

Ozone Nucleolysis for Management of Pain and Disability in Prolapsed Lumbar Intervertebral Disc

A Prospective Cohort Study

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Key words: prolapsed intervertebral disc, ozone nucleolysis, oxygen-ozone therapy, low back pain

Summary

The prevalence rate of low back pain in a number of studies ranged from 22% to 65% in one year, and lifetime prevalence ranged from 11% to 84%. Over the years many percutaneous minimally invasive therapeutic modalities have evolved. Intradiscal oxygen-ozone therapy has also showed promising results. We undertook a prospective cohort study to evaluate the therapeutic outcome of oxygen-ozone therapy on patients with lumbar disc herniation in the Indian population.

After obtaining ethical committee and investigational review board permission, 53 consecutive patients complying with selection criteria were treated with a single session of oxygen-ozone therapy. All presented with clinical signs of lumbar nerve root compression supported by CT and MRI findings. All patients received 3-7 ml of ozone-oxygen mixture at an ozone concentration of 29-32 mc/ml of oxygen. Therapeutic outcome was assessed after three weeks, three months, six months, one year and two years on a visual analog scale and Oswestry low back pain disability questionnaire.

Pain intensity was significantly reduced following treatment (VAS baseline 7.58 ± 0.86 , after three weeks 2.75 ± 1.42 and after two years 2.64 ± 2.14). Similarly the Oswestry disability index showed a remarkable improvement in the functional status of the patients ($p < 0.05$). No major complication was observed in this case se-

ries. Oxygen-ozone treatment is highly effective in relieving low back pain due to lumbar disc herniation.

Introduction

The prevalence rate of low back pain in a number of studies ranged from 22% to 65% in one year and the lifetime prevalence ranged from 11% to 84%¹. In 1934 Mixter and Barr drew worldwide attention by stating that herniated disc or nucleus pulposus is one of the important causes of low back pain². Various treatment modalities for herniated disc include conservative management, minimally invasive procedures such as intradiscal steroids, chemonucleolysis, intradiscal decompression, laser discectomy, annuloplasty and surgical management. Non-invasive conservative treatment is the first choice in most cases, but when patients fail to respond, minimally invasive percutaneous measures or surgery is warranted. The success rate of lumbar disc surgeries ranges from 49% to 95%. Therefore, there has been continuous search for safer alternative methods. Use of medical ozone for treatment of low back pain was advocated by orthopaedic surgeon Verga in the 1980s. In 1998 Muto and Avella suggested intradiscal injection of ozone for disc herniation under CT guidance³. After that successful outcome have been reported by many European centers^{4,6}. Therefore the present study was carried out in an Indian popula-

tion to establish the efficacy of oxygen-ozone therapy:

- For relieving pain due to disc prolapse.
- For reducing disability of patients due to disc prolapse.

Material and Methods

This open label prospective study was carried out after obtaining permission from the ethical committee and investigational review board between March 2006 and December 2008 at the Pain Clinic, Charnock Hospital, Kolkata, India. Fifty-six consecutive adult patients with low back pain due to lumber disc

prolapse were included in this study over a period from March 2006 to December 2008. There was a drop-out of three patients during follow-up.

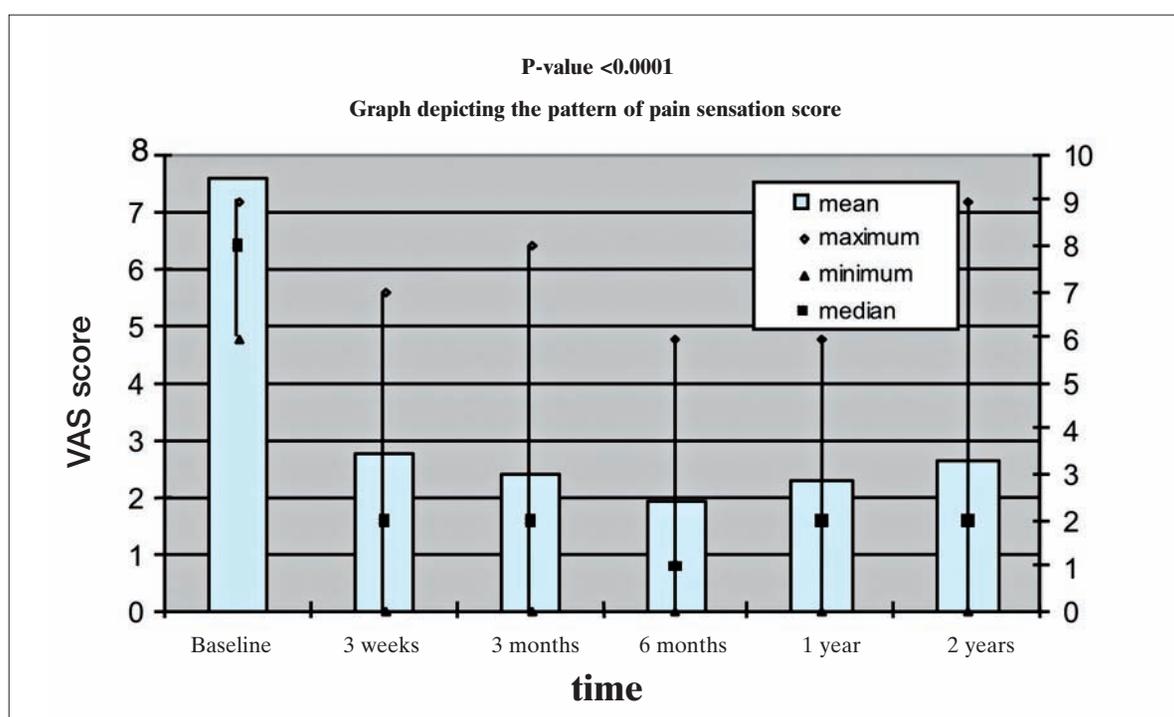
Selection criteria

All patients were referred after failure to respond to conservative therapy for four weeks and refusal or non-feasibility of surgical intervention. To our knowledge/review no such study has been undertaken among the Indian population. So we included all the patients available during the recruitment period of six months. The period of study was from March 2006 to December 2008 with a follow-up period fixed at intervals of three weeks, three months, six months, one year and two years. Patients with the following inclusion criteria were selected in this study:

- VAS score ≥ 6 .
- Radicular pain concurring with imaging for more than four weeks and less than one year.
- MRI/CT images concurring with dermatomal pattern of pain.
- SLR $\leq 45^\circ$.
- Femoral stretch test positive.
- Dural stretch test positive.
- Functional impairment.

Table 1 Changes in VAS score over time.

	Obs	Total	Mean	Variance	Std Dev
Baseline	53	402.0000	7.5849	.7475	.8646
3 weeks	53	146.0000	2.7547	2.0348	1.4265
3 months	53	128.0000	2.4151	3.0552	1.7479
6 months	53	103.0000	1.9434	3.3621	1.8336
1 year	53	123.0000	2.3208	3.6067	1.8991
2 years	53	140.0000	2.6415	4.5806	2.1402



Exclusion criteria

- Positive red flag.
- Presence of bleeding disorder.
- Local infection.
- G6PD deficiency.
- Uncontrolled diabetes.
- Caries spine.
- Hyperparathyroidism.
- Pregnancy.
- Patient refusal.

Informed consent was obtained from all the patients. Intravenous cannulation was done and midazolam 0.05 mg/kg was injected for conscious sedation. Patients were turned to a prone position and a pillow was placed under the lower abdomen. The procedure was performed under C-arm guidance. The C-arm was first focused to an antero-posterior view for identification of the diseased disc. Then the C-arm was angled cranially or caudally to abolish any double end-plates and to achieve the widest possible view of the disc space. Then the C-arm was rotated obliquely so that the image of the facet joint appeared at the centre of the end plates. At this stage needle entry point was just lateral to the superior articular process, which corresponds to the centre of the disc. The needle puncture site was identified and marked on the skin.

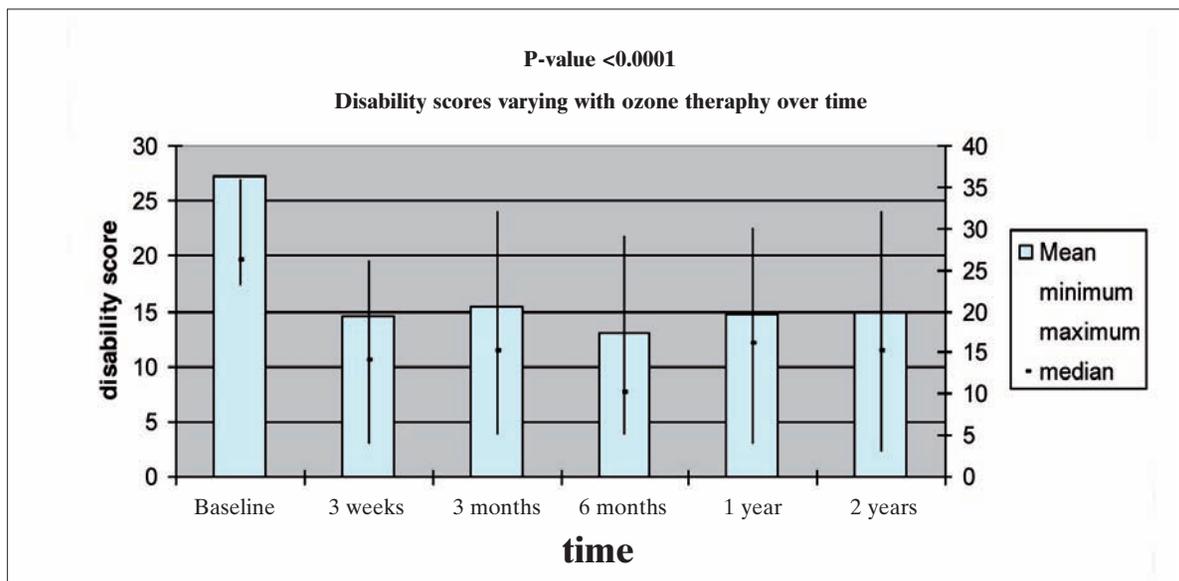
After antiseptic dressing and draping, the proposed site was infiltrated with local anaesthetic agent. A 22 gauge 12 cm long needle was

introduced needle through needle into the affected disc using the tunnel view under fluoroscopic guidance. The position of the needle was confirmed by AP and lateral view of the spine and 3-7 ml of oxygen-ozone mixture at a concentration of 29-32 mc/ml was injected in the disc by ozone resistant syringe over a period of 15-20 seconds.

At the end of the procedure, patients were advised to rest in supine decubitus position for at least two hours. All patients were discharged on the same day evening, and were advised to gradually resume motor activity. All patients underwent follow-up examination at three weeks, three months, six months, one year and two years after the procedure. Pain intensity was assessed by 0-10 points visual analog scale (VAS) and Oswestry low back pain disability questionnaire⁷ was used to assess functional

Table 2 Changes in Oswestry disability index over time.

	Obs	Total	Mean	Variance	Std Dev
Baseline	53	1445.0000	27.2642	8.3904	2.8966
3 weeks	53	768.0000	14.4906	32.4470	5.6962
3 months	53	816.0000	15.3962	45.3592	6.7349
6 months	53	690.0000	13.0189	46.6343	6.8289
1 year	53	785.0000	14.8113	53.4253	7.3093
2 years	53	792.0000	14.9434	50.2083	7.0858



impairment. Oswestry disability index was used on a 0-5 point score to assess limitations of daily activities due to pain.

The index includes;

- 1 pain intensity
- 2 personal care (washing, dressing)
- 3 lifting of weight
- 4 walking
- 5 sitting
- 6 standing
- 7 sleeping
- 8 social life
- 9 traveling
- 10 changing degree of pain.

Statistical analysis was done using ANOVA test. Microsoft Epi info. Version 3.4.1 software was used for data analysis, and results were considered statistically significant if p value < 0.05 .

Results

Patients' range of age was 21-65 (average 46.04) years. There were more men than women (male: female ratio 32: 21). Intensity of pain was significantly reduced following ozone therapy (Table 1). The reduction of VAS score from baseline to three weeks following treatment was 7.58 ± 86 to 2.75 ± 1.42 , and at the end of the study, that is two years after treatment 2.64 ± 2.14 , p value was < 0.0001 which is significant. Oswestry low back pain disability score showed a significant improvement in functional status of the patients. Reduction of Oswestry disability index from baseline to three weeks and two years following treatment was 27.26 ± 2.89 to 14.49 ± 5.69 and 14.94 ± 7.08 , p value was < 0.0001 (Table 2).

There were no complications such as systemic hypotension, bradycardia, vagal shock, meningeal irritation or neurological deficit observed in this series.

Discussion

The intervertebral discs occupy one third of the height of the spinal column and consist of an outer annulus fibrosus and inner nucleus pulposus. The nucleus pulposus is sandwiched inferiorly and superiorly by cartilage endplates. In childhood the annulus fibrosus is separated from the nucleus pulposus by a transitional zone. In the growing phase during skeletal mat-

uration the boundary between annulus and nucleus becomes less obvious. The nucleus pulposus is a ball of transparent jelly which consists of collagenous fibres, cells and mucopolysaccharides.

Disc prolapse results from herniation of soft disc material from the nucleus pulposus through a tear in the annular ligament. Pain and inflammation develop from the pressure of the herniated material on the posterior longitudinal ligament and the dura mater, which may ultimately affect the nerve roots.

About 90% of patients respond to medical treatment including analgesics and physiotherapy. The remaining 10% require decompression of nerve roots either by surgery or some percutaneous intradiscal procedure.

Chemonucleolysis using chymopapain was the first intradiscal therapy done in human in 19638. Subsequently some other percutaneous therapeutic options evolved. The use of medical ozone in the treatment of low back pain was developed by orthopaedic surgeon Verga in 1980s. He has treated about 8000 patients over 15 years, and relapse of pain has occurred in less than 2% of cases. The injection is generally made into the paravertebral musculature and in the hernia zone. Ozone nucleolysis by intradiscal injection under CT guidance was first suggested by Muto et Al in 1998³. The action of ozone is due to the active oxygen atom released by the breakdown of the ozone molecule. This active oxygen atom or singlet oxygen is attached to the proteoglycan bridges of the nucleus pulposus. Due to this reaction proteoglycans in the nucleus pulposus is no longer able to hold water and there is shrinkage or mummification of the disc leading to decompression of nerve roots.

Based on this theory of ozone nucleolysis, this prospective study was undertaken in 53 adult patients suffering from lumbar disc prolapse for more than four weeks duration. Three to seven ml of oxygen-ozone mixture at a concentration of 29-32 mc/ml were injected into the disc. The mean concentration of ozone was 30.2 mc/ml in this series, which is absolutely safe for the patient. Viebahn reported that the nontoxic concentration of ozone varies from one to 40 microgram per milliliter of oxygen and concentration should not exceed 40 mc/m³. The dose of ozone is crucial and must not exceed the capacity of antioxidant enzyme and glutathione to prevent accumulation of

the superoxide anion and hydrogen peroxide, which can cause cell membrane degradation^{10,11}.

Following intradiscal administration of ozone-oxygen mixture, patients were followed-up for two years using the visual analog scale and Oswestry low back pain disability index. A significant improvement was observed in the functional status of the patients and severity of pain was also significantly reduced (Tables 1 and 2). Bonetti et Al also reported excellent results in 74.4% patients after six months⁵.

Ozone not only attenuates nerve root compression by reducing the size of the disc, it also helps to reduce venous stasis caused by compression of vessels and hence improves the microcirculation and supply of oxygen. This reduces pain associated with neuronal hypoxia.

Ozone has analgesic as well as anti-inflammatory effects¹² as it inhibits synthesis of proinflammatory prostaglandins, release of bradykinins and algogenic compounds. Ozone also increases the release of antagonists to proinflammatory cytokines¹³.

Patients who did not show much improvement following ozone therapy and whose Oswestry disability index remained high even after three months were referred to a neurosurgeon for surgical intervention if indicated.

To conclude, ozone nucleolysis provides excellent pain relief in most herniated disc patients who failed to respond to conservative therapy. The limitations of this study are lack of control and lack of blinding. Further study is necessary to evaluate the long-term outcome of ozone nucleolysis therapy.

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Initial Clinical Experience with a New Biointegrative Cement for Vertebroplasty in Osteoporotic Vertebral Fractures

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Key words: vertebroplasty, biointegrative cement

Summary

Polymethylmethacrylate, as a widely used material for vertebroplasty, has several drawbacks such as heat development and high allergenic potential. In order to avoid these drawbacks ceramic cement materials have been developed.

The purpose of this study was to evaluate a new biointegrative material for vertebroplasty in osteoporotic vertebral fractures regarding pain relief, safety aspects and technical feasibility.

The injectable bone substitute Cerament™ SpineSupport has been developed for vertebroplasty of osteoporotic vertebral fractures. The aim of the product is to provide mechanical stability by cured calcium sulfate dehydrate during a period of several weeks and to act as an osteoconductive support by hydroxyl apatite particles.

Inclusion criteria were a stable single vertebral fracture at levels Th5 to L5, verified by CT and MRI, and not older than four weeks, in osteoporotic patients aged 60 years or older. Bipedicular vertebroplasty technique was used. Follow up included CT directly after treatment and after two months and pain assessment (VAS) pre and post procedure after two weeks and one month.

Seven patients (age range 62 – 96 years, mean 73.9, five women, two men) were treated at levels T8 (n=1), T12 (n=4) and L1 (n=2). The average injected volume was 1.9 ml (range 0.2 - 4 ml). No material or procedure-related complications were observed. An average height loss of the treated vertebral bodies of 3.6 mm (range 1.5 - 5.4)

was seen two months after treatment as compared to pre-treatment CT. Pain assessment by VAS resulted in an improvement from mean 69 prior treatment to 37 the day post treatment, 42 after two weeks and 30 after one month.

Initial results indicate that Cerament™ SpineSupport is safe and effective in the treatment of acute osteoporotic vertebral body fractures. Further studies with long-term follow-up are needed to confirm these results and to prove the concept of osteoconduction with hydroxyl apatite particles.

Introduction

Vertebroplasty is a widely use method for pain treatment and vertebral augmentation in osteoporotic vertebral fractures. The method was introduced by Galibert and Deramont initially for the treatment of painful vertebral hemangiomas and metastases¹. Later the indication was expanded to painful osteoporotic vertebral fractures, which today is by far the most frequent indication for vertebroplasty^{2,3}.

Since the introduction of vertebroplasty polymethylmethacrylate (PMMA) based cement materials have been used almost exclusively⁴. There are a number of PMMA cements available adapted to the specific needs in vertebroplasty such as fluoroscopic visibility, injectability and working time. In spite of some differences in mixture composition, the basic properties of PMMA cement materials are rather sim-

ilar. The use of PMMA is well documented and several studies have shown its effectiveness in vertebral augmentation and pain relief^{5,6}.

However there are a number of drawbacks which query PMMA as an ideal cement material for vertebroplasty for osteoporotic vertebral fractures. PMMA has a high allergenic potential and is locally toxic before hardening. The heat development during hardening may damage nerve structures in case of leakage^{4,7}. Both the toxicity and the heat development are potentially harmful for the local bone viability which might further degrade the bone in the osteoporotic vertebrae.

In order to avoid these problems related to PMMA several cement materials based on ceramics have been developed. Beside their good biocompatibility these materials are also potentially osteoconductive⁴.

The aim of this prospective patient study was to evaluate a new biointegrative material for

vertebroplasty in osteoporotic vertebral fractures regarding pain relief, safety aspects and technical feasibility.

Method and Materials

The investigational bone substitute Cerament™ SpineSupport (BoneSupport AB, Lund, Sweden) based on calcium sulfate hemihydrate, hydroxyl apatite and Iohexol has been developed for percutaneous treatment of osteoporotic vertebral fractures. The basic concept of this cement material is to provide instant mechanical stability by the formation of cured calcium sulfate dehydrate during a period of several weeks and to act as an osteoconductive support for ingrowths of new bone by the hydroxyl apatite particles.

Cerament™ SpineSupport consists of a powder phase comprising calcium sulfate hemihydrate (60 weight %) and hydroxyapatite (40 weight %) and a liquid phase consisting of Iohexol 180 mg Iodine/ml. The powder phase of the cement is provided in a prefilled mixing device and the mixing procedure is started by adding the Iohexol. The injectable paste can thereafter be loaded into 1 ml syringes for injection into the vertebral body.

The mixing time is approximately 1 min, the working time up to 10 min and the setting time is approximately 30 min. In contrast to PMMA none of the components is highly allergenic and no significant heat development occurs during the hardening. The compression strength of Cerament™ SpineSupport is 25 MPa in vitro as compared to 50 - 100 MPa for typical PMMA materials⁸.

The study was approved by the local Ethics Committee and the Swedish Medical Products Agency. Informed consent was obtained from all patients. Inclusion criteria were:

1. Stable, painful vertebral fracture at a single level from T 5 to L 5, verified by computed tomography (CT) and magnetic resonance imaging (MR).

2. Age of the fracture not older than four weeks confirmed by patient history.

3. Signs of osteoporosis verified by radiography, CT or by medical history (e.g. bone density measurements).

4. Patients aged 60 years or older. Seven patients (mean age 73.9 years, range 62 - 96, five women, two men) were included and treated at levels T 8 (n=1), T 12 (4) and L 1 (2) (Table 1).

Table 1 Patient age, treated level, injected cement volume and anterior vertebral height loss two months after treatment compared to preprocedural imaging.

Patient No.	Age	Level	Injected volume	Height loss, mm	Height loss, %
1	78	T 12	0.2	2.6	17
2	96	T 8	1.5		
3	65	T 12	0.6	2.9	16
4	62	L1	0.8	1.5	8
5	73	L1	2.2	5.0	29
6	68	T 12	3.9	5.4	25
7	75	T 12	4.0	4.3	32
mean	73.9		1.9	3.6	21

Table 2 VAS values the day before treatment, within one day after treatment, after two weeks and one month.

Patient No.	Preop	Postop	2 weeks	1 month
1	65	5	90	49
2	30	15	0	1
3	80	18	10	0
4	70	45	30	37
5	89	54	65	42
6	70	80	100	77
7	80	40	0	6
mean	69	37	42	30

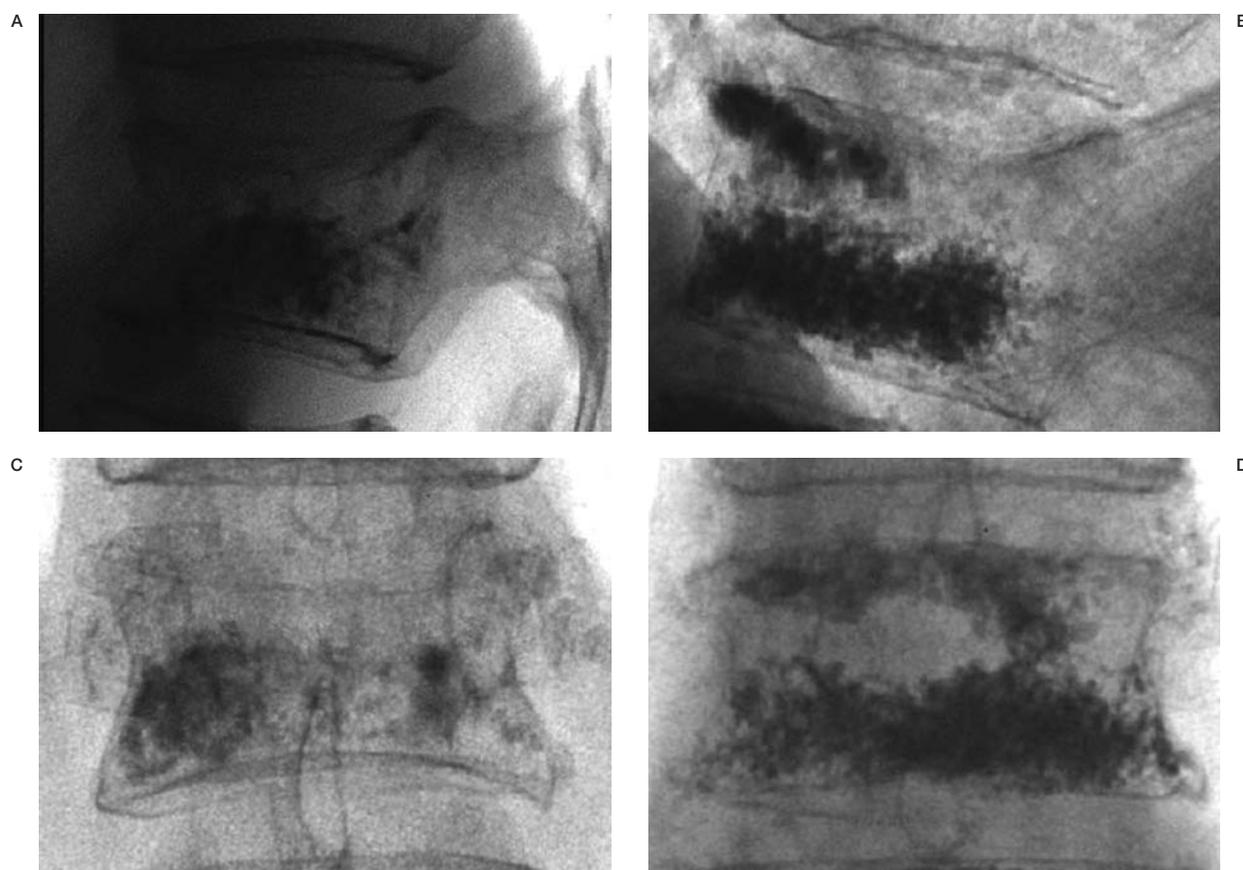


Figure 1 Radiographic visibility of 4.0 ml Cerament™ SpineSupport (A,C) as compared to 4.2 ml PMMA (Osteofirm™; Cook Europe, Bjaeverskov, Denmark) (B,D) directly postprocedural in two different cases.

Bipedicular vertebroplasty technique was used with 13G or 11G needle size and Cerament™ SpineSupport was used exclusively in all patients. The procedure was performed under conscious sedation. Periprocedural arterial blood gas sampling was performed to monitor pulmonary embolisation.

Preprocedural and postprocedural imaging included x-ray one month after treatment, CT the day before treatment, within one day after treatment and after two months. MRI within two weeks before treatment.

Postprocedural compression of the treated vertebral body was assessed by measuring the anterior vertebral height on mid sagittal reconstructions on the CT examinations before treatment and after eight weeks.

Pain was assessed on a 100 graded (0 = no pain, 100 = worst imaginable pain) visual analogue scale (VAS) on the day before treatment, within one day after treatment, after two weeks and one month. The patients were also asked to

assess their general health status using a visual analogue global self-rated health assessment (EQ5Dvas, 0 = worst imaginable health status, 100 = best imaginable health status) on the day before treatment, within one day after treatment, after two weeks and one month⁹.

Results

Procedural behavior of the material

Due to the prefilled mixing device the mixing procedure was convenient. In contrast to PMMA no measures to prevent monomere fume exposure were needed. The injection was performed with 1 mm syringes.

During the treatment of the first cases plugging of the injection needles occurred, which ruled out further injection of the cement. Because of this, the injected cement volumes were unintentionally low in the first four cases (Table 1). Probably a separation of the powder and liquid phase caused by filter pressing creat-

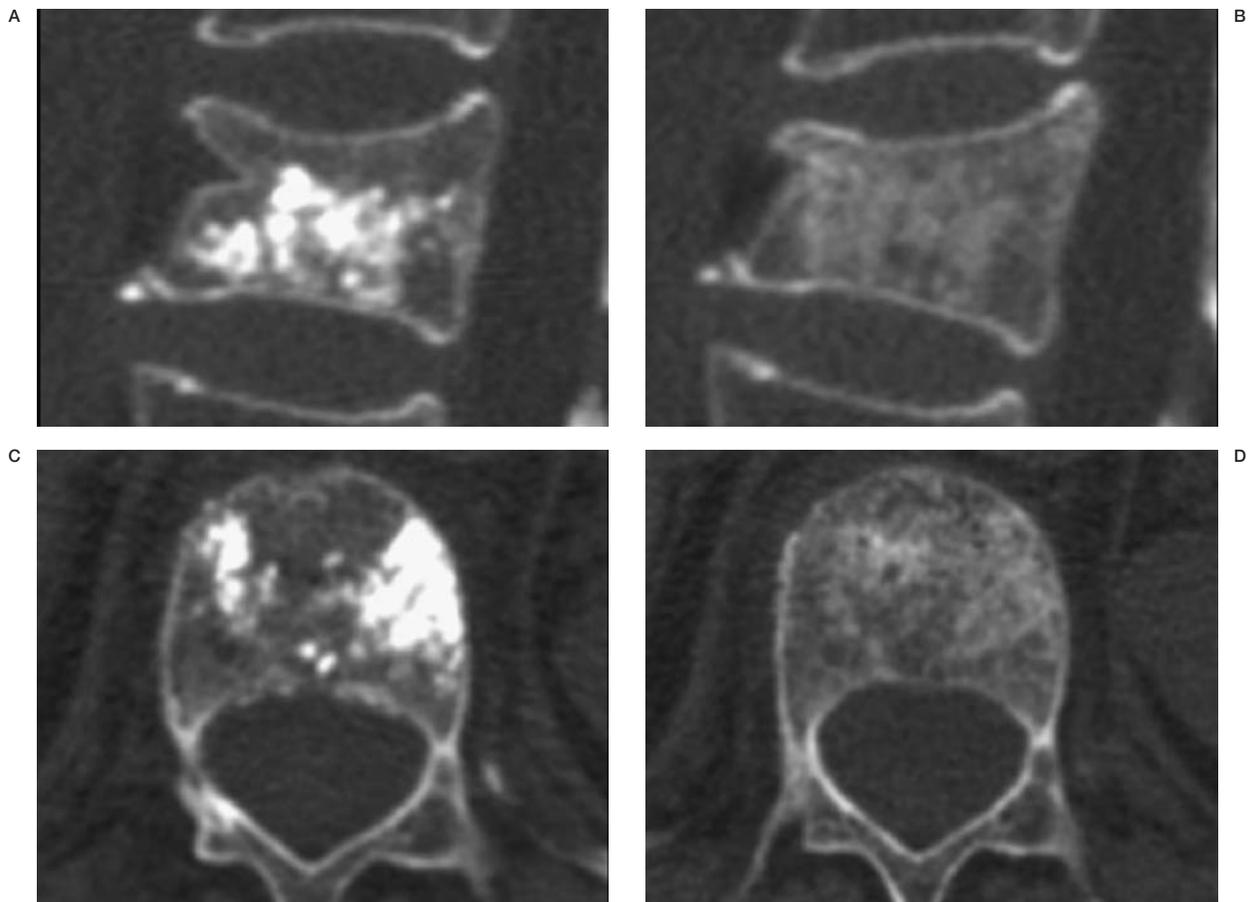


Figure 2 Visibility on CT of Cerament™ SpineSupport directly after treatment (A,C) and after 2 months (B,D). The markedly decreased visibility after 2 months is probably due to the resorption of the Iohexol. As in this case, in all measured cases an additional anterior compression was seen after 2 months (B).

ed a particle jam inside the injection needle. These initial problems were partially solved by a minor modification of the cement material decreasing its susceptibility to pressure and by saline flushing of the vertebral body through the vertebroplasty needles prior to the cement injection. These measures markedly reduced the occurrence of needle plugging. The average injected volume was 1.9 ml (range 0.2 – 4.0) (Table 1). The fluoroscopic visibility of the cement was inferior to typical PMMA cements for vertebroplasty, which made fluoroscopic monitoring of the injection difficult especially in obese patients (Figure 1).

The visibility on CT directly after the procedure was good without any difficulties ruling out material leakage. However on CT two months after treatment almost nothing of the material was seen, probably due to resorption and elimination of the Iohexol, indicating that

the remaining components barely contribute to the radioopacity of the material (Figure 2).

Pain relief, quality of life

The VAS score was reduced for all patients by at least 50% except for two patients. In patient 1, treated at level T 12, a marked increase in pain was seen at follow-up at two week caused by a new fracture at level L 2. Patient 6 had no pain reduction but an increase in the VAS score was seen both the day after treatment and at two and four weeks follow-up. CT at eight weeks revealed the development of an osteonecrosis in the treated level. The mean VAS score decreased from 69 preoperatively to 30 after four weeks. However this improvement was not statistically significant ($p > 0.05$; Wilcoxon signed rank test) (Table 1).

Regarding the self-assessed general health status (EQ5Dvas) the mean status improved

from preprocedural 45 (range 20-60) to 54.7 (range 20-81) at two weeks with a further improvement to 71.1 (range 51-95) at four weeks. The improvement from preprocedural to four weeks was statistically significant ($p < 0.05$; Wilcoxon signed rank test).

Height stabilization

Measurements of the anterior height of the treated vertebral bodies on CT before and eight weeks after treatment showed an increased anterior compression in all cases. The mean height loss was 3.6 mm (range 1.5 – 5.5) or 21% (range 8 – 32). Due to medical complications follow-up CT after eight weeks was not performed in patient 2, so the height loss could not be assessed in this case (Table 1, Figure 2).

Safety

Measurement of periprocedural arterial blood gases showed no signs of pulmonary embolism. Patient 2 was admitted 11 days after treatment because of sudden onset of paraparesis. Subsequent MRI showed edema in the thoracic medulla and further investigation revealed a thoracic aortic aneurysm. The condition was interpreted as medullary ischemia due to the thoracic aneurysm and not related to the vertebroplasty. Due to the complicated course no follow-up CT after eight weeks was performed in this patient. In patient 1, treated at level T 12, a new vertebral fracture occurred at level L 2. Patient 6 showed the typical radiological features of osteonecrosis on follow-up CT eight weeks after treatment. The patient did not show any pain relief following the treatment.

Discussion

The presented study shows that vertebroplasty in osteoporotic vertebral fractures with the ceramic bone substitute Cerament™ SpineSupport is feasible with promising results.

The use of ceramic cements like Cerament™ SpineSupport in vertebroplasty in osteoporotic vertebral fractures avoids some of the drawbacks related to PMMA, namely the toxic and thermal effect during the procedure and the allergenic effect especially for personnel. However further improvements of the material are needed to reach injectability and fluoroscopic visibility comparable with PMMA for vertebroplasty.

As a consequence of this study the liquid phase in the final CE marked product Cerament™ SpineSupport has been changed to Iohexol 300 mg Iodine/ml.

Regarding the therapeutic effect, the results indicate that the efficiency in pain relief within the first month after treatment is comparable to results reported with PMMA⁶. A slight to moderate additional anterior compression of the treated vertebrae was seen in all measured cases indicating that the stabilizing effect probably is less than that of PMMA¹⁰. On the other hand, the physiological compression strength of Cerament™ SpineSupport might help to prevent new fractures at adjacent levels, which has been discussed as a consequence of vertebroplasty with PMMA^{11,12}. These aspects are still speculative and have to be evaluated with larger studies with long-term follow-up.

No complications likely related to the procedure or the material were seen. The new vertebral fracture in patient 1 occurred at a non adjacent level and was most probably related to the osteoporosis. The osteonecrosis at the treated level in patient 6 was primarily judged as spontaneous. Osteonecrosis is a known complication of vertebral fractures. However a contribution of the cement material to the development of the osteonecrosis cannot be ruled out and the lack of pain relief in this patient indicates that Cerament™ SpineSupport probably is not suitable for this fracture type.

Regarding the basic concept of Cerament™ SpineSupport, with a short-term stabilizing effect with pain relief provided by cured calcium sulfate dehydrate and a long-term osteoconductive effect by the hydroxyl apatite particles, only the pain relief could be demonstrated in our study with short-term follow-up. Whether this bone substitute is able to induce a local increase in bone mass in an osteoporotic patient has to be shown with long-term follow-up studies including longitudinal measurements of the local bone mass.

Conclusions

Initial results indicate that Cerament™ SpineSupport is safe and effective in the treatment of acute osteoporotic vertebral body fractures. Further studies with long-term follow-up are needed to confirm these results and to prove the concept of osteoconduction with hydroxyl apatite particles.

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Endovascular Management for P2 Aneurysms of the Posterior Cerebral Artery

Experience on Proximal Occlusion of the P2 Segment

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Summary

This study evaluated the outcomes of endovascular management for P2-segment aneurysms. From 2003 to 2008, 14 consecutive patients with P2 aneurysms were treated endovascularly by proximal P2 segment occlusion at our institution. The aneurysms included 12 P2a and two P2p aneurysms. Presenting symptoms were caused by subarachnoid hemorrhage (SAH) in six patients, stroke in five, and isolated headaches in three. Mean follow-up was 14 months. Twelve aneurysms were treated with proximal P2 segment occlusion without parent artery revascularization. Twelve aneurysms were at the P2a and two aneurysms at the P2p. Two patients developed hemianopsia after the procedure and one recovered completely within six months follow-up with one still persistent at 22-month follow-up. Proximal parent vessel occlusion was a relatively safe, effective treatment for P2 aneurysms that posed low risk for early or delayed ischemia or infarction.

Introduction

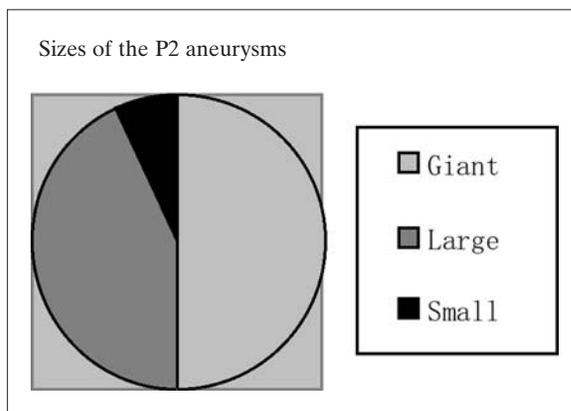
Aneurysms of the posterior cerebral artery (PCA) account for 0.3 to 2.3% of all intracranial aneurysms¹. Most PCA aneurysms arise from P2 region (e.g. spanning from the posterior communicating artery (PCoMA) to the point at which the PCA enters the quadrigeminal cistern), including P2a, and P2p (divided

by the posterior aspect of the cerebral peduncle)¹⁻⁴. Clearly this is a subclass of very complicated aneurysms, in which endovascular treatment may have significant advantages over surgical treatment. The P2 segment is such a location. Terasaka et al⁴ reported that 36% of the patients who underwent a surgical procedure in their series experienced a moderate or severe disability. If it is possible to treat an aneurysm in this location with proximal occlusion of the posterior cerebral artery, then such an approach may be preferable to an open surgical technique^{2,3,5}. Coil embolization of an aneurysm in this location may also make sense if the surgical difficulties are viewed as insurmountable⁶. There will certainly continue to be cases in which endovascular treatment is not the best option for an individual patient, i.e., if the patient cannot tolerate proximal P2 occlusion⁷. However, evaluation of the anastomotic collateral channels prior to a planned artery occlusion is not easily recognizable on routine subtraction angiography. The aim of this study was to retrospectively review our experience with 14 P2 aneurysms treated by proximal P2 occlusion.

Material and Methods

P2 segment

The P2 segment of the PCA was classified according to Krayenbuehl and Yasargil's classification⁸. The P2 segment extends from the



PComA to the take-off of the major inferior posterior temporal trunk. The P2 segment is subdivided into P2a and P2p by the posterior aspect of the cerebral peduncle. P2 aneurysms were arbitrarily defined as aneurysms located at the P2a or P2p segment.

Patient population

Between 2003 and 2008, 14 consecutive patients presenting with aneurysms of the P2 segment treated by proximal coil occlusion of the parent vessel were reviewed retrospectively. There were three females and 11 males ranging in age from four to 56 years (mean age, 30.6 years). Aneurysms arose from the P2 as follows: 12 (85.7%) P2a, two (14.3%) P2p (Figure 1). Clinical presentation included isolated headaches in three patients (21.4%). In five patients (35.7%), the aneurysm caused symptoms of ischemia and compression of midbrain. Six patients (42.9%) presented with SAH. Clinical grading at admission in six patients with SAH, according to the Grade I–V scale of Hunt and Hess, revealed Grade I in four patients, Grade II in two patients. Of the 14 aneurysms, one was small, six were large ($\geq 10\text{mm}$, $< 25\text{ mm}$), and seven were giant ($\geq 25\text{ mm}$).

Radiologic evaluation

All 14 patients underwent cerebral angiography to determine the exact location and configuration of the aneurysm. Computed tomography (CT) and, when available, magnetic resonance imaging (MRI) were used to determine the aneurysm size and the degree of intraluminal thrombosis. Four-vessel angiography was performed to assess the size, shape, configuration, and relationship of the aneurysm neck to the parent artery before the intervention and

the temporal branches of the MCA were evaluated for the potential ipsilateral flow from the anterior circulation to the involved PCA territory.

Treatment

All patients were treated under general anesthesia. Systemic heparinization was achieved during the procedures with heparin 5000U bolus followed by 1000U of heparin every hour. The intravascular procedures were performed in the neurointerventional room under general anesthesia with direct fluoroscopic guidance. The femoral artery was catheterized via the Seldinger technique.

After an 6.0 French sheath was inserted into the femoral artery, 70 mg/kg heparinization sulfate was administered, titrating the activated clotting time to two to three times baseline. Next, a 5.0 French guiding catheter was passed into the cervical vertebral artery, through which a microcatheter (Echelon 10, M.T.I-ev3, CA, USA/ SL-10, Boston Scientific, CA, USA) was passed in a coaxial fashion through the guiding catheter followed by selective catheterization of the artery with the aneurysm in each case. The tip of the catheter was placed in the aneurysm. Coils were selected on the basis of the size of the aneurysm and artery to be occluded. The smallest coil was 2x40 mm (Microvention, Tustin, CA, USA). Angiography was performed after coil placement to confirm occlusion of the aneurysm and the parent vessel. No tolerance test of occlusion was performed in any patient. Patients received anticoagulation therapy for 24 hours.

Follow-up

Eight patients were evaluated at mean 11-month follow-up (range, three months to four years) after treatment including angiography neurological examination. Clinical follow-up was obtained through a telephone interview. The mean duration of follow-up was 14 months (range, two months to four years). The outcomes of the 14 patients are presented in Table 1 according to their modified Rankin Scale (mRS)⁹.

Results

Clinical results

Fourteen aneurysms were dissecting aneurysms. Five patients presented with hemiparesis

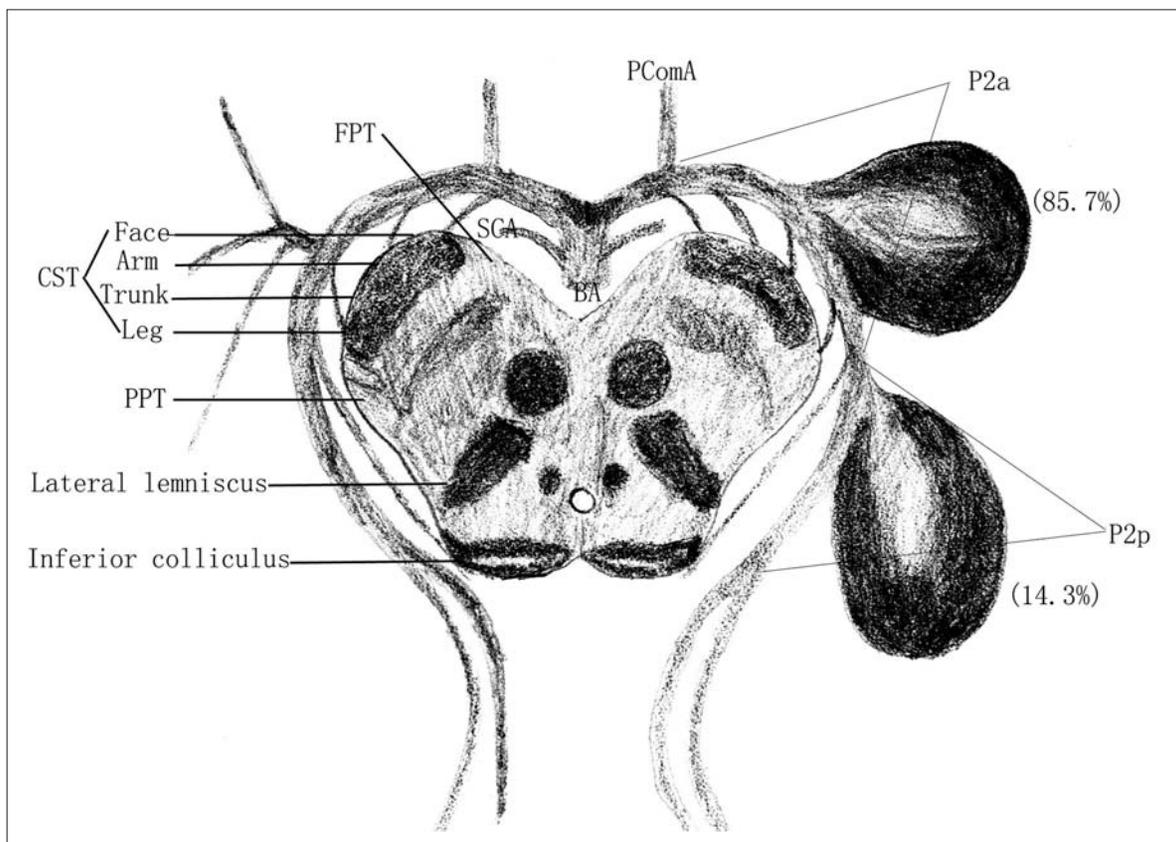


Figure 1 The chart summarizes the location of aneurysms on the P2 in 14 patients: 12 (85.7%) P2a and two (14.3%) along the P2p segment. The frontopontine tract (FPT), corticospinal tract (CST) and parieto-temporal pontine tract (PPT) ranked on the sequence from anterior-medial to posterior-lateral in the cerebral peduncle. Corticospinal fibers to the face, arm, trunk and leg ranked on the sequence from anterior to posterior in the CST. This can explain why patients with P2a aneurysms presented with hemiparesis and palsy of the arm was worse than the leg.

caused by ischemic stroke and the palsy of the arm was worse than the leg. Two patients had hemianopsia postoperatively. In this series, we found no correlation between the size of P2 aneurysms and neurologic signs and symptoms. Arm palsy persisted in two patients, despite a documented shrinkage in aneurysm size and alleviation of the mass effect in one patient and a small aneurysm in other patient.

Resolution of signs and symptoms

Table 1 lists the symptomatology in the 14 patients treated by intravascular coil occlusion for aneurysms of the P2 and shows the number of patients whose symptoms improved after treatment. Hemiparesis, hemihypoesthesia, memory loss and CNIII (oculomotor nerve) palsy were demonstrated in seven patients. After treatment, six of the seven patients had improved movement function. One patient who

had memory and CNIII involvement on presentation improved function of this nerve and memory after treatment.

Complications

Two patients developed hemianopsia after intravascular parent vessel occlusion treatment. One responded to volume expansion and anticoagulation followed by a short course of antiplatelet treatment with no further evidence of hemianopsia. In this series, the overall complication rate was 7.1% (1/14); one patient developed permanent hemianopsia as a result of ischemia.

Illustrative cases

Patient 12

A 46-year-old female patient who presented with acute headaches and left hemiparesis un-

