## CASE REPORT

# Graft-versus-host disease following transobturator tape procedure with small intestinal submucosa (Surgisis): a case report

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Received: 12 January 2009 / Accepted: 15 February 2009 / Published online: 12 March 2009 © The International Urogynecological Association 2009

**Abstract** Transobturator tape procedure using small intestinal submucosa (SIS) is designed for the diminishment of the complications of tension-free vaginal tape procedures, and SIS can lower the erosion rate of mesh. However, we here report a case which developed graft-versus-host disease following the use of SIS for the transobturator procedure.

**Keywords** Graft-versus-host disease · Transobturator tape · Small intestinal submucosa

## Introduction

The tension-free vaginal tape (TVT) procedure has been one of the most popular procedures for the treatment of stress urinary incontinence (SUI) since the introduction by Ulmsten in 1995 [1]. In order to lower the complications of TVT procedures, such as vascular injuries and postoperative urinary retention [2], transobturator tape procedure was introduced by Delorme in 2001 [3].

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Graduate Institute of Medicine, Faculty of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan Graft-versus-host disease (GVHD) includes inflammatory and/or fibrosing manifestations that may arise at various times after transplantation of any organ containing lymphoid cells. Graft-versus-host disease is divided into two forms: acute GVHD and chronic GVHD. Acute GVHD involves only the epithelia and is induced by the recognition of host-specific antigens. It is characterized by a selective epithelial inflammation that can affect the skin, digestive tract, and liver. Cutaneous involvement is the most common. Lymphocytic infiltration and cytopathic changes of keratinocytes are the major features of acute GVHD.

Small intestinal submucosa (SIS) is an acellular, nonimmunogenic, resorbable, xenogenic, and collagen-based biomaterial that is derived from the extracellular matrix of porcine small intestinal submucosa. A previous study had demonstrated that a vigorous response to implanted SIS can occur, as evidenced by an early, acute inflammatory response consisting mostly of polymorphonuclear cells. Cytokine and antibody isotype analysis has demonstrated the presence of a T helper-2 response and the absence of a T helper-1 response, which is typically associated with tissue acceptance rather than rejection [4].

However, here, we report a woman who developed GVHD in the perineal incision wound within 1 month after the application of SIS sling for SUI. To our knowledge, this is the first case reporting this complication.

## **Case report**

A 44-year-old woman presented to our institution with the complaint of involuntary urinary leakage during exertion for more than 2 years. SUI had been proven by urodynamic study and positive pad test. Transobturator sling procedure

with Surgisis (Cook Inc., West Lafayette, IN, USA) was then performed. A single dose of prophylactic antibiotics with 1 g of Cefazolin (Cefamezin, Fujisawa, Tokyo, Japan) had been given 30 min before procedure. The intra- and postoperative course had been uncomplicated, with reasonable operating time, minimal bleeding, and without any sign of infection or fever. No antibiotics had been given after the operation. The wound healing was uneventful. Unfortunately, she reported left perineal swelling on postoperative day 22. The patient noted no pain and fever, and she was continent. Pelvic examination revealed an ulcer and an exudate developed at the left perineal incision site (Fig. 1). Tracing back her history, it was found that she had a history of drug allergy to aspirin.

At the same day, surgical debridement and irrigation was made to facilitate healing after bacterial culture and tissue biopsy had been done. After primary treatment of the wound. amoxicillin (Amoxicillin, Yung Shin, Taiwan) was given in order to provide coverage against a wide spectrum of aerobic, anaerobic, and facultative anaerobic organisms. Unfortunately, the ulcer and exudate did not improve after 5-day use of Amoxicillin. No bacteria were isolated from the discharge 1 week after debridement. The pathology revealed the pictures of GVHD (Fig. 2). A subepithelial cleft and an apoptotic keratinocyte in the squamous epithelium with lymphocyte infiltration (exocytosis) and focal hydropic change (spongiosis) simulating grade 3 GVHD. Therefore, 1 mg/Kg/day of Prednisolone (Donison, China chemicals, Taiwan) was given for 1 month and a maintenance dose of 30 mg/day for one more month. Fortunately, the wound resolved gradually after a 2-month course of treatment.

After follow-up of 2 years, she had a complete remission of symptoms and remained continent so far.

### Discussion

The new minimally invasive TOT procedure provides good results at short-term follow-up and high cure rates [3]. Synthetic mesh may also lead to the erosion of vaginal wall. This complication appears in about 0.7~1.0%. The SIS tape was developed to overcome the possibility of erosion and rejection. Small intestine submucosa (SIS) is an acellular, non-immunogenic, resorbable, xenogeneic, and collagen-based biomaterial that is derived from the extracellular matrix of porcine small intestinal submucosa. It had been shown that the SIS implantation is typically associated with tissue acceptance rather than rejection [4]. Unfortunately, GVHD developed in our patient within 1 month after operation. Tracing back her medical history, she had a history of drug allergy to aspirin. The wound could heal after only 2-month course of oral steroid may be due to the local epithelial reaction rather than systemic disease.



Fig. 1 Twenty-two days after operation, ulcerous and erythematous change developed at the left perineal incision site (*arrow*)

Characteristically, pathologic findings of GVHD include clustered lymphocytes around dyskeratotic and/or dead keratinocytes (satellite cell necrosis), with the presence of an activated donor lymphocyte recognizing a host cell. In more severe forms, clefts and spaces after necrosis of the basal cell layer result in separation of the dermoepidermal junction. Histological signs are classified into four grades, as follows: grade 1, basal cell vacuolization; grade 2, basal

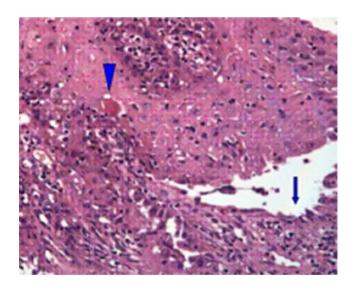


Fig. 2 Histological finding: A subepithelial cleft (*thick arrow*) and an apoptotic keratinocyte (*arrow head*) in the squamous epithelium with lymphocyte infiltration (exocytosis) and focal hydropic change (spongiosis) simulating grade 3 GVHD. (H&E stain; original magnification,  $\times$ 40)

cell vacuolization and single necrotic keratinocytes; grade 3, superepidermal clefts and numerous necrotic keratinocytes; and grade 4, necrosis of the entire epidermis and complete separation from the dermis [5].

Shiohara and Kano had shown that in drug-induced hypersensitivity syndrome, sequential reactivations of several herpesviruses can be detected coincident with various clinical symptoms in the same order as demonstrated in GVHD [5]. In this report, we referred this case as an acute GVHD due to the similarity of clinical symptoms and pathologic findings. Therefore, making a diagnosis of acute GVHD is difficult because the clinical symptoms, histological aspects, and composition of the lymphocytic infiltrate are not specific. The similar histological findings can be observed in cutaneous reactions to chemotherapy or radiation therapy, in adverse drug reactions, and even in some viral infections [5].

In sum, we must be aware of the risks and maintain a high index of suspicion in a patient with history of any type of allergy. Moreover, patients and her families should be informed about the possible complications of this procedure. This underlies the need for careful evaluation of the biocompatibility of any new implantable mesh tape before it becomes available for clinical application. Acknowledgements The authors appreciate Mrs. Chen for her assistance of artwork.

Conflicts of interest None

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