Title	Double-bundle anterior cruciate ligament reconstruction using autologous hamstring tendon hybrid grafts in a patient with hypermobile Ehlers-Danlos Syndrome : A case report
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1 Double-bundle anterior cruciate ligament reconstruction using autologous hamstring tendon hybrid grafts in a patient with hypermobile Ehlers-Danlos Syndrome: a case 2 3 report 4 Ryosuke Hishimura¹, MD, PhD, Eiji Kondo², MD, PhD, Masatake Matsuoka¹, MD, PhD, 5 Koji Iwasaki³, MD, PhD, Yasuyuki Kawaguchi⁴, MD, PhD, Yuki Suzuki¹, MD, PhD, 6 Tomohiro Onodera¹, MD, PhD, Daisuke Momma², MD, PhD, 7 and Norimasa Iwasaki¹, MD, PhD 8 9 ¹ Department of Orthopaedic Surgery, Faculty of Medicine and Graduate School of Medicine, 10 11 Hokkaido University, North 15 West 7, Kita-Ku, Sapporo 060-8638, Japan ² Centre for Sports Medicine, Hokkaido University Hospital, North 15 West 7, Kita-Ku, 12 Sapporo 060-8638, Japan 13 ³ Department of functional reconstruction for the knee joint, Hokkaido University, North 15, 14 15 West 7, Kita-ku, Sapporo, Hokkaido 060-8638, Japan ⁴ Sports and Arthroscopy Center, Hanna Central Hospital, Ikoma, Nara, Japan 16 17 **Corresponding author** 18 Name: Eiji Kondo, MD, PhD 19 Institutional address: Centre for Sports Medicine, Hokkaido University Hospital, 20 North 15 West 7, Kita-Ku, Sapporo 060-8638, Japan 21Phone: (+81) –11–706–5937 22 Email: eijik@med.hokudai.ac.jp 23 24

Declarations:

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The authors declare no conflicts of interest associated with this study.

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• Ethical approval

The protocol of this study was approved by the Institutional Review Board of our medical institution.

• Informed consent

Informed consent for the use of medical information was obtained from all patients in this study.

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• Authors' contribution

EK was involved in the design of the study, performed the clinical assessment, analysis and interpretation of data, and drafted and revised the manuscript. RH and MM were involved in the design of the study, assisted with data interpretation, and revised the manuscript for important intellectual content. KI, YK, YS, TO, DM, and NI were involved in the design of the study and the data acquisition and revised the manuscript critically for important intellectual content. All authors have read and approved the final manuscript.

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ABSTRACT

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Background: Ehlers-Danlos syndrome (EDS) is a connective tissue disorder characterized by skin hyperextensibility, joint hypermobility, and tissue friability. Hypermobile type Ehlers-Danlos syndrome (hEDS) is considered one of the EDS subtypes characterized by generalized joint hypermobility. Although there have been a few case reports which described surgical considerations for anterior cruciate ligament (ACL) reconstructions in patients with other types of EDS, no reports have described those in patients with hEDS. Case presentation: We report a case of ACL injury in an 18-year-old male patient with hEDS. The patient was successfully treated with an anatomic double-bundle ACL reconstruction using autologous hamstring tendon hybrid grafts which consist of hamstring tendons connected in a series with commercially available polyester tape. The autogenous tendon portion of the anteromedial and posterolateral bundles were composed of 4 and 2 strands of hamstring tendons, respectively. After 2 weeks of knee joint immobilization, continuous passive motion exercise of the knee joint and partial weight-bearing was allowed. A hinged knee brace was used for a period of 5 months postoperatively. Second-look arthroscopy at 30 months showed that the ACL graft had no laceration and an excellent coverage of the synovium. At 36 months after surgery, the side-to-side differences in the anterior laxity was remarkably improved. The operated knee showed negative Lachman test and had a full range of motion. Conclusions: To the best of our knowledge, this represents the first report of anatomic doublebundle ACL reconstruction in patients with hEDS and demonstrates excellent clinical and functional outcomes.

Introduction

73	Ehlers-Danlos syndrome (EDS) is a connective tissue disorder characterized by skin
74	hyperextensibility, joint hypermobility, vascular fragility, and tissue fragility [1, 2]. The overall
75	incidence has been reported as approximately 1.0 per 5000 in the general population [2]. EDS
76	was classified into six types as the following; classical, hypermobile, vascular, kyphoscoliosis,
77	arthrochalasia, and dermatosparaxis [3].
78	The hypermobile EDS (hEDS) has been described in those with musculoskeletal disorders
79	including joint hypermobility, joint subluxations/dislocations, and ligament and tendon rupture
80	[1, 4]. There were some reports regarding joint laxity and pain in the patient with hEDS [5, 6].
81	Orthopedic surgeons may encounter joint trauma patients with hEDS due to joint instability
82	associated with inferior biomechanical properties of the innate collagen-containing structures.
83	According to previous studies, the treatment of knee injury in patients with hEDS can be
84	challenging [5, 6].
85	There have been only a few case reports which described the surgical considerations for
86	anterior cruciate ligament (ACL) reconstructions in patients with EDS [7-9]. However, it
87	remains controversial whether operative or conservative treatment of ACL injury yields a better
88	functional outcome. In particular, no reports have described surgical consideration and graft
89	selection for ACL reconstruction in patients with hEDS.
90	Recently, we encountered a case of ACL injury in a patient with hEDS. We successfully
91	treated the patient by double-bundle ACL reconstruction using hamstring tendon hybrid
92	autografts [10-13]. To the best of our knowledge, this is the first report of double-bundle ACL
93	reconstruction in patients with hEDS.

Case report

An 18-year-old male sustained an acute twisting injury to his left knee by slipping on ice. The patient was first diagnosed by a pediatric physician as hEDS at 2-years-old with a history of poor wound healing and elastic skin after inguinal hernia surgery. The patient at the age of 18 visited our affiliate hospital on the day of the accident. Physical examination showed knee effusion, a positive Lachman test, and an anterior drawer test. Anteroposterior and lateral plain radiographs of the left knee demonstrated no fracture (Fig. 1A, B). Magnetic resonance imaging (MRI) of the left knee detected a complete rupture of the ACL with a bone bruise of the lateral femoral condyle (Fig.1C, D). Considering the inherent joint laxity in a patient with hEDS, there was concern whether the ACL reconstruction could restore sufficient stability of the affected knee. Immediately after injury, conservative treatment was chosen for the time being. Although conservative treatment was continued by a rigid hinged knee brace for a period of 5 months, the patient had repeated episodes of giving way in activities of daily living (ADL) as well as participation with university theater club. Six months after injury, the patient was referred to our hospital for surgical treatment. The left knee showed not only a positive Lachman test and anterior drawer test but also a positive pivotshift test. The anterior laxity was measured using a Kneelax3 (MR Systems, Haarlem, The Netherlands) with 30° of knee flexion under an anterior drawer force of 133 N. The anterior laxity of the left knee was 18.4 mm, showing predominant laxity compared to that of the right knee (the right side was 13.6 mm). The preoperative side-to-side differences in the anterior laxity was calculated as + 4.8 mm. According to Beighton criteria [2], which is often used to assess joint hypermobility, the total score was 6 points. Considering the predominant laxity of the affected knee and the decrease in ADL, we made the decision to proceed with ACL reconstruction of the left knee. At the seven months after injury, anatomic double-bundle ACL reconstruction using hamstring tendon hybrid autografts was performed with the trans-tibial tunnel technique [10,

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11]. Arthroscopic examination showed complete rupture of the ACL without remnant tissue (Fig. 2A). The ipsilateral semitendinosus and gracilis tendons were harvested. In the graft preparation, the doubled semitendinosus and gracilis tendons were created as an anteromedial (AM) bundle, and the doubled semitendinosus tendon was created as a posterolateral (PL) bundle (Fig. 2C). Thus, the autogenous tendon portion of the AM and PL bundles was composed of 4 and 2 strands of tendons, respectively. A commercially available polyester tape (Leeds-Keio artificial ligament; Neoligaments, Leeds, England) was mechanically connected in a series at an unlooped end of the folded tendon [12, 13]. An Endobutton CL BTB (Smith & Nephew, Andover, MA) was attached to the looped end [14]. The diameter of the AM and PL grafts were 7 mm and 6.5 mm, respectively. To insert a guidewire for the tibial PL tunnel, we used a hole-in- one guide (Wire-navigator, Smith & Nephew, Tokyo, Japan) [10]. Then, a guidewire was drilled in the tibia. A guidewire for AM bundle reconstruction was inserted in the same manner. Two tibial tunnels were made with a cannulated drill. To create two femoral tunnels, a guidewire was drilled at the femoral attachment of the AM bundle by using an offset guide (Transtibial Femoral ACL Drill Guide; Arthrex, Naples, FL,). Then, a guidewire was inserted at the PL bundle attachment on the femur. Two femoral sockets were created with cannulated drills. Finally, the grafts for the AM and PL bundles were fixed with 30 N tension to each graft using two tensiometers (Yufu Itonaga Co., Ltd., Tokyo, Japan) at 10° of knee flexion (Fig. 2B). The plain radiograph after ACL reconstruction was shown in Fig. 3. Considering its intrinsic joint laxity, accelerated rehabilitation was not applied to this patient. After 2 weeks of knee joint immobilization, continuous passive motion exercise of the knee joint and partial weight-bearing were allowed after 3 months. A hinged knee brace with 30° extension block was applied for a period of 3 months after surgery. A knee brace was used for a period of 5 months postoperatively. At 24 months after surgery, MRI showed a thick double-

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bundle of the ACL graft (Fig. 4A, B). Thirty months later, second-look arthroscopy and staple removal were performed. It showed that the ACL graft had no laceration and an excellent coverage of the synovium (Fig. 4C) [15]. After 36 months postoperatively, the side-to-side anterior laxity was improved from + 4.8 mm to - 4.2 mm. Lysholm knee score was 100 points. The objective International Knee Documentation Committee was determined as grade A. Knee injury and Osteoarthritis Outcome Score was 94.4, 92.8, 98.0, 85.0, and 87.5 in Pain, other Symptoms, Function in daily living, Function in Sport and Recreation, and knee related Quality of Life, respectively. The left knee showed a negative Lachman test, a negative pivot-shift test, and had a full range of motion with no loss of hyperextension (5°). This patient subsequently had no flexion contracture and could sit comfortably in the Japanese style (seiza). However, there was early extension deficit during the first 6-8 weeks which can lead to a "more stable knee", which is not always an advantage for the patient without knee joint laxity. The patient had returned to a preinjury level of daily activity and participated in theater club activities.

DISCUSSION

We reported a case with ACL injury in the patient with hEDS. Anatomic double-bundle ACL reconstruction using hamstring tendon hybrid autografts was performed in this case and had a favorable clinical outcome as a short-term result.

There was concern about using an autograft-native tissue procedure, considering its intrinsic joint laxity. Previous reports which demonstrated that patients with EDS showed spontaneous tendon ruptures that pointed toward weaker tendon biomechanical properties [6, 16]. Considering the weakness of an autograft-native tissue procedure in patients with EDS, the use of allografts could be a feasible option. However, in Japan, the use of allografts is severely restricted.

In this case, we first considered the selection of a hamstring tendon, a bone-patellar tendon-

bone (BTB), and quadriceps tendon grafts as the autologous tendon graft. During the remodeling phase, the structural properties of the graft deteriorate, and the reduced properties are not completely restored even at 12 months after surgery [17-19]. Previous studies generally confirmed that remodeling process of the graft was known to entail cellular repopulation, revascularization and collagen deposition [20, 21]. Considering the graft remodeling phase, each graft will be reconstructed with the similar ligamentization process. To overcome the weakness of an autograft-native tissue, we focused on using hamstring tendon 'hybrid' autografts [22, 23]. It is well known that the weak points of a hamstring tendon graft fixed with sutures to the bone are (1) low stiffness of the graft-suture-bone complex, (2) rapid relaxation of graft tension after surgery, and (3) difficulty in tension control during graft fixation [23-25]. The "hybrid graft" was used to improve upon these weak points. Namely, the femur-hamstring graft-tibia complex with polyester tapes involves the following advantages according to our biomechanical studies [24, 26, 27]: (1) the maximal load of hamstring tendon hybrid graft was significantly greater than that of the BTB grafts. (2) higher stiffness and stronger ultimate loads than the hamstring complex with the suture method; (3) acceptably long and thick hybrid grafts for double-bundle reconstruction can be fashioned by surgeons with a relatively short or thin autogenous tendon; (4) the hybrid graft can be more resistance to graft tension relaxation, and easily fixed to the bone, applying a tension quantified using a tensiometer to the graft. Although there are no reports of the results of ACL reconstruction in hEDS, several papers regarding the other types of EDS were reported. Choi et al. [8] reported that single-bundle ACL reconstruction using Achilles tendon allograft was performed in a patient with the classical type of EDS. At 2 years postoperatively, the patient continued to participate in regular preinjury activities. Williams et al. [7] demonstrated the effectiveness of single-bundle ACL reconstruction using the hamstring autograft combined with a Ligament Advanced Reinforcement System (LARS) in a patient with an unknown type of EDS. At one year post

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surgery, the patient had resumed sport activities.

Several biomechanical studies have shown that double-bundle ACL reconstruction produces better stability in the knee, compared with single-bundle reconstruction [28-30]. However, controversy remains regarding the clinical utility of anatomic double-bundle reconstruction in comparison with single-bundle reconstruction [31]. Recently, many comparative studies have demonstrated significant superiority in anterior and/or rotatory stability of the knee after double-bundle reconstruction [11, 32, 33]. Therefore, we considered that double-bundle ACL reconstruction procedure with hamstring tendon hybrid autografts could obtain suitable anterior and rotatory stability of the knee in a case of hEDS. A single-bundle reconstruction with an extra-articular stabilization may be one option to this case [34].

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Conclusion

To the best of our knowledge, this represents the first report of anatomic double-bundle ACL reconstruction using hamstring tendon hybrid autografts in patients with hEDS and demonstrates excellent clinical and functional outcomes.



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Fig. 1. Preoperative plain radiograph and magnetic resonance imaging (MRI) scan at three months after injury.

- (a) Anteroposterior and (b) lateral radiographs of the left knee demonstrating no fracture and avulsion.
- (c) Coronal fat saturated proton density image of the left knee. Bone bruise of the lateral femoral condyle was detected. (d) Sagittal T2-weighted image of the left knee. The complete discontinuity of the ACL shows a full-thickness tear.

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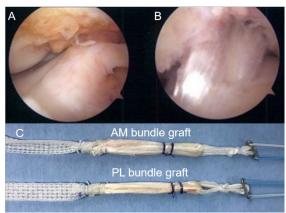


Fig 2. Arthroscopic observation of the ACL reconstruction and the intraoperative photograph of the hamstring tendon hybrid autograft.

- (a) Arthroscopy showed complete rupture of the ACL without remnant tissue. (b) Two grafts transplanted across knee joint at time of surgery at 90° of knee flexion in arthroscopic view by use of lateral infrapatellar portal.
- (c) AM and PL bundle grafts fashioned for anatomic ACL reconstruction. The tendon portion of the AM and PL bundles was composed of 4 and 2 strands of tendons, respectively.

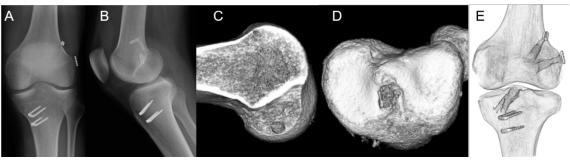


Fig. 3. Postoperative radiograph and imaging of computed tomography (CT) of the left knee. (a) Anteroposterior radiograph of the left knee joint. (b) Lateral view of the left knee joint. (c) Postoperative 3-dimensional CT image of the femur and (d) the tibia showed that the 2 tunnels were created at the expected positions. (e) The transparent 3-dimensional CT image of the left knee represents 2 tunnels intuitively.

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Fig. 4. Magnetic resonance imaging (MRI) scan at 24 months postoperatively and intraoperative finding of second-look arthroscopic evaluation at 30 months postoperatively.

(a) Sagittal and (b) coronal T2-weighted image of the left knee showing the reconstruction to be a thick ACL graft.

(c) ACL graft had no laceration and was completely covered with the thin synovial and thick fibrous tissues.

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