Such a report raises discussion about the etiopathophysiology of this type of tremor. In my experience, tremor of attitude is produced by a lesion of the striatum, mainly the caudate nucleus on the opposite side. The authors are postulating a dysfunction of the ipsilateral basal ganglia caused by direct pressure of the SDH superimposed on a preexisting silent lesion of the contralateral basal ganglia. Although deep lacunar infarction may not be visible on the computerized tomography scan, there seems to be a widening of the left sylvian operculum. Displacement by the contralateral SDH may have produced an ischemic lesion of the left basal ganglia responsible for the right-sided tremor.

It is even more intriguing that, although the authors postulate that there might be a dysfunction of the right basal ganglia, the patient did not present with tremor of the right arm. In my opinion, this is caused by pressure from the SDH on the right side of the cortex, which interrupts a pathway in the loop from basal ganglia to the cortex, as originally postulated by Bucy in his assertion that the integrity of the cortex must be intact for contralateral tremor to be present. Like the case I reported more than 30 years ago, this case provides an interesting exercise in reasoning about the neurophysiological mechanism of tremor. As noted by Arthur Koestler: “Science is a glorious entertainment.”

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RESPONSE: We appreciate Dr. Hardy’s interest regarding our report of tremor caused by ipsilateral chronic subdural hematoma (SDH). We agree in part with his comments. Although tremor is the most common movement disorder when considered clinically, its pathophysiological mechanism is still uncertain. It has been believed that connections between the basal ganglia, thalamus, and cortex (corticostriatopallidothalamicocortical loop) play an important role in the control of motor behavior. Damage to one of these structures may contribute to the genesis of tremor. A recent study has even emphasized that the cerebellum may also affect the pathophysiological mechanism of tremor.

In our reported case, the patient’s computerized tomography scan revealed a lateral right frontoparietal chronic SDH as well as a small hematoma in the left frontal region; however, his tremor improved dramatically after removal of the right-sided SDH. We therefore hypothesized that there was a close relationship between his right hand tremor and the direct pressure effect of the ipsilateral SDH, which was not related to the left frontal hematoma. Moreover, our patient was at high risk of experiencing stroke, with the possibility of an existing silent lesion on the left basal ganglia. Therefore, a “release phenomenon” could be reasonably explained to be a possible mechanism for genesis of his tremor.

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References

Spine Fusion With Demineralized Bone

To The Editor: On reading the contribution by Helm and colleagues (Helm GA, Sheehan JM, Sheehan JP, et al: Utilization of type I collagen gel, demineralized bone matrix, and bone morphogenetic protein-2 to enhance autologous bone lumbar spinal fusion. J Neurosurg 86:93–100, January, 1997), we were surprised by the seemingly counterintuitive finding that a composite graft of autologous bone and allogeneic demineralized bone matrix (DBM) performed markedly worse than autologous bone alone with respect to histological, radiographic, and biomechanical evidence of bone union in a canine model of spinal fusion. Proper removal of the calcium constituent of bone yields an organic matrix (that is, DBM), which has been shown uniformly to possess both osteoinductive and osteoconductive characteristics. Indeed, the balance of clinical experience is encouraging and suggests that DBM grafts in humans may decrease the necessity for harvesting autologous bone from a secondary operative site in some clinical applications, including spinal fusion.4,5

On careful inspection of the processing methods reported in this study, however, we noted no mention of use of an appropriate demineralizing agent to decalcify the allogeneic cortical bone tissue properly. By far, the most commonly used demineralizing agent is HCl.1 In fact, in describing their DBM processing methods, Helm and coworkers specifically provide citation of previous studies in which HCl was used. They cite as an example Bolander and Balian,2 who found that critical-size long bone defects in rabbits that underwent DBM graft placement showed similar biomechanical integrity 12 weeks postoperatively to contralateral defects grafted with autologous bone. Prior to implantation, the DBM had been decalcified in 0.6 M HCl for 3 to 4 hours.2 Helm, et al., extracted the bone tissue in a 1:1 chloroform/methanol solution. The purpose of this processing step is to reduce any residual lipidic and adipocytic components in the matrix; it is not a decalcifying method.1 In fact, nondemineralized allograft bone has been shown to offer less satisfactory graft performance than either autologous bone or DBM when directly compared in a rabbit model of spinal fusion.6

Failure to demineralize properly the bone tissue used in the study by Helm, et al., would call into question the validity of their findings with respect to the effectiveness of DBM for spinal fusion. If it is indeed true, this is a critical oversight in either reporting or conducting this study. We recommend that the authors engage an independent mon-
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itor to audit the study records to determine whether such an omission actually occurred.

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References


RESPONSE: We appreciate the interest of Drs. Block and Russell in our lumbar spinal fusion research. In the Materials and Methods section of our paper, the preparation of demineralized bone matrix (DBM) was presented in an abbreviated form. As referenced, the DBM was processed using the same techniques as Bolander and Balian, which included decalcifying the tissue with HCl.

There continues to be great interest in identifying materials that can be added to autologous bone grafts to improve both the rate and strength of spinal fusions. One such material is DBM containing a cocktail of proteins, some of which are osteoinductive. Because of differences in bone processing techniques used to produce DBM, the various preparations that have been studied to date have given variable results, some showing excellent osteoinduction and others showing limited bone formation. Because of this batch-to-batch variability, it is imperative that extensive preclinical testing be performed not only in the rodent, but also in such larger animals as the dog and nonhuman primate before these materials are used in the clinical setting.

One specific form of DBM, Grafton Allogeneic Bone Matrix (GABM) Osteotech, Shrewsbury, NJ has been studied in several clinical trials. Lowery, et al., conducted a retrospective study to compare the radiographic changes between two groups of patients who underwent posterior lateral lumbar or lumbosacral spinal fusions in which either autologous bone alone or a composite graft of autologous bone combined with GABM were used (unpublished data). In an oral report they stated that the “radiographic index scores were not significantly different between study groups at any postoperative follow-up interval.” These investigators stated that 87% of the patients who received autologous bone alone required iliac crest graft compared with 64% of the patients who received a composite graft, indicating that GABM significantly decreased the need for iliac crest bone graft harvest. It is our opinion that these results do not support the use of GABM in autologous bone spinal fusions. First, radiographic density studies alone cannot be used to determine whether the operative region is solidly fused. In our experience, autologous bone spinal fusions that appear to be solid when viewed on three-dimensional computerized tomography reconstructions may be found to contain pseudoarthroses on postmortem examination. Therefore, plain radiographs alone can be quite misleading when evaluating bone graft substitutes in spinal fusions. Second, Lowery, et al., did not report the amount of autologous bone used in each treatment group or how patients were selected for iliac crest grafting, leading them to draw unsubstantiated conclusions. In a separate study, An, et al., reported a study in which autograft alone was compared with allograft plus GABM for anterior cervical fusions. Pseudoarthrosis was seen in 47.4% of the allograft plus GABM group compared with 26.3% of the autograft group. In addition, graft collapse was demonstrated in 19% of the allograft plus GABM group compared with 11% of the patients in the autograft group. These authors concluded that allograft plus GABM grafts were inferior to autografts for anterior spinal fusions. In summary, no clinical studies have demonstrated with certainty that the use of GABM can lead to improved spinal arthrodesis compared with autologous bone alone.

In the past, osteoinductive proteins were isolated and purified by using biochemical methods. The application of molecular techniques has made it possible to sequence and clone the genes for these various proteins, which can be used to produce large quantities of growth factors that are pure, highly concentrated, and have little risk of viral contamination. One such osteoinductive factor is bone morphogenetic protein-2 (BMP-2). It has been demonstrated in numerous studies that this recombinant human protein can form bone in virtually every in vivo assay system. Our laboratory and numerous others have demonstrated that the addition of BMP-2 to autologous bone grafts can consistently and markedly improve bone deposition at the graft site. It is becoming clear that many of the technical issues involved in DBM production and use no longer need to concern the practicing neurosurgeon, because the application of recombinant human BMPs will certainly be the future of basic science and clinical research efforts in which osteoinductive materials are used.

The excellent results that have been obtained with rhBMP-2 both in rodents and larger animals have prompted us to look into using gene therapy to deliver the BMP-2 gene to increase local BMP-2 production and initiate endochondral bone formation. Preliminary studies in our laboratory in which an adenoviral vector is used to deliver the universal promoter-driven BMP-2 gene have demonstrated excellent bone deposition in a rodent model of spinal fusion. The results are provocative, because if stable transfection of cells at a fusion site can be achieved and an inducible promoter used to drive the BMP-2 gene, the amount of BMP-2 gene expression could be upregulated or downregulated postoperatively to control the amount of bone deposition at the fusion site. Clearly, basic science research in spine fusion is headed into the molecular arena and greater emphasis should be placed on...