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Bone histomorphometric evaluation of a clinically fused titanium tumour cage in a child

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Abstract An intervertebral titanium tumour cage was implanted in a 2-year-old-girl after T11 spondylectomy due to Ewing sarcoma. After 2-years' follow-up without evidence of recurrence, the titanium cage was explanted to correct spinal deformity and to allow normal spinal growth development. Radiological follow-up and surgical exploration at the time of retrieval suggested fusion of the segment. Histologic evaluation, however, demonstrated ingrowth of trabecular bone, but without bridging trabecular bone. The distance between the opposing bone fronts measured 1.5 mm and the viable bone volume (BV/TV) within the cage was 36%. Histologic evaluation

demonstrated that bone formation was still an ongoing process in the fusion zone 2 years after implantation.

Keywords Histomorphometry · Interbody fusion · Tumour cage · Titanium

Introduction

Over the last decade, the use of interbody cage devices has attracted progressive interest in the treatment of degenerative disorders of the spine and in spinal reconstruction after trauma or tumour resection [6, 15]. Despite initial favourable outcome compared to interbody fusion with the use of bone graft alone [1, 2, 5, 10], concerns may arise because the long-term effects of cage devices on the spinal segment are still unknown. In addition, post-operative complications such as cage migration and pseudarthrosis, leading to revision procedures, have recently been reported [3, 7, 11, 12]. Retrieval studies of failed cages showed ingrowth of bone along one side of the cages, but fibrous and fibrocartilage tissue at the opposite side, indicating that these cages were fixated only on one side [7, 11].

Histologic and bone histomorphometric evaluation of an apparently fused titanium cage device in humans has never been reported. The presented case may deepen the current knowledge on bone formation and bone remodeling occurring in cage devices after longer follow-up intervals.

Case report

A 2-year-old girl was referred to our hospital with a 2-week history of progressive gait disturbance. Physical examination revealed a paraparesis with a sensory level at T11 and sphincter disturbance. Magnetic resonance imaging (MRI) showed an epidural tumour with involvement of T11 and anterior compression of the spinal cord (Fig. 1). Emergency decompression laminectomy T10–12 was performed with debulking of the tumour mass around the spinal cord. Pathological evaluation of the surgical specimens and subsequent screening for metastasis demonstrated an isolated Ewing sarcoma. Adjuvant chemotherapy (protocol EICESS-92) was

Fig. 1 Preoperative T1-weighted magnetic resonance (MR) image of the spine, showing destruction of the T11 vertebra and anterior compression of the spinal cord

Fig. 3 Anteroposterior (A) and lateral (B) plain radiographs showing incorporation of the vascularised fibular graft 11 months after surgery, but still a significant non-progressive thoracolumbar kyphoscoliosis

Fig. 2 Anteroposterior (A) and lateral (B) plain radiographs showing the titanium tumour cage in situ with a significant thoracolumbar kyphoscoliosis

Fig. 4 Contact lateral radiograph of the explanted cage demonstrating mineralised tissue through the fenestrations of the cage

administered. After three cycles of chemotherapy, however, the tumour response was classified as non-responding. After consulting the EICESS Study Centre (Münster, Germany) and the hospital's sarcoma team, it was decided to perform a surgical intervention (i.e. vertebrectomy and reconstruction). A custom-made titanium

Fig. 5 Histological transverse sections of the explanted cage. The proximal (A) and distal (C) side of the cage show trabecular bone formation without direct apposition towards the cage. (B) Centre of the cage shows mainly fibrous and fibrocartilage tissue in the fusion zone (basic fuchsin and toluidine blue $\times 25$)

cage [14] to replace the T11 vertebra was chosen rather than a biological reconstruction (e.g. autologous bone), because of the uncertainty of the prognosis. Accordingly, a spondylectomy T11 was performed using a combined posterior and anterolateral approach. Anterior reconstruction was achieved with a cylindrical titanium cage (height: 18 mm, outer diameter: 13 mm, Stryker-Howmedica-Osteonics, Kiel, Germany) packed with rib graft and stabilised with custom-made anterior instrumentation (Fig. 2). A non-vascularised split fibular graft (length: 8 cm) was fixated to the spinous processes and lamina of T9–L1 as posterior stabilisation [8]. The postoperative course was uneventful and adjuvant chemotherapy was continued. The patient made a complete neurological recovery without evidence of recurrence at 2-years' follow-up. However, a progressive junctional kyphosis of 55° combined with a 25° thoracolumbar scoliosis developed. Radiographs disclosed resorption and dislodgement of the proximal site of the fibular graft, but without signs of cage migration or loosening in the instrumented area. A second intervention through an anterior approach rather than a posterior approach was chosen: explantation of the titanium cage, correction of the deformity, stabilisation of the defect by a double-folded vascularised fibular graft, and anterior instrumentation was performed [16]. At the time of surgery, the cage demonstrated solid anchorage on both sides, suggesting complete fusion of the spinal segment. The postoperative course was uneventful. At 11 months follow-up, radiographs showed complete incorporation of the fibular graft, but still a non-progressive scoliotic and kyphotic deformity (Fig. 3).

Contact radiographs of the explanted cage were obtained and the specimen was further processed for undecalcified bone histology [13]. Although contact radiographs suggested bridging trabecular bone (Fig. 4), midsagittal and transverse histological sections disclosed no bridging of trabecular bone in the centre of the cage and a fibrocartilage gap of 1.5 mm (Fig. 5, Fig. 6). In addition, histological sections demonstrated a fibrous tissue layer along the cage walls without bone apposition directly to the cage. Histologi-

cally, the non-fusion zone consisted of dispersed enchondral bone formation and partially resorbed bone graft particles, which were incorporated in cartilage matrix. Features of ongoing bone formation, but not of a pseudarthrosis, were found. On both sides along the walls of the cage, intramembranous bone formation was observed. The viable bone volume (BV/TV) within the cage was 36% of the total volume within the cage. The total bone volumes within consecutive transverse fields of 1 mm height throughout the entire cage (total: 17 fields) are summarised in Fig. 6. The total bone volume decreased from 56% at the periphery to 5% towards the fusion zone. The percentage of lamellar bone ranged from 99% at the periphery to 49% at the fusion zone, while the percentage of woven bone ranged from 1% at the periphery to 51% at the fusion zone.

In summary, the presented case represents a unique treatment of a Ewing sarcoma patient. The histological and bone histomorphometric results clearly demonstrate that bone formation is still an ongoing process after 2 years' follow-up, which was evidenced by the presence of enchondral bone formation and by bone remodeling adjacent to the fusion zone within the cage.

Discussion

There is a lack of data about apparently successfully fused cages in humans. The current report, therefore, may deepen our knowledge about ongoing bone formation and bone remodelling within a retrieved cage, and can be used for comparison with histological findings of failed cage fusions.

Togawa and Bauer reported histological findings of 50 failed fusion cages: similar to our report, little to no bone apposition to the inner surface of the cages was present [11]. Contrary to the present report, the failed cages showed only ingrowth of viable bone along one side of the cage, while the other side showed only fibrocartilage tissue. Unlike our findings, hyaline cartilage was not associated with bone formation. The histological findings of

Fig. 6 Trabecular bone formation and percentage of woven and lamellar bone throughout the cage, measured within consecutive transverse fields of 1 mm height (total: 17 fields), are summarised in the graph. A longitudinal histological section of the titanium cage is presented below. The scale of the x-axis corresponds with the scale (i.e. height) of the cage, and thus with the measured transverse fields within the cage (see arrows)

Togawa and Bauer were confirmed in another study on failed cage fusions [7]. In addition, in this latter study, the mean percentage of trabecular bone within the cage was calculated: there was a mean percentage of 28.6% (range 15–40%), comparable with the bone volume in the current report (BV/TV: 36%). Analysis of bone volume formed within cage devices may provide further insight into the stress-shielding effect of metal and titanium cages, and may confirm recently reported biomechanical data demonstrating the stress-shielding effect of cage devices [4].

The histological findings in this study may be explained by several underlying components. First, adjuvant chemotherapy may have negatively influenced the process of bone formation and remodeling. Secondly, the height of the cage may be a critical size defect preventing complete fusion. Thirdly, an evident mismatch of the modulus of elasticity existed between the titanium cage and vertebral bone, leading to a stress-shielding effect. Another explanation may be that a relative instability of the spinal construct influenced the rate of interbody fusion, although the cage was not evidently loose at the time of retrieval – a phenomenon not well understood. Similar problems with respect to stand-alone cages were reported by Nilsson et al. [9]. Finally, the spinal segment may eventually fuse after a longer follow-up period, considering bone formation was still going on after 2 years' follow-up.

Based on the results of this retrieval, we conclude that bone formation within a cage can still be an ongoing process even after several years of implantation. However, it should be taken into account that no definitive statements on the process of histological fusion and bone remodeling can be made based on one case report. Further investigations of apparently fused interbody cages are needed for improving our understanding of the process of bone formation and remodeling within cage devices.

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