

Iliac crest bone graft: a 23-years hystory of infection at donor site in vertebral arthrodesis and a review of current bone substitutes

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Abstract. – OBJECTIVE: This is an exemplary case report underlining a relevant morbidity which could be associated to the use of autologous iliac crest bone graft (ICBG) for spine fusion.

CASE REPORT: Starting from 1990, a 25-years-old woman underwent two subsequent surgical treatments for non-Hodgkin lymphoma vertebral localizations. In the second surgery, arthrodesis was obtained with autograft through right posterior iliac crest osteotomy. During the chemotherapy treatment following the surgery, the patient suffered from infection at posterior iliac crest scar, the site of previous graft, caused by methicillin-resistant *Staphylococcus aureus*. She was subjected to surgical debridement and specific antibiotic treatment with local healing and phlogosis index reduction. Chemotherapy protocol was concluded and the patient healed with definitive lymphoma remission. After 22 years the patient had a relapse of donor site infection, requiring a new antibiotic therapy and a new surgical debridement.

RESULTS: The relapsed infection at donor site lasted for a long period, more than one year, despite of specific care. It finally healed after another accurate surgical debridement and post-operative antibiotic therapy.

CONCLUSIONS: This case report underlines the possible consequences on the patient's quality of life of a long-term disease affecting the iliac crest bone graft donor site. Literature concerning alternatives to autograft for spine fusion is also reviewed.

Key Words:

Spine fusion, Iliac crest bone graft, Bone substitutes, Donor site, Morbidity.

ognized drawbacks on iliac crest bone graft, including increased operative time, increased blood loss, increased donor site morbidity, and a limitation to the amount that can be realistically harvested for multilevel fusion¹. Successful fusion has been demonstrated following iliac crest bone grafting in various applications in lumbar spine surgery^{2,3}. However, the morbidity rates associated with the use of ICBG remain high, with some studies reporting up to a 50% rate of persistent donor site pain, paresthesias, hematoma and infection⁴. Other authors⁵⁻⁸ describe a complication rate ranging from 2.4% to 5.8% for major complications and from 9% to 37.9% for minor complications. Because of donor site morbidity, spine surgeons have increasingly used synthetic and recombinant bone graft extenders, and a whole industry has arisen from this market⁹: local autograft, allograft, demineralized bone matrix (DBM), synthetic bone grafts (ceramics), bone morphogenetic proteins (BMPs), autogenous growth factors (AGFs), bone marrow aspirate (BMA) and collagen-based matrices are the most popular bone graft substitutes gaining popularity and being increasingly used in the lumbar spine. We report here a peculiar case of a 25 years ICBG site infection in a patient submitted to revision surgery because of a T10 non-Hodgkin lymphoma: the intention of this exemplary case report is to remind how the morbidity in autograft shouldn't be underestimated and it also represents an occasion to review the synthetic alternatives and report our experience in this field.

Case Report

A 49-years-old woman presented at admission with worsening pain at right pelvis and recurrent fever. Twenty-two years before, she underwent a surgical debridement for an infection due to Methicillin-Resistant *Staphylococcus aureus* (MR-

Introduction

Iliac crest bone autograft (ICBG) has long been considered the gold standard for fusion procedures in spine surgery. However, there are rec-

SA) occurring at iliac crest in the site of a previous bone autograft. Microbiological results from needle biopsy confirmed an active MRSA local infection at posterior iliac crest where a fistula appeared.

The patient's history was collected: in July 1990 the patient (aged 25-years-old) was referred to our unit because of a T10 neoformation compressing the epidural space and submitted to T10 posterior decompression and secondary T9-T11 stabilization with Hartshill hardware. Twenty months later a T8 wedge fracture occurred and the patient was urgently admitted to our unit and underwent hardware removal and new arthrodesis with T6-T12 Roy-Camille plates. Arthrodesis was obtained with autograft through right posterior iliac crest osteotomy. The histological exam revealed a high-grade non-Hodgkin lymphoma and patient was addressed to the Onco-Hematologic Unit. Two months after discharge the patient began chemotherapy according to the F-MACHOP protocol consisting of 6 cycles, but soon after the first cycle a fistula appeared in the wound scar at the right iliac crest, the site of the previous graft. Phlogosis blood index increased. Subsequent hospitalization was necessary and microbiological diagnosis of methicillin-resistant *Staphylococcus aureus* (MRSA) infection at posterior iliac crest scar was made after swab. A surgical debridement of the abscess was performed, washing drains were left in place for few days and a treatment with specific antibiotic was performed for other 8 days with local healing and phlogosis index reduction.

Chemotherapy protocol was concluded and the patient healed with definitive lymphoma remission. The patient underwent regular clinical and radiological follow-up; she stayed asymptomatic, both at lumbar and iliac crest sites, for several years until Summer 2014 when symptoms and local signs of donor site infection relapsed.

At this time an antibiotic specific therapy with Daptomycin, Oxacillin and Linezolid started, and a new surgical debridement was performed.

Despite the specific care, the infection was still present in Autumn 2015, after 23 years from the graft, when the patient came back to our attention. At admission, she presented painful at the right side with a purulent fistula at the donor site (Figure 1).

Surgical debridement was performed (Figure 2) with wide curettage of the pathological area and copious washings. A postoperative specific antibiotic therapy started and continued until

blood phlogosis index negativity. Currently, the body scan is negative, the wound healed and the patient is asymptomatic.

Discussion

In order to achieve fusion in vertebral surgical procedures, the instrumentation can stabilize the spine at first and then the final success depends on both biological and host factors, which determine fusion to the adjacent bone segment. Many spinal fusion procedures require the use of bone grafts, and spinal fusion largely depends on the osteoconductive and osteoinductive properties of bone grafts or their substitutes.

The massive amount of cancellous bone that can be obtained from the inner table of the pelvis provides all the desired properties of osteoconduction, osteoinduction and osteogenicity, necessary to obtain a solid arthrodesis. The large surface area of this bone graft has the optimal chemistry, structure, and porosity to serve as an excellent scaffold for new bone formation. Similarly, it contains all the necessary bone-forming growth factors and it is inherently osteoinductive. Fur-

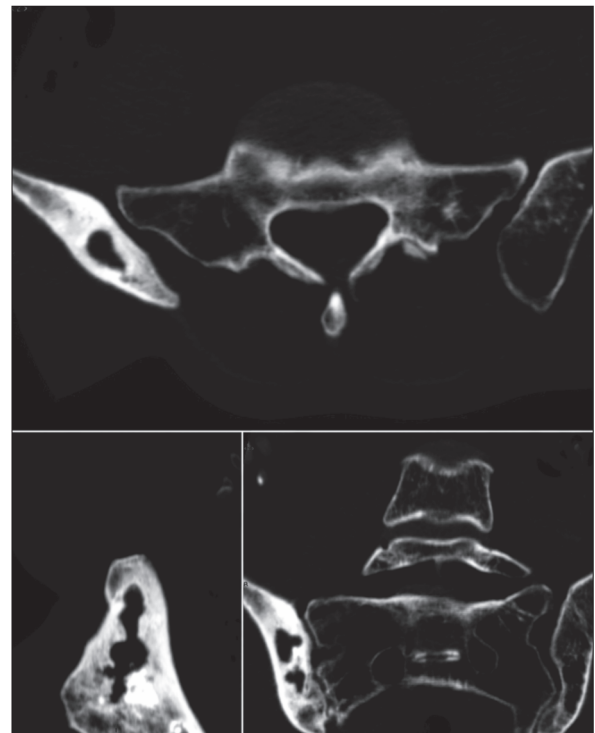


Figure 1. Preoperative CT images of iliac donor site infection 23 years after grafting. A central large osteolysis is surrounded by sclerotic bone.

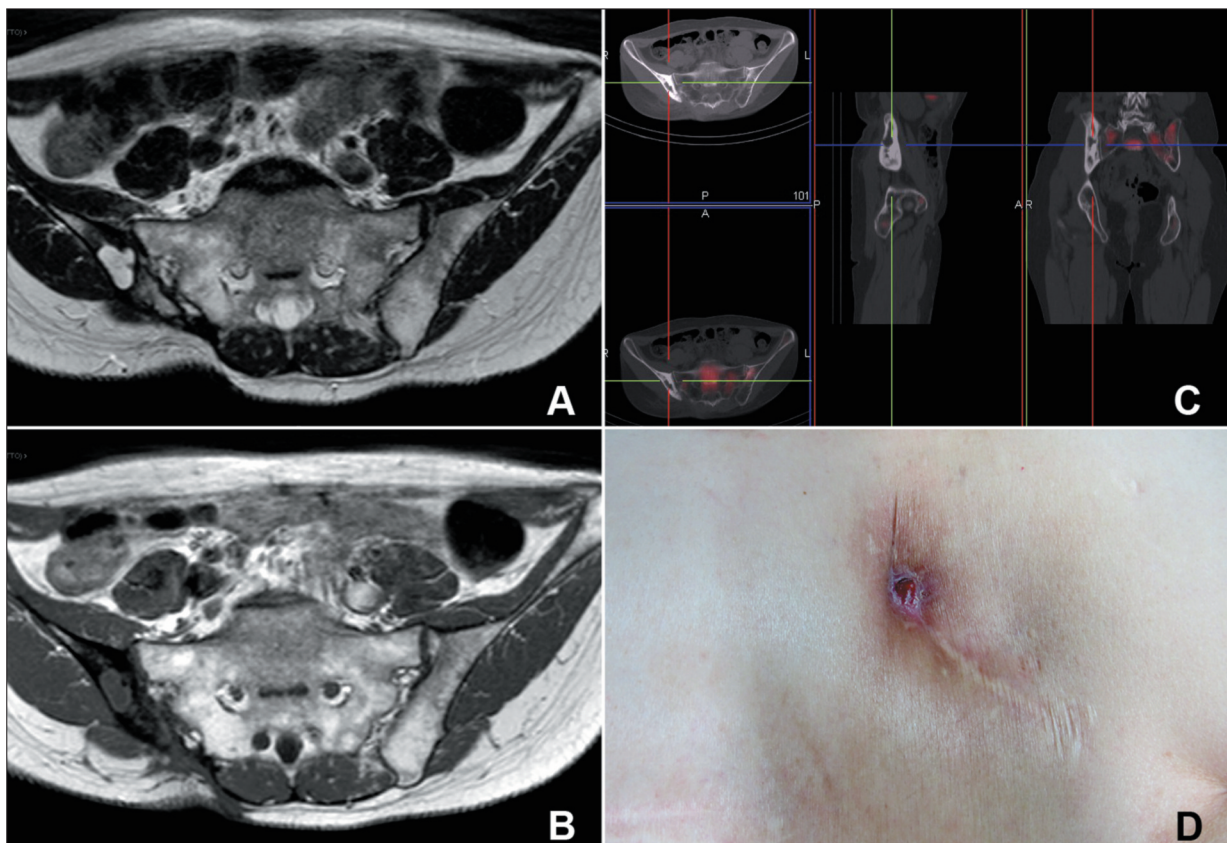


Figure 2. Preoperative MRI (A, B) shows liquid at iliac crest contest hyperintense in T2 and hypointense in T1, compatible with purulent material. PET scan (C) confirms contrast enhancement at iliac right site. D, Preoperative cutaneous fistula.

thermore, cancellous bone is easily re-vascularized and rapidly incorporated at the host site. There are no concerns for disease transmission and no risks of immunogenicity¹⁰. The use of iliac crest bone graft (ICBG) has been well-supported in the literature^{2,3,11,12} with fusion rates as high as 93%. Nowadays, it is considered the gold standard in spine fusion.

Morbidity associated with its use is also well reported. Donor site morbidity can be attributed to the harvesting procedure of the ICBG. This procedure is associated with longer operative times, increased estimated blood loss, and a longer hospital stay^{13,14}. Major complications have been reported ranging from 0.7% to 25%, including infection, prolonged wound drainage, large hematomas, reoperation, pain lasting more than 6 months, sensory loss, scar, joint subluxation, gait disturbances, sacroiliac joint destabilization, herniation of abdominal muscles and contents, iliac or pelvis fracture, and heterotopic bone formation^{15,16}. Minor complications are more common, with a reported complications

rates ranging from 4 to 49%. These complications included superficial infection, minor wound problems, temporary sensory loss, and mild or transient pain. Swan and Goodacre¹⁷ studied the complications of iliac bone harvesting in 72 patients. The postoperative donor site complications included persistent pain at the donor site in 7% of cases (all resolved within 6 months) and superficial wound infections in 3% of cases (successfully treated with oral antibiotics). In all of the studies reviewed, there were no reports of long-term infective complications at the iliac crest donor site.

In the literature there are others example of wound/donor site infection after ICBG procedures: Calori et al¹⁸ found local infections at the donor site in 14.28% cases of ICBG group; according to Pirris et al⁹, one patient (4%) of his series developed a deep wound infection that required operative irrigation and debridement. Armaghani et al¹⁹ report one superficial wound infection and a postoperative hematoma, both of which were treated successfully with close obser-

vation and oral antibiotics; they register no deep wound infections requiring a revision surgery or a readmission to the hospital.

Similarly to our case report, De Riu et al²⁰ report an unusual complication: a huge iliac abscess that appeared 4 years after bimaxillary surgery involving iliac bone grafts. Concerning our case report, at our knowledge 25 years delayed abscess has never been described before as a complication in ICBG donor site morbidity.

For these reasons, much progress has been made in the field of bone graft alternatives for spinal fusion; approximately 1,400 products are available on the international market for use as bone void fillers. We briefly review the main ICBG alternatives.

Local autograft: Park et al²¹ have shown equivalent fusion results for local laminectomy bone autograft (ALB) and ICBG in a single level posterolateral fusion.

Allograft bone has been the most widely used as a substitute to avoid complications of donor site morbidity, but its use is associated with an increased risk of infection and rejection, and it has poor osteoinductive properties²². The reported fusion rates with the use of fresh-frozen or

freeze-dried allograft bone in posterolateral lumbar fusions have wide variability in the literature²³, probably due to its poor osteogenic or osteoinductive properties that do not induce new bone formation in the same manner as the autogenous bone graft. Moreover, they generally provide no initial mechanical support and must be used in conjunction with a scaffold or fixation^{24,25}.

Ceramics are osteoconductive and biodegradable bone graft scaffolds²⁶⁻³⁰. These agents consist of coralline hydroxyapatite, β -tricalcium phosphate, silicate-substituted calcium phosphate, calcium sulfate, or a combination of these minerals. Ceramics have several advantages; they are nontoxic, nonimmunogenic, easy to sterilize, and have limitless availability. Their disadvantages are that they are brittle and have a little shear strength or fracture resistance. Because they offer minimal mechanical stability in the immediate postoperative period, ceramics are usually insufficient as scaffolds in lumbar fusion surgery^{22,30}.

Platelet gels are osteoinductive and are used as bone graft enhancers in conjunction with ICBG, ALB, or allograft bone. It would make logical

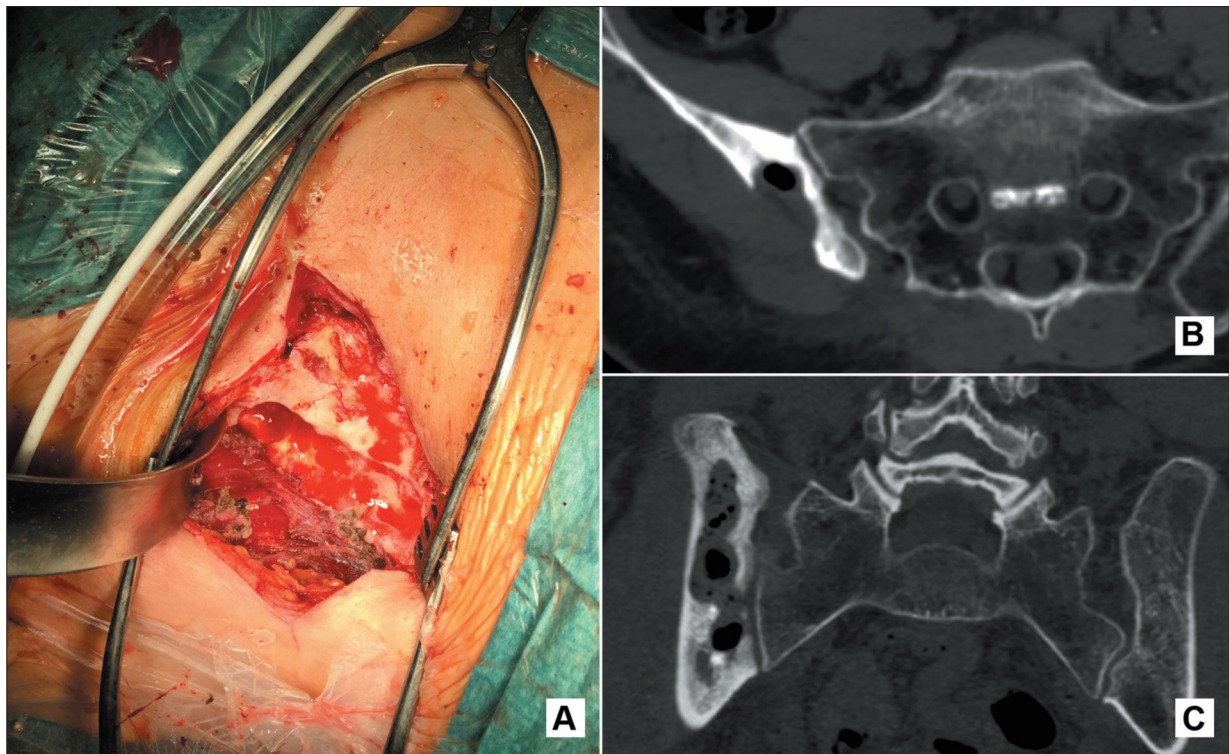


Figure 3. *A*, Intraoperative debridement with iliac crest bone milling. *B*, *C*, Postoperative CT showing bone defect after donor site debridement.

sense that the addition of platelet gel to autologous iliac crest would enhance fusion rates due to the presence of TGF- β and PGDF. However, clinical study findings refute this hypothesis. Potential reasons for these results include rapid dissolving of the platelet gel and diffusion of growth factors²⁹.

With reported fusion rates of 95% to 98%, bone morphogenetic proteins have revolutionized the ability to achieve successful fusion in the lumbar spine. BMP induces bone formation by influencing mesenchymal stem cells. Disadvantages include ectopic bone formation in the neural foramen and the central canal after BMP use; radiculitis, occurring just days after surgery, is also a known complication of BMP use, osteolysis also a serious complication following BMP use. Wound dehiscence and infection have been reported in multiple papers³¹.

Bone marrow aspirate (BMA) is both osteoinductive and osteogenic. It is typically used with a structural graft to give it mechanical strength. Its inherent advantages are the minimal harvesting site morbidity and the high amount of Demineralized Bone Matrix (DBM) which has emerged to enhance, and often supplant, the use of freeze-dried allograft. DBM retains the same properties as freeze-dried allograft but without the mineral content. It serves as an effective osteoconductive scaffold and contains type I collagen and non-collagenous proteins. Much like allograft it is relatively inexpensive and unlimited in quantity compared to ICBG. Its main disadvantage is the inherently variable osteoinductive properties. The osteoinductivity of DBMs has been well documented in preclinical studies³²⁻³⁴. However, few clinical studies have evaluated the efficacy of DBM as a bone graft extender in instrumented posterolateral fusion with respect to an iliac crest bone autograft alone^{35,36}. Our experience consists on an *in vivo* study aimed to carry out an evaluation of the osteoinductive and osteoconductive properties of two bone substitutes composed of MgHA granules or HDBM-MgHA dispersed in a biomimetic matrix, which has previously shown *in vitro*^{37,38} biocompatibility and biological proprieties similar to an autograft. The osteogenic ability of these compounds was evaluated and compared with a cortical-cancellous bone autograft in an ovine model of lumbar spine instrumented fusion to reproduce a model as close as possible to the surgical procedure performed on humans. Our histomorphometric results showed that MgHA stimulated the deposition of newly formed bone

tissue similar to autologous bone in a higher amount with respect to HDBM-MgHA. Finally, the bone surface to volume ratio parameter, a useful basic 3-dimensional parameter in characterizing the complexity of structures, showed that newly formed trabecular bone around MgHA biomaterial presented a greater surface than autologous bone³⁹. The Authors considered the combination of osteoinductive and osteoconductive materials such as DBM and concluded it can be a valid alternative to the autologous/homologous bone, thus perhaps overcoming the limitation of current therapeutic strategies.

Conclusions

Major and minor complications at donor site are described in the literature. An ideal bone graft substitute with little or no associated complications and risks does not exist at this time. Currently, autograft is considered to be the gold standard but it shows few limitations: this case report describes a 25-years disabling ICBG donor site morbidity that required revision surgeries during years. The recent development of bone graft substitutes represents a great advance in caring for these patients. Each graft alternative has advantages and disadvantages, and the options must be considered on an individual, risk-benefit basis to select the best option for each patient undergoing spinal fusion. This case report also underlines the possible consequences on the quality of life in patients with rare, but still possible, chronic long-term donor site disease.

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Conflict of Interest

The Authors declare that there are no conflicts of interest.

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