RAB27A was evolutionary conserved among all species available in the database (Fig. D). Polymorphism phenotyping-2 (http://genetics.bwh.harvard.edu/pph2/) and sorting intolerant from tolerant (http://sift.jcvi.org/) predicted that it was "probably damaging" and "deleterious", respectively. In addition, it was absent in 250 unrelated Thai controls.

In conclusion, we found two novel mutations in the *RAB27A* gene in a Thai boy with GS2. The identified mutations enabled us to perform a prenatal diagnosis for the subsequent pregnancy. The fetus was found to carry only one mutation. We reported the first case of a successful prenatal diagnosis for GS2.

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References

1 Griscelli C, Prunieras M. Pigment dilution and immunodeficiency: a new syndrome. Int J Dermatol 1978;17:788-791.
2 Meeths M, Bryceson YT, Rudd E, Zheng C, Wood SM, Ramme K, et al. Clinical presentation of Griscelli syndrome type 2 and spectrum of *RAB27A* mutations. Pediatr Blood Cancer 2010;54:563-572.
3 Menasche G, Pastural E, Feldmann J, Certain S, Ersoy F, Dupuis S, et al. Mutations in *RAB27A* cause Griscelli syndrome associated with haemophagocytic syndrome. Nat Genet 2000;25:173-176.
4 Westbroek W, Tuchman M, Tinloy B, De Wever O, Vilboux T, Hertz JM, et al. A novel missense mutation (G43S) in the switch I region of *Rab27A* causing Griscelli syndrome. Mol Genet Metab 2008;94:248-254.
5 Rossi A, Borroni RG, Carrozzo AM, de Felice C, Menichelli A, Carlesimo M, et al. Griscelli syndrome type 2: long-term follow-up after unrelated donor bone marrow transplantation. Dermatology 2009;218:376-379.
6 Mamishi S, Modarressi MH, Pourakbari B, Tamizifar B, Mahjoub F, Fahimzad A, et al. Analysis of *RAB27A* gene in griscelli syndrome type 2: novel mutations including a deletion hotspot. J Clin Immunol 2008;28:384-389.
7 Cetica V, Hackmann Y, Grieve S, Sieni E, Ciambotti B, Coniglio ML, et al. Patients with Griscelli syndrome and normal pigmentation identify *RAB27A* mutations that selectively disrupt MUNC13-4 binding. J Allergy Clin Immunol 2015;135:1310-1318.e1.
8 Singh A, Garg A, Kapoor S, Khurana N, Entesarian M, Tesi B. An Indian boy with griscelli syndrome type 2: case report and review of literature. Indian J Dermatol 2014;59:394-397.
9 Ohbayashi N, Mamishi S, Ishibashi K, Maruta Y, Pourakbari B, Tamizifar B, et al. Functional characterization of two *RAB27A* missense mutations found in Griscelli syndrome type 2. Pigment Cell Melanoma Res 2010;23:365-374.
10 Sanal O, Ersoy F, Tezcan I, Metin A, Yel L, Menasche G, et al. Griscelli disease: genotype-phenotype correlation in an array of clinical heterogeneity. J Clin Immunol 2002;22:237-243.

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Crohn's disease with anorectal stenosis successfully treated with vedolizumab

Anorectal stenosis (ARS) is a rare complication of Crohn's disease (CD) and a risk factor for both fecal diversion (FD) and proctectomy,[1,2] especially in patients who failed anti-tumor necrosis factor-α (anti-TNF) therapy.[3,4] Herein, we presented a case of a 17-year-old female diagnosed with CD at age 7, with inflammation located in the small bowel and colon (Paris classification: L3L4b). Due to corticosteroid dependency, infliximab with concomitant azathioprine was introduced at age 9 and discontinued two years after, because of the appearance of a 3 cm tumor-mass, which resembled a lymphoma, in the oral cavity. The histopathologic examination confirmed orofacial granulomatosis. The therapy with anti-TNF agent (adalimumab) was continued. While treated with adalimumab and azathioprine, she presented with symptoms of ileus at the age of 14. The cause of the obstruction was ARS (4 cm in length), impassable by the coloscope, which was resolved by endoscopic balloon dilatation (EBD). The dose of adalimumab was increased to 80 mg per week and azathioprine was continued. Despite this therapy, she needed EBD every 3-5 months because of repeated obstructive ARS. She suffered from extreme fatigue and was not able to attend school. Pediatric Crohn's disease activity index (PCDAI) was 45. At that time, surgical therapy with FD was planned. Colonoscopy revealed severe proctitis with ARS and a simple endoscopic score for CD (SES-CD) of 11 in the rectum (Fig. A). However, a trial with vedolizumab (VDZ) was started prior to surgical therapy at age 16. The response to VDZ was assessed at week 10; she was in clinical remission (PCDAI=5), feeling energetic and again able to attend school. Colonoscopy revealed a dramatic endoscopic improvement (Fig. B) with SES-CD of 3.

The management of CD with ARS is challenging. Our patient had failed anti-TNF therapy, therefore a trial involving the biologic agent VDZ with a different mechanism of action was a logical treatment option. VDZ is a selective monoclonal antibody against

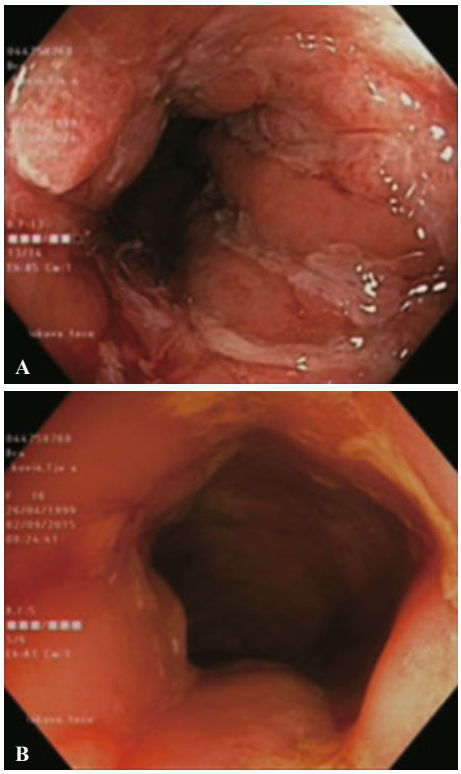

Fig. The endoscopic picture. **A:** Before therapy with vedolizumab, deep ulcerations of anorectal mucosa with anorectal stenosis; **B:** Endosopic improvement after three infusions of vedolizumab.

$\alpha 4\beta 7$-integrin, which targets leukocyte trafficking in the gastrointestinal tract (GIT).[5] VDZ has not been approved for use in pediatric CD, although there are clinical trials that report its effectiveness and safety in adult CD.[6] Our case demonstrates that VDZ may represent a viable treatment option in severe pediatric CD patients with refractory ARS intended for surgical therapy. After one year of the VDZ therapy, our patient remains in clinical and endoscopic remission without the need for EBD or surgical treatment.

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References

1 Galandiuk S, Kimberling J, Al-Mishlab TG, Stromberg AJ. Perianal Crohn disease: predictors of need for permanent diversion. Ann Surg 2005;241:796-801.
2 Brochard C, Siproudhis L, Wallenhorst T, Cuen D, d'Halluin PN, Garros A, et al. Anorectal stricture in 102 patients with Crohn's disease: natural history in the era of biologics. Aliment Pharmacol Ther 2014;40:796-803.
3 Singh S, Ding NS, Mathis KL, Dulai PS, Farrell AM, Pemberton JH, et al. Systematic review with meta-analysis: faecal diversion for management of perianal Crohn's disease. Aliment Pharmacol Ther 2015;42:783-792.
4 Strong S, Steele SR, Boutrous M, Bordineau L, Chun J, Stewart DB, et al. Clinical practice guideline for the surgical management of Crohn's disease. Dis Colon Rectum 2015;58:1021-1036.
5 Bryant RV, Sandborn WJ, Travis SP. Introducing vedolizumab to clinical practice: who, when, and how? J Crohns Colitis 2015;9:356-366.
6 Sandborn WJ, Feagan BG, Rutgeerts P, Hanauer S, Colombel JF, Sands BE, et al. Vedolizumab as induction and maintenance therapy for Crohn's disease. N Engl J Med 2013;369:711-721.

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