expected to expose any cases of CAA occurring after obstetric epidurals. The data obtained is inconsistent, with the retrospective studies showing an association between epidurals and postpartum backache, and the prospective studies refuting this. This illustrates more about the potential for bias in retrospective studies than the link between epidurals and postpartum backache. Few researchers have examined their patients, and no study involved MRI scanning, making it difficult to determine the prevalence of CAA. However, Russell examined those who complained of new onset backache in his retrospective study,[90] and found that most back pain was mild and not suggestive of serious pathology, which would seem to exclude CAA. A recent randomized study of long-term outcome after epidural analgesia during labour found no evidence of a causal link between epidural analgesia during labour and low back pain.[56] Patients in this study were examined (although not MRI scanned), and none diagnosed with CAA. Back pain is common in the population as a whole and during pregnancy. Swedish studies have found between 49 and 67% of pregnant women suffer from back pain; most improved within 6 months of delivery, but 7% had serious backache 18 months after delivery.[10 78] Aetiological factors for back pain during pregnancy include mechanical factors, sacroiliac dysfunction, hormonal influence on joint laxity, and local factors, with a small fraction suffering a herniated disc.[6] The current evidence suggests no causative link between epidural analgesia and back pain.[56] As back pain is a cardinal feature of CAA, it would appear unlikely that epidural analgesia in labour is a major cause of CAA.

Evidence for neurological deficit after epidural analgesic

The true incidence of neurological sequelae attributable to epidural anaesthesia is difficult to quantify.[20 84] Studies of neurological complications after epidural anaesthesia are not designed to specifically discover CAA, particularly as MRI scanning is often not undertaken. However, a large survey would be expected to uncover cases of CAA if it were prevalent after epidural anaesthesia.

A review of adverse drug reactions in Sweden over 30 yr included 21 reports of neurological abnormalities secondary to epidural analgesia.[80] Since 1965, it has been compulsory to report all suspected new or adverse drug reactions to the Swedish Adverse Drug Reactions Advisory Committee. All reports from this large database concerning peripheral nerve injury associated with epidural or subarachnoid administration were reviewed. No cases of CAA were reported from

this large database. There was only one case of an obstetric epidural leading to neurological deficit. This patient had a plain bupivacaine epidural for labour analgesia. She developed low back pain radiating to both legs with perineal dysaesthesia and incontinence, 27 months after delivery. Complicating factors included blood in the epidural catheter on first insertion and a forceps delivery. The incidence of peripheral neurological deficit is increased by use of the lithotomy position,[110] and instrumental delivery.[45 77] Indeed, Murray found that 85% of postpartum obstetric paralyses were associated with instrumental deliveries.[73]

The Patient Injury Act in Finland provides a 'no fault' scheme for all patients. Claims are therefore made against the Patient Insurance Association (PIA) rather than the party implicated. A review spanning 5 yr uncovered 38 reports of neurological damage after central nerve block among the 23 500 claims for compensation filed with the PIA.[7] It was estimated that 55 000 spinals and 170 000 epidurals were performed during this time. This large study revealed no documented cases of CAA. Two obstetric cases were reported in this review. After epidural analgesia for labour, one patient suffered an L5 lesion whilst the other had an unspecified permanent neurological deficit. There are no details as to the clinical findings or investigations, making it difficult to determine the cause or type of neurological deficit.

Scott and Hibbard published the results of an extensive retrospective questionnaire sent to all obstetric units in the UK, requesting data of any serious adverse events during and after extradural block in the previous 5 yr.[95] Information was received from 203 units covering 516 000 deliveries, thus representing 78% of all births reported to the Royal College of Obstetricians and Gynaecologists during that time. Scott and Hibbard estimated that 506 000 epidurals for labour were performed during the 5 yr. There were 38 cases of neuropathy, all of which were a result of the damage of a single nerve or nerve root. They were of limited duration (up to 3 months), except for one case of permanent peripheral nerve damage. No cases of CAA were reported.

A multidisciplinary prospective audit in North-West Thames had 35 notifications of neurological deficits.[54] During the 1-yr study period, notification of any postpartum neurological deficit was requested from obstetricians, anaesthetists, neurologists, rheumatologists, urologists, orthopaedic surgeons, GPs, and health visitors. Of 48 066 deliveries, 13 007 patients had an epidural and 629 had a spinal. An independent neurologist reviewed the notes of the 35 women with neurological deficits. Seven women had no neurological problems (joint problems), eight had no clinically identifiable lesion, one had multiple sclerosis, and 19 had neurological problems associated with pregnancy and delivery (an incidence of one in 2530). Seven of these patients had deficits persisting at 1 yr. No anaesthetic technique could be identified as a contributory factor. However, none of the women were examined or given an MRI scan, and no diagnosis was given to the neurological deficits.

Conclusions

CAA is an extremely rare condition with a wide variety of presentations. Criteria for diagnosis are: back pain that increases with exertion, with or without leg pain, which may be bilateral; some neurological abnormality on examination, most often hyporeflexia; and characteristic MRI findings. Its quoted incidence varies depending upon the criteria used for diagnosis and the prevalence of the most common aetiology at that time. Often it presents many years after the suspected causative event. This highlights the need for meticulous records of epidural interventions, including documentation of pre-existing neurological abnormality, complications during epidural insertion, details of drugs used, and any post-epidural neurological deficit.

It is now generally accepted that contrast media can lead to CAA, ethyliodophentylate in particular.[57 61 102 105] A link has been suggested between the use of epidural steroids and CAA.[75] It would seem that meningeal irritation can be caused by blood or its breakdown products in the CSF.[48 58 76 106] The epidural catheter itself may lead to inflammation of the meninges.[114] There is no evidence to suggest that this meningeal inflammation causes long-term problems, including CAA. It is possible that bupivacaine with epinephrine may cause CAA, although the evidence is not conclusive.[16 24] There is fairly good evidence to link the use of preservatives with CAA.[99 106] From Burnstein's survey, it would seem that local anaesthetics containing preservatives or epinephrine are not used regularly in anaesthetic practice in the UK.[21]

Prospective studies show that epidurals do not cause chronic backache.[56 70 81] Studies of backache or neurological complications after central nerve block do not show a link between epidural anaesthesia and CAA. However, all are lacking in detail, and do not cover a sufficient time period to be sure that they would detect CAA. Reviews of insurance claims,[7] adverse drug reactions,[80] and reports of adverse events after epidurals,[95] rely on a connection being made between the symptoms of CAA and the epidural. We cannot be certain that this connection would have been made, as CAA presents in a wide variety of ways and often many years after the aetiological event.

There are a few cases in the literature of CAA after epidural anaesthesia (Table 2). However, only one case has been reported after an uncomplicated (non-obstetric) epidural using bupivacaine without preservatives, detergents, or vasoconstrictors.[41] This report contains insufficient detail to be used as scientific evidence of a link between epidural bupivacaine and CAA.

To discover if obstetric epidurals lead to CAA, an enormous prospective study would need to be undertaken, over many years. It would need to look at any neurological abnormality in detail, including full clinical examination

and MRI scan. Such a study, unsurprisingly, has not yet been done. Current evidence does not support the claim that epidural analgesia in obstetrics using preservative-free, low concentration bupivacaine with opioids or plain bupivacaine, if performed in the standard way with disposable equipment, causes CAA.

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