Spontaneous Osteonecrosis of the Knee Treated with Autologous Chondrocyte Implantation, Autologous Bone-Grafting, and Osteotomy

A Report of Two Cases with Follow-up of Seven and Nine Years

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Spontaneous osteonecrosis of the knee is a disease whose primary etiology remains unknown. First described by Ahlbäck et al.[1] in 1968, it is now categorized as either primary (spontaneous) or secondary osteonecrosis[2]. Primary osteonecrosis usually presents in people over the age of fifty years, with sudden onset of pain, most frequently in the medial femoral condyle. Secondary osteonecrosis is associated with certain risk factors, such as corticosteroid therapy and alcohol use, and is usually encountered in younger people.

In patients with advanced disease or for whom nonoperative treatment has failed, surgery is recommended, typically partial or total joint replacement[3-5]. Reports of non-arthroplasty procedures are limited. Debridement, curettage, microfracture surgery, osteochondral allograft, bone-grafting, and isolated high tibial osteotomy (HTO) have been proposed[6-12], but none have demonstrated proven clinical outcomes in long-term follow-up studies. The recent widespread introduction of autologous chondrocyte implantation (ACI) into clinical practice has renewed interest in biologic treatment options for osteonecrosis of the knee. Recently, Adachi et al.[13] showed excellent short-term results with the use of ACI in conjunction with interconnected porous hydroxyapatite (IP-CHA) bone substitute for the treatment of steroid-induced osteonecrosis. In our patients, the abnormal subchondral bone was addressed with an autologous bone graft because of its superior osteogenic, osteoconductive, and osteoinductive properties. We describe two cases of spontaneous osteonecrosis of the knee that were treated with ACI, autologous bone-grafting, and osteotomy and followed for seven and nine years. The patients were informed that data concerning their cases would be submitted for publication, and they provided consent.

Case Reports

CASE 1. A fifty-year-old man with a history of seizures treated with Keppra (levetiracetam), Depakote (valproic acid), and Lamictal (lamotrigine) experienced spontaneous onset of sharp pain in the medial aspect of the knee in June 2000. He had not experienced knee trauma and did not have a history of corticosteroid therapy or alcohol abuse. The pain gradually increased, resulting in persistent limitations with weight-bearing activities. In addition, he described mechanical symptoms (mostly catching of the knee). In October 2000, he underwent arthroscopy at an outside institution for a presumptive diagnosis of meniscal tear; however, a chondral flap of the medial femoral condyle was encountered instead. In 2001, a diagnosis of spontaneous osteonecrosis of the medial femoral condyle was made on the basis of clinical and radiographic findings.

On presentation to us, the physical examination demonstrated varus alignment of the left knee, stable ligaments, and knee motion of 0° to 130°. Radiographs revealed radiolucent areas surrounded by sclerotic rims in the medial femoral condyle (Fig. 1-A). The lateral and patellofemoral compartments were normal. Weight-bearing long leg alignment radiographs demonstrated 50% medial joint space narrowing and collapse of the medial femoral condyle (Ficat stage III). The mechanical axis passed through the most medial aspect of the medial compartment. Magnetic resonance imaging (MRI) revealed a large osteonecrotic area in the medial femoral condyle (Fig. 1-B).

After thorough discussion of the treatment options, the patient decided to undergo correction of the varus malalignment through HTO and ACI with bone-grafting to address the osteochondral defect. In November 2001, after detailed informed consent was obtained, we proceeded with diagnostic arthroscopy, cartilage biopsy, and chondroplasty. A large collapsed area was encountered in the medial femoral condyle. The lesion was 400 mm long, 200 mm wide, and 10 mm deep and was circumferentially shouldered by intact articular cartilage. We harvested

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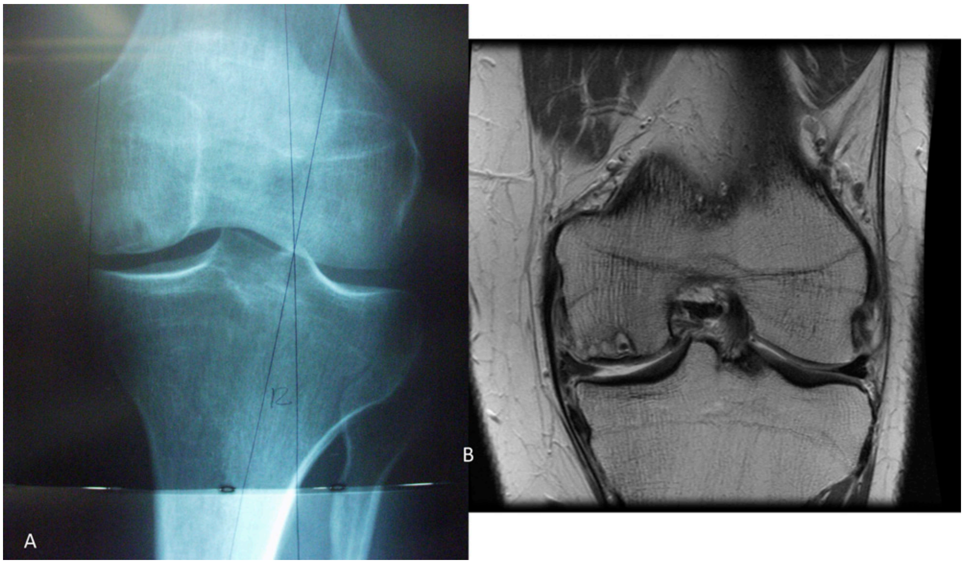

Fig. 1

Figs. 1-A and 1-B Preoperative imaging studies of the knee. **Fig. 1-A** Anteroposterior radiograph of the knee showing radiolucent areas surrounded by sclerosis in the medial femoral condyle. **Fig. 1-B** Coronal MRI showing an area of osteonecrosis involving the medial femoral condyle.

180 mg of articular cartilage from a lesser-weight-bearing area (the superior and lateral aspect of the intercondylar notch proximal to the sulcus terminalis of the lateral femoral condyle). The cartilage was enzymatically digested, and the chondrocytes were grown to confluence. After two weeks, the cells were cryopreserved while the patient awaited insurance approval and scheduling of the second-stage procedure. After cryopreservation, the approximately 200,000 to 300,000 cells contained in the initial cartilage biopsy specimen were grown to approximately twelve million cells per 0.4 mL of culture medium, with an additional culture time of approximately four weeks.

Four months after the arthroscopy, reimplantation of the chondrocytes was performed. We used a 12° closing-wedge HTO. The treatment plan involved use of autologous bone graft for the subchondral bone defect and ACI for the overlying cartilage defect. Intraoperatively, a full-thickness patellar defect also was observed; thus, an anteromedialization osteotomy of the tibial tubercle was performed, as described by Fulkerson[14]. After arthrotomy, the chondral defect was excised and the necrotic bone was debrided back to healthy tissue with a high-speed burr under constant irrigation. Bone retrieved from the closing-wedge HTO was used to graft the resulting defect, which measured 10 mm in depth at its deepest extension (Fig. 2-A). A periosteal patch was harvested from the proximal part of the tibia and was circumferentially microsutured over the bone graft with 6-0 resorbable sutures, with the cambium layer facing out (Fig. 2-B). A second periosteal patch was harvested and was microsutured at intervals of 3 to 5 mm with the cambium layer facing the defect (Fig. 2-C). After the suture line was sealed with fibrin glue and checked for water integrity, the chondrocyte suspension was aspirated from the two transport vials and injected between the two periosteal membranes, hence the

Fig. 2

Fig. 2-A Medial femoral condyle defect measuring 10 mm in depth. **Fig. 2-B** Microsuturing of the first periosteal patch to the base of the defect over the bone graft. **Fig. 2-C** Second periosteal patch microsutured at intervals of 3 to 5 mm.

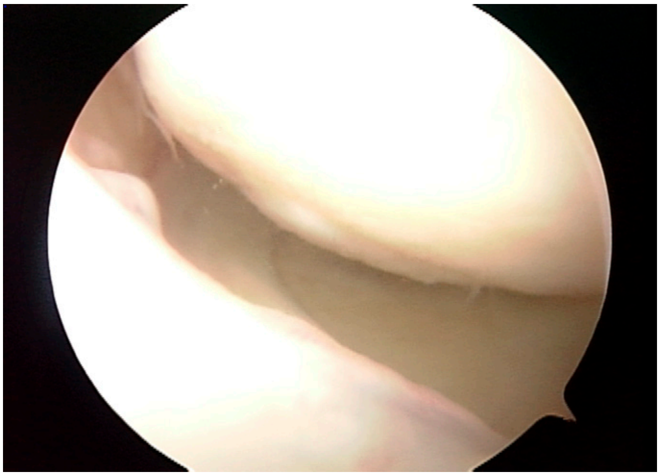

Fig. 3

Second-look arthroscopy at one year postoperatively showing integration of the cartilage repair tissue.

term *sandwich technique*[15]. An ACI was also performed for the small (15 × 15-mm) patellar defect, as previously described[16].

The patient followed a three-phase rehabilitation protocol, as previously described[17]. During the initial phase, toe-touch weight-bearing and six to eight hours per day of continuous passive motion were prescribed for six weeks after the surgery. During the second phase, the patient progressed to full weight-bearing and functional closed-chain exercises, excluding leg presses and squats. At one year postoperatively, the patient resumed normal activities, including light running, but was advised to refrain from cutting sports.

At six weeks postoperatively, the patient had decreased pain and knee motion was from 0° to 120°. At twelve months, we performed a second-look arthroscopy to evaluate the integrity of the graft, which was fully incorporated and firm (Fig. 3). MRI at twenty-four months postoperatively demonstrated repair tissue filling the medial femoral condyle graft site with minimal surface irregularity posteriorly. The bone graft had incorporated, and there was no bone marrow edema. Radiographs and MRIs revealed solid bone-healing of the osteotomy site (Figs. 4-A, 4-B, and 4-C). At the time of the latest follow-up, seven years after surgery, the patient was pain-free and able to participate in recreational sports without limitations.

Case 2. A forty-seven-year-old man was referred to us with a presentation similar to that described in Case 1. He had sharp pain in the medial aspect of the left knee and was unable to walk without a cane. The ligaments were stable and knee motion was from 0° to 110°. A previous MRI report had suggested osteonecrosis in the medial femoral condyle, and a subsequent arthroscopy at an outside institution confirmed the diagnosis. He presented to us after two unsuccessful arthroscopic surgical procedures for chondroplasty.

Preoperative radiographs showed 10° of varus malalignment at the knee (Fig. 5-A). After an initial arthroscopic procedure for cartilage biopsy (harvesting of 240 mg), the patient was subsequently treated in June 2001 with a 10° closing-wedge HTO and ACI (three vials of chondrocytes) with bone-grafting for a lesion measuring 10 cm^2 in area and 10 mm in depth.

Postoperative radiographs demonstrated a solidly healed osteotomy site (Fig. 5-B). MRI four years after surgery showed complete filling of the defect with bone and restoration of the articular surface (Fig. 6-B). A second-look arthroscopy at the same time confirmed the imaging findings (Fig. 6-A).

The patient did not experience any postoperative complications and was allowed to return to unrestricted activities after twelve months. Nine years after the procedure, he was doing well, able to stand a full day working as an orthodontist and biking, running, and playing tennis for exercise. He did not report any pain in the knee and demonstrated only minimal osteoarthritic changes on radiographs (Figs. 7-A through 7-D).

Results

Clinical Scores

Our patients were assessed with a range of functional scores, including the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), the modified Cincinnati Knee Rating Scale, and the Knee Society Score. They also answered questions regarding their self-rated knee function and satisfaction

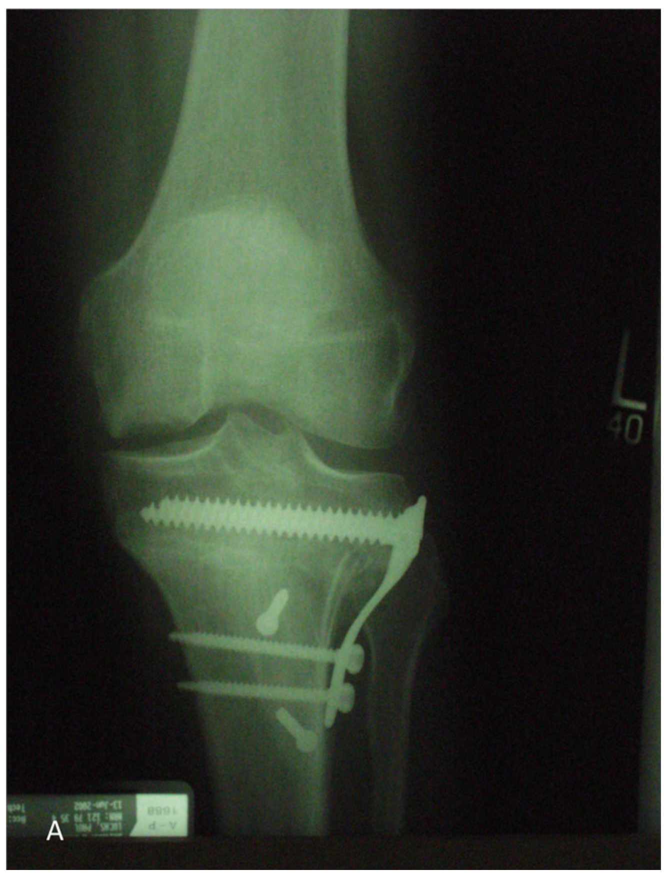

Fig. 4-A

Postoperative anteroposterior radiograph at twenty-four months showing solid bone healing at the osteotomy site.

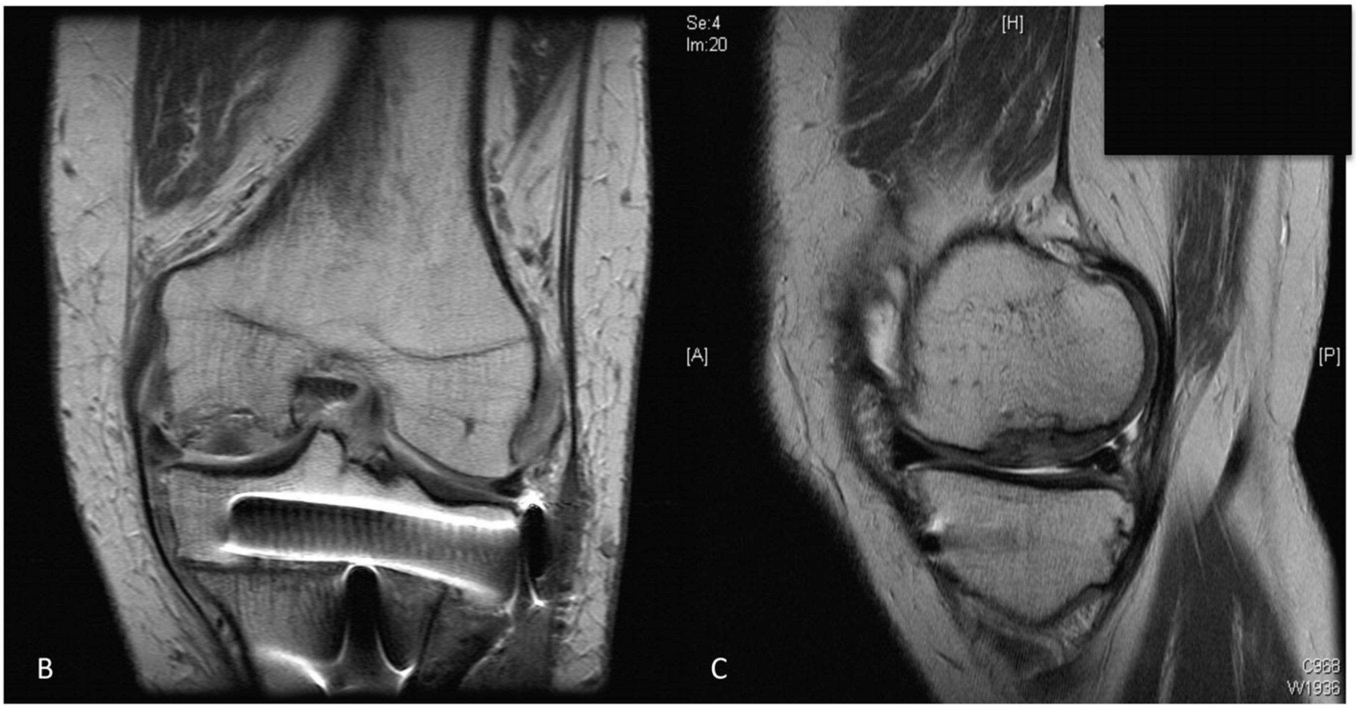

Fig. 4-B Fig. 4-C

Postoperative coronal (**Fig. 4-B**) and sagittal (**Fig. 4-C**) MRIs at twenty-four months showing good filling, with repair tissue filling the medial femoral condyle graft.

with the procedure. Scores were collected preoperatively and at yearly intervals postoperatively during an office visit or by mailed questionnaire (Table I).

In both our patients, the results of physical examination, including knee motion and swelling, correlated with clinical scores; the findings gradually improved over the first two years

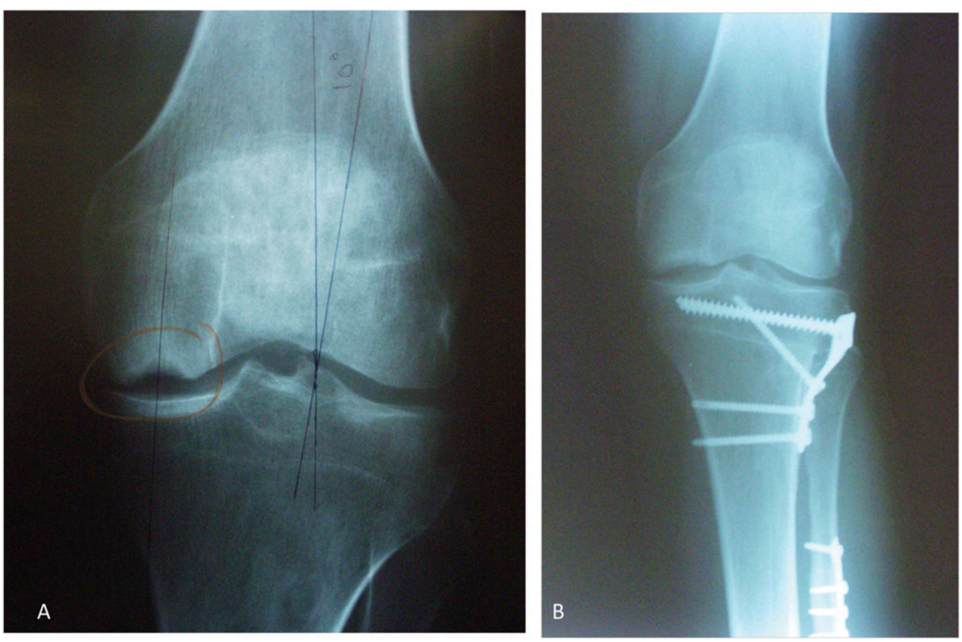

Fig. 5

Fig. 5-A Preoperative anteroposterior radiograph demonstrating a collapsed crescentic defect at the articular surface of the medial femoral condyle (Ficat stage III). **Fig. 5-B** Postoperative anteroposterior radiograph revealing solid bone-healing of the osteotomy sites at the tibia and fibula.

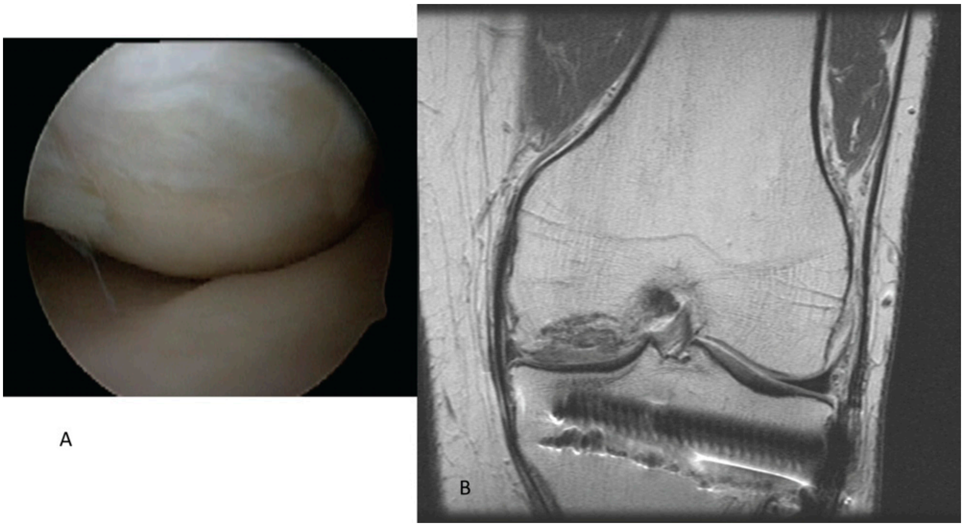

Fig. 6

Fig. 6-A Second-look arthroscopy at four years postoperatively demonstrating excellent graft firmness and incorporation.
Fig. 6-B Postoperative coronal MRI at four years revealing complete coverage of the bone graft with cartilage repair tissue and no evidence of delamination.

Fig. 7

Postoperative radiographs at ten years demonstrating minimal osteoarthritic changes without evidence of joint effusion or additional focal abnormality.

TABLE I Clinical Scores

	Modified Cincinnati Knee Rating Scale	WOMAC Score	Knee Society Pain Score	Knee Society Functional Score
Case 1				
Preop.	2	60	50	50
12 mo	6	33	80	60
24 mo	6	20	90	80
36 mo	6	17	90	80
48 mo	6	9	80	70
60 mo	6	11	80	70
72 mo	6	10	80	70
84 mo	6	10	80	70
Case 2				
Preop.	4	34	75	40
12 mo	8	26	70	60
24 mo	8	17	100	90
36 mo	8	18	100	100
48 mo	8	17	100	100
60 mo	7	16	100	100
72 mo	7	16	100	100
84 mo	6	16	95	90
96 mo	6	16	95	90
108 mo	6	16	95	90

and remained stable thereafter. Swelling and effusion had resolved by six months postoperatively; motion quickly improved to 120° by three months, with continued gradual improvement to nearly normal values at one year. After osteotomy site healing was confirmed during the early postoperative period, no additional radiographs were obtained for the first patient, since he was essentially asymptomatic. At the last postoperative evaluation, both patients rated their surgery as having provided excellent results.

Discussion

We describe two patients with spontaneous osteonecrosis of the medial femoral condyle treated with ACI in conjunction with autologous bone-grafting and closing-wedge HTO. Peterson et al.[18] initially described the use of isolated ACI for the treatment of more shallow osteochondral lesions of less than 6 to 8 mm without the use of bone-grafting. A combination of ACI and concurrent autologous bone-grafting, termed a *sandwich technique,* was first reported by Peterson and Minas to address even deeper osteochondral defects, such as large osteochondritis dissecans lesions[19,20]. Bartlett et al.[21] also described the use of concurrent ACI and bone-grafting for osteochondral defects deeper than 6 to 8 mm, with good results at six months and one year. Adachi et al.[13] described two-year results of a related technique with use of ACI and an IP-CHA bone-graft substitute for treatment of steroid-induced osteonecrosis in one patient. To our knowledge, there are no previous reports in the literature on the long-term outcomes of the sandwich ACI technique with autologous bone-grafting for spontaneous osteonecrosis of the knee.

Our study has the obvious limitations of a case report, with only two patients treated with a combination of ACI, bone-grafting, and realignment osteotomy. It is impossible to determine with certainty which of these treatments provided the most pain relief. However, it is our belief that biologic reconstruction should address all structural deficits present in a knee joint, which, in our two patients, consisted of a chondral defect on the surface with associated osseous deficiency and knee malalignment.

The etiology of osteonecrosis and, more specifically, spontaneous osteonecrosis of the knee is poorly understood. Whereas secondary osteonecrosis is associated with a number of known risk factors, such as corticosteroid therapy and alcohol use, the pathophysiologic changes leading to spontaneous osteonecrosis remain controversial. One hypothesis is that vascular compromise of the subchondral bone results in ischemia and subsequent bone edema, which can lead to subchondral insufficiency; others have proposed insufficiency fracture as the initiating event[22-24]. Ficat was among the first to describe osteonecrosis, originally in the femoral head[25]. Depending on the Ficat stage, several non-arthroplasty treatment options have been described for osteonecrosis of the knee[6-12,26]. However, most studies have not provided consistent long-term clinical outcomes, resulting in arthroplasty being considered as the treatment of choice for more advanced stages of osteonecrosis. While many patients with osteonecrosis of the knee are appropriately treated with partial or total knee replacement, certain patients are candidates for biologic reconstruction, provided they are physiologically young and active and have a knee joint that is intact outside the affected area and without diffuse arthritic changes. Recently, corticosteroid-induced osteonecrosis of the knee has been treated with osteochondral allograft transplantation[27-29]. Sandwich ACI provides an all-autologous treatment alternative for patients unwilling to receive allograft tissue, or for patients treated in countries where allograft tissue is not readily available.

In conclusion, the treatment of osteonecrosis of the knee in younger patients remains challenging. We believe that every reasonable attempt should be made to delay the need for knee replacement in this group. Treatment of osteonecrosis with sandwich ACI and osteotomy in our two patients yielded excellent long-term results. However, a much larger series is needed to confirm the reproducibility of this biologic treatment option for osteonecrosis. ■

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