CORR Insights

CORR Insights®: What Is the Role of Allogeneic Cortical Strut Grafts in the Treatment of Fibrous Dysplasia of the Proximal Femur?

Richard W. Nicholas Jr MD

Where Are We Now?

One deformities in patients with fibrous dysplasia can be potentially disabling and difficult to treat. When involving the proximal femur, fibrous dysplasia is often progressive; resulting in pain, varus angulation of the hip (shepherd's crook deformity) and potentially, pathological fractures [6, 7]. The disease process is caused by a postzygotic (somatic) mutation of the *GNAS* gene, manifesting in poorly functioning osteocytes, which produce an inferior quality fibro-osseous bone [9]. The

extent of the disease, as well as its extraskeletal manifestations (such as McCune–Albright Syndrome), depends upon the eventual location of the migrating, abnormal embryonic cells [2, 10].

Traditional treatment with curettage and grafting has been associated with resorption of the graft and replacement with newly formed, dysplastic bone produced by the persistent population of abnormal osteoblasts [7]. Enneking and colleagues [3] have suggested that cortical allografts may provide superior outcomes when treating lesions of the femoral neck. The suggestion was

that incorporation (or replacement) of the cortical bone would be limited in comparison to cancellous grafting thus maintaining structural support the femoral neck. Evaluation of retrieved bulk allografts, previously implanted for tumor reconstructions confirmed (at least adjacent to normal bone) that allografts demonstrated delayed and incomplete incorporation [4]. Such findings suggest that the premise might also be valid in fibrous dysplasia.

Shortly after the Majoor and colleagues paper was accepted for publication, a similar article was published—also from a national referral center (NIH)—maintaining a longitudinal database for patients with fibrous dysplasia [5]. Leet and colleagues reviewed surgical management of long bone lesions in their patients, comparing various grafting techniques including cortical allografts. They identified no differences in outcome comparing patients treated with the cortical grafts versus other techniques, concluding that both allografting and autograft are of “limited value in ablating lesions of fibrous dysplasia” [5].

This CORR Insights® is a commentary on the article “What Is the Role of Allogeneic Cortical Strut Grafts in the Treatment of Fibrous Dysplasia of the Proximal Femur?” by Majoor and colleagues available at: DOI: 10.1007/s11999-016-4806-3.

The author certifies that he, or a member of his immediate family, has no funding or commercial associations (eg, consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted article.

All ICMJE Conflict of Interest Forms for authors and *Clinical Orthopaedics and Related Research®* editors and board

members are on file with the publication and can be viewed on request.

The opinions expressed are those of the writers, and do not reflect the opinion or policy of *CORR®* or The Association of Bone and Joint Surgeons®.

This *CORR Insights®* comment refers to the article available at DOI: 10.1007/s11999-016-4806-3.

R. W. Nicholas Jr MD (✉)
Department of Orthopaedic Surgery,
University of Arkansas Medical
Sciences, 4301 West Markham, Slot 531,
Little Rock, AR 72205, USA
e-mail: rnicholas@uams.edu

CORR Insights

The two seemingly parallel studies show that controversies remain. In fact, there are potentially important differences between the two studies, most notably in patient demographics (more polyostotic disease, concurrent endocrinopathies and younger patients in the NIH review). The Netherlands study lacks a comparison group for surgically treated patients, but was instead structured to investigate the potential differences between successful allografts and those that failed. Additionally, the current paper specifically reviews a select population of patients with proximal femur lesions and not a variety of long bone lesions.

Where Do We Need To Go?

The authors' exclusion criteria indicate that advanced disease was not considered amenable for treatment with cortical allografting, a presumption that may be correct based on their findings of higher failure rates even in patients with nondisplaced fractures and extensive disease in the femoral head. Clearly questions remain on the best means to treat the complex and vexing clinical problem of proximal femoral fibrous dysplasia. Drawing from the information in the current study, orthopaedists could anticipate that cortical allograft reconstruction of the proximal femur—in selected

individuals with fibrous dysplasia—can be used successfully with approximately 50% of treated patients achieving stability, at least for a substantial period of time. However, currently there is no adequate biological solution for the underlying disease process, and progression is likely for many patients.

How Do We Get There?

Because additional surgery or disease-related complications will result in many patients, a method of controlling fibrous dysplasia is desirable. Considering that the underlying disease process is responsible for the structural weakness and lack on integrity of the proximal femur, future treatments may best be focused on the disease rather than the deformity. Bisphosphonates alter bone remodeling and have been shown useful at modifying painful symptom in fibrous dysplasia [8]. However, a subsequent carefully designed, randomized control trial has failed to demonstrate an ability of these compounds to prevent disease progression [1].

Although initially promising in the case reports (and anecdotally successful in several of my own patients) I do not think that bisphosphonates will be the answer to fibrous dysplasia. One logical question can be raised as to why such

drugs, which alter osteoclast function, would ultimately control a disease of disordered osteoblast bone formation. Investigations into medically altering the abnormal bone production, the rate of bone turnover, or preventing the accumulation of abnormally produced osteoid are possible avenues for intervention. Genetic manipulation of the abnormal cells themselves may hold the most promise for future study and therapeutic intervention.

References

1. Boyce AM, Kelly MH, Brillante BA, Kushner H, Wientroub S, Riminucci M, Bianco P, Robey PG, Collins MT. A randomized, double blind, placebo-controlled trial of alendronate treatment for fibrous dysplasia of bone. *J Clinical Endocrinology & Metabolism*. 2014;99:4133–4140.
2. Dumitrescu CE, Collins MT. McCune-Albright Syndrome. *Orphanet J Rare Dis*. 2008;3:12.
3. Enneking WF, Gearen PF. Fibrous dysplasia of the femoral neck. Treatment by cortical bone-grafting. *J Bone Joint Surg Am*. 1986;68:1415–1422.
4. Enneking WF, Mindell ER. Observations on massive retrieved human allografts. *J Bone Joint Surg Am*. 1991;73:1123–1142.
5. Leet AI, Boyce AM, Ibrahim KA, Wientroub S, Kushner H, Collins MT. Bone-grafting in polyostotic fibrous dysplasia. *J Bone Joint Surg Am*. 2016;98:211–219.

CORR Insights

6. Parekh SG, Donthineni-Rao R, Ricchetti E, Lackman RD. *J Am Acad Orthop Surg.* 2004;12:305–313.
7. Stanton RS. Surgery for fibrous dysplasia. *J Bone Miner Res.* 2006;21 Suppl 2:105–109.
8. Weinstein RS. Long-term aminobisphosphonate treatment of fibrous dysplasia: Spectacular increase in bone density. *J Bone Miner Res.* 1997;12:1314–1315.
9. Weinstein LS, Shenker A, Gejman PV, Merino MJ, Friedman E, Spiegel AM. Activating mutations of the stimulatory G protein in the McCune–Albright syndrome. *N Engl J Med.* 1991;325:1688–1695.
10. Weinstein LS, Yu S, Warner DR, Liu J. Endocrine manifestations of stimulatory G protein α -subunit mutations and the role of genomic imprinting. *Endocr Rev.* 2001;22:675–705.