Osteolysis following resorbable poly-L-lactide-co-D, L-lactide PLIF cage use: a review of cases

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Abstract

Study design Report of case series

Objective To report a problem with bioabsorbable poly-L-lactide-co-D, L-lactide, PLDLLA, posterior lumbar instrumented fusion (PLIF) cage implants.

Summary of background data Synthetic bioabsorbable implants have recently been introduced to spinal surgery and their indications and applications are still being explored. There is evidence that the use of bioabsorbable cages may be of benefit in interbody spinal fusion.

Methods We present a case series of nine patients who have undergone PLIF with bioabsorbable cages in the lumbar spine.

Results At follow-up over at least 1 year, four of these patients were found to have osteolysis around the implant on CT scanning. One of these patients underwent an operation to remove the cage and histology sent during surgery suggested that the implant had caused the bone loss and there was no evidence of infection. Another patient had ongoing pain in relation to the lysis, while the other two patients with lysis remained asymptomatic.

Conclusions PLDLLA cage, which has high osteolytic nature, is considered not suitable as a fusion cage.

Keywords Bioabsorbable cage · PLIF · Osteolysis

Introduction

Synthetic bioabsorbable implants have recently been introduced to spinal surgery however, their indications and applications are still being explored. There are reports of successful use of bioabsorbable interbody cages in both the lumbar [1, 2] and cervical fusions [3, 4]. There are also a number of animal studies that report encouraging outcomes. These demonstrate good resorption of the cage with excellent bony incorporation and bone remodelling leading to a sound arthrodesis [5–7]. There is evidence, however, that resorbable cages may cause osteolysis [8, 9]. In the study by Jiya et al., 2 out of the 12 patients undergoing interbody fusion with resorbable poly-L-lactide-co-D, L-lactide (PLDLLA) cages developed osteolysis.

In this report we present nine patients who underwent posterior lumbar interbody fusion (PLIF) using bioabsorbable PLDLLA cages. At follow-up, four of these patients (44%) had developed osteolysis around the interbody cage. We describe the potential management of this problem in this particular group of patients.

Materials and methods

The patients in the series are aware that the information regarding their cases have been submitted for publication, and have consented to this.

A number of patients underwent posterior instrumented fusion of lower lumbar vertebrae using PLIF cages between 2004 and 2005 in our institution. All the patients had canal stenosis giving symptoms of claudication as well as low back pain. All the cases were performed by a single experienced consultant spinal surgeon. All the patients underwent fusion with a PLDLLA cage along with

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decompression and laminectomy. All the cases in our institution that used PLDLLA cage were included in the series with no exclusions. A total of nine cases were performed. All the procedures were carried out via a posterior approach using the same pedicle screw system to instrument the adjacent vertebrae on each side of the interbody cage. All the cases used the same resorbable Telamon PLDLLA Hydrosorb (Medtronic Sofamor Danek, Memphis, Tennessee, USA). The published surgical technique for the cages was followed. The cages were sized using a trial before inserting a pre-packed implant direct from the manufacturer.

All the patients were followed up routinely in outpatients and imaging in the form of plain radiographs and computed tomography were performed as deemed necessary by the surgeon in charge.

Results

There were six female and three male patients in our series. The mean age was 52, range 37–66. The fusion was at L4/5 in six of these patients, at L5/S1 in two and at L3/4 in one patient. The reason for fusion was degenerative spondylolisthesis in six patients, degenerative disc disease in two patients and a lytic spondylolisthesis in one patient (see Table 1 for further details). To our knowledge none of the patients in the series were taking bisphosphonates and none of the above patients in the series had any bone erosive or destructive diseases.

At a mean of 4-year follow-up, range 3–5 years, five patients have had a sound radiographic fusion with no evidence of osteolysis and a good clinical outcome. The remaining four patients have evidence of osteolysis around the cage. There was no evidence of instability on flexion/extension views in any of these patients nor was there any significantly measurable subsidence of the cages. There was no obvious lucency around the pedicle screws. In all

the four cases, CT scanning demonstrated a sound posterolateral fusion mass with no signs of pseudarthrosis; there was also no sign of cage subsidence. At 4-year follow-up, two of these patients are asymptomatic and have had a good clinical outcome. However, two of these patients had ongoing pain and one required revision surgery.

Illustrative cases

Patient 1 was a 52-year-old woman who underwent a posterior instrumented fusion of L4/L5 in January 2005 for back pain secondary to L4/L5 degenerative spondylolisthesis. An episode of significant bleeding was encountered intraoperatively. The procedure was, therefore, abandoned prematurely in order to get the patient stabilised. This meant that only the left PLDLLA cage was inserted, the right side was packed with bone graft after discectomy alone. The left side cage was inserted in the usual manner using autologous bone graft from the iliac crest. The patient stabilised and further intervention was not required. The patient then went on to make an uneventful recovery and was discharged from hospital 2 days later.

The patient was seen back in clinic 5 months post operatively when it was noted that the patient's symptoms were improved. Radiographs at that point demonstrated a slight subsidence and loss in correction of the spondylolisthesis, but were otherwise unremarkable. At the 10-month review, the patient developed back pain again. Further investigations including a CT scan in December 2005 (11 months from the surgery) revealed that there had been a failure of fusion. Osteolysis was seen with no demonstrable bony incorporation (see Fig. 1). This was at L4/L5 and restricted to the left side only. The patient then went on to have an MRI scan that confirmed osteolysis with a large cavity where the cage should have been, but had not incorporated with the bone.

Table 1 Details of patients who received PLIF surgery using PLDLLA Hydrosorb cages at our institution

Patient sex	Age at surgery	Level of PLIF	Lysis	Symptoms	Length of follow-up (years)
Female	52	L4/5	CT 11 months post-op showed lysis	Ongoing pain declined revision	5
Female	37	L5/S1	CT 16 months post-op showed lysis	Ongoing pain revision surgery	5
Male	56	L4/5	CT 16 months post-op showed lysis	No symptoms	4
Female	63	L4/5	CT 15 months post-op showed lysis	No symptoms	4
Female	66	L4/5	No lysis good fusion	No symptoms	4
Female	46	L3/4	No lysis good fusion	No symptoms	3
Male	39	L4/5	No lysis good fusion	No symptoms	5
Male	57	L5/S1	No lysis good fusion	No symptoms	4
Female	50	L4/5	No lysis good fusion	No symptoms	3

Investigations for low-grade infection were carried out. Inflammatory markers on different occasions did not show any elevation of white cell count, C-reactive protein or erythrocyte sedimentation rate. A labelled white cell scan of the spine did not suggest any infection.

After discussion, the patient opted for no further operative intervention. The patient continues follow-up with annual reviews and CT scans of her lumbar spine, which has continued to show a lucent area on the left side. The CT also showed a satisfactory posterolateral fusion mass with no evidence of pseudarthrosis. Flexion/extension radiographs neither demonstrate any instability nor any sign of subsidence of the cage. The patient has ongoing pain, but no increase in symptoms and prefers continuing opioid analgesics to reoperation. She has stopped working, but manages daily activities. The osteolysis has not increased with time, nor has been improvement.

Patient 2 was a 37-year-old woman that underwent an instrumented fusion of L5/S1 for a spondylotic spondylolisthesis; this was performed in February 2005. An L5/S1 posterolateral instrumented fusion and PLIF were performed using the Hydrosorb cages and autologous iliac crest graft. The procedure and the post-operative recovery were uneventful. She initially felt some benefit from the operative procedure and felt her back pain had improved in the first 3 months after the surgery. However, she had a gradual deterioration over the ensuing 9 months and by a year post operatively she felt that her back pain was worse than ever.

She had further imaging including a CT scan and MRI of her spine carried out in June 2006, 16 months after her

initial surgery, which revealed that all the implants were in an excellent position with no sign of subsidence of the cage. There were erosive changes on the inferior endplate of L5 and the superior endplate of S1 (see Fig. 2). Investigations for low-grade infection including white cell count, C-reactive protein levels and ESR were all within the normal limits. A labelled white cell isotope scan was not suggestive of infection.

The patient continued to complain of progressive back pain not responding to analgesics. In February 2007, 2 years after her initial surgery, she was taken back to theatre. An L5/S1 anterior debridement with insertion of a STALIF (Depuy Spine, Raynham, Massachusetts, USA) PEEK interbody fusion device was performed. The STALIF cage was packed with autologous bone graft. Screw grip was satisfactory.

Histological samples from the debridement revealed fibrocartilage and hyaline cartilage as well as the fragments of collagenous connective tissue containing an infiltrate of histocytes and lymphocytes as well as numerous foreign body type multinucleated giant cells containing large intracytoplasmic vacuoles marking the site where material has leaked out during processing. There was also fibrin deposition and a mild chronic inflammatory infiltrate. There was no active or granulomatous inflammation. Chronic inflammatory cells mainly comprised of lymphocytes. Lymphocytes amounted to more than five cells per high power field (see Fig. 3).

Microbiological assessment of samples revealed no organisms on microscopy or extended cultures. Following this revision procedure, the patient's symptoms settled.

Fig. 1 Computerised tomography scans showing resorption of the bone around the cage. Note on the coronal cut that the bone is only resorbed on the same side as the Hydrosorb cage, the opposite side is unchanged

Fig. 2 Computerised tomography scans showing resorption of the bone around the cage. Note in this patient the whole vertebral body was involved (bilateral cages)

A CT scan in October 2007 showed bony incorporation in the interbody space. She has returned to non-manual work, and has returned to most of her normal activities.

A further two patients underwent posterolateral instrumented fusion and PLIF using PLDLLA cages in early 2005. At follow-up, these patients have had satisfactory clinical outcomes with resolution of their symptoms. However, CT scans have shown osteolysis around their cages in a similar distribution to illustrative case 2 above. The lysis was detected in 15 and 16 months after the surgery, which is a similar post-operative interval as the illustrative cases above i.e. 11 and 16 months. There appeared to be satisfactory posterolateral fusion mass with no evidence of pseudarthrosis present in either case on CT scanning. Both of these patients continue to attend regular follow-up but do not appear to have any problems in

association with the osteolysis. It has been over 4 years since the time of surgery and nearly 3 years since lysis was first noticed. The osteolysis is not progressive. As such it has not been felt necessary to suggest revision surgery as yet. It is not clear why these patients are asymptomatic while others were not.

Discussion

Telamon Hydrosorb PLDLLA cages (Medtronic Sofamor Danek, Memphis, Tennessee, USA) are manufactured from a resorbable polylactide polymer composed of the isomers poly L-lactide (70%) and an equal (racemic) mixture of both poly L-lactide and poly D-lactide (30%). The cage is designed to resorb and according to the company literature retains 100% of its compressive strength for up to 9 months after implantation and completely resorbs between 18 and 36 months.

There is evidence that the use of bioabsorbable cages may be of benefit in interbody spinal fusion. Nonresorbable cages (PEEK or titanium) are exposed to stress shielding, corrosion and may require extraction at some point. Theoretically, a resorbable cage would not suffer from these problems.

An ideal resorbable cage is the one that provides structural support along with loading of the bone graft and resorbs allowing bone graft consolidation without subsidence or osteolysis. The fact that an osteolytic response has occurred makes the use of such bioabsorbable implants questionable in the spine as they have not only failed to promote fusion, but actually may have lead to more bone loss. Although there are reports of successful use of bioresorbable cages being used in both human patients and

Fig. 3 Showing the histology from the tissue removed at the surgery. Note the presence of giant cells (arrow)

animal models [1–7]; our series have shown a 44% rate of osteolysis in use of the PLDLLA PLIF cages (4 out of 9 cases). Jiya et al. [8] describe a 16% osteolysis rate in their paper and a worrying rate of subsidence and failure of fusion compared to PEEK cages. Herceg et al. [9] presented a similar results at the North American Spine Society meeting. Jiya raises the possibility that osteolysis may be due to low-grade infection, but we feel the supplementary evidence from this report does not support this hypothesis.

PLDLLA degrades in a number of ways through chemical, thermal, mechanical and physical mechanisms [10] of these the chemical degradation is the most important and is primarily through hydrolysis and metabolism in the citric acid cycle [10]. Disintegration of the PLDLLA cages into multiple fragments and initial absorption of small PLDLLA fragments are observed 1 year after the implantation. Bone formation rate and bone remodelling are elevated at 12 months, probably because of disintegration of the PLDLLA cages. Thereafter, PLDLLA cages were replaced with trabecular bone and dispersed fibrous tissue progressively [11, 12].

These PLDLLA cages have caused problems in the animal models. Kandziora et al. [13] showed that PLDLLA cages were associated with the osteolysis in a sheep model post operatively after only 12 weeks. They found a severe foreign body reaction causing osteolysis around the PLDLLA cage and suggested scepticism over the value of PLDLLA as an implant. A further study a sheep model using 16 sheep with PLDLLA cages demonstrated no fusion present in any animal between 12 and 24 months follow-up. There was an associated foreign body reaction accompanied by severe cage degradation [14]. This is similar to the histology taken from patient 2 showed that there numerous foreign body type multi-nucleated giant cells containing large intra-cytoplasmic vacuoles with no active or granulomatous inflammation. It is likely that the cases with osteolysis in the above series are initiated by these PLDLLA fragments. They may cause more osteoclastic than osteoblastic activity, therefore, bringing about bone lysis rather than laying down trabecular bone.

We report on 4 out of the 9 patients who had biore-sorbable PLDLLA PLIF cage insertion for lumbar spine fusion and would appear to have undergone an osteolytic reaction to the resorbable cage or as a consequence of the resorption process.

Patient 1 was interesting as only a left-sided PLIF cage was inserted into the patient. It was only this half of the vertebral body that was expansively lucent as seen on the CT scan (see Fig. 1). This strengthens the hypothesis that the cage is directly responsible for the osteolysis.

It is possible that the osteolysis could have occurred as a result of infection. The histological features from the

second case with the presence of numerous foreign body type multinucleated giant cells containing large intra-cytoplasmic vacuoles is highly suggestive of the PLIF cage causing the osteolytic response rather than an infective process. Furthermore, the specimens sent for microscopy culture and sensitivity from patient 2 failed to identify the presence of any organisms. Along with this the inflammatory markers from both the patients were all within the normal limits and the labelled white cell scans did not suggest any infection. None of these patients suffered from bone erosive or destructive diseases.

It is also possible that the osteolysis was secondary to mechanical failure of the implants resulting in the instability and osteolysis. While this is a possible explanation we feel that the lack of movement on flexion/extension radiographs along with the fact that there was no obvious subsidence of the cages goes against this. The post-operative CT scans taken that show the osteolysis around the cage also demonstrate a satisfactory posterolateral fusion mass with no evidence of pseudarthrosis. It, therefore, seems unlikely that the osteolysis of the vertebral body is secondary to instability.

It was also of interest that of the four cases with established osteolysis, all had features of this within 16 months. However, only 2 of the 4 cases had significant symptoms warranting further surgical intervention. The one patient that underwent revision surgery had a successful anterior procedure with no further osteolysis using a PEEK anterior implant with autologous graft. The remainder of the patients (including one that declined further surgery) have not had deteriorating symptoms and importantly no increase in the osteolysis. It seems that revision surgery is not absolutely necessary when osteolysis appears in this patient group and we are guided by the patient's severity of symptoms. As yet the osteolysis is not progressive; all of these patients have evidence of a solid posterolateral fusion on CT scans. This may explain why they have managed or even been asymptomatic despite the lysis around the vertebral body.

Some patients seem to go on to develop a sound fusion in the presence of the PLDLLA implant. The demographic details and medical co-morbidity of these patients who went on to fuse were not different to those who developed osteolysis. None of them was on bisphosphonates. We do not understand why some patients seem to develop lysis while others do not. It is possible that they respond differently to the PLDLLA fragments. The PLDLLA fragments seem to cause osteolysis in a significant subgroup of patients. This is in keeping with animal models where only some of the animals developed osteolysis while, others appeared to progress to fusion [13]. Further work is necessary to determine what is different in the subgroup that undergoes osteolysis.

The implanted cages were all pre-packed and direct from the manufacturer. Therefore, changes to the material from repeated or inappropriate sterilisation methods did not contribute to the osteolysis seen.

We conclude by suggesting caution when using this PLDLLA implant as part of a lumbar fusion. With an osteolysis rate of 44%, we did not feel that resorbable cages should be used in the spine.

Conflict of interest None.

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