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タイトル	Toho Journal of Medicine Vol. 6 No. 3 掲載論文の紹介
別タイトル	PUBLISHED ARTICLES IN THE TOHO JOURNAL OF MEDICINE Vol. 6 No. 3
作成者（著者）	東邦大学医学会編集委員会
公開者	東邦大学医学会
発行日	2020.09.01
ISSN	00408670
掲載情報	東邦医学会雑誌. 67(3). p.112 114.
資料種別	その他
著者版フラグ	publisher
メタデータのURL	https://mylibrary.toho u.ac.jp/webopac/TD44209383

Toho Journal of Medicine Vol. 6 No. 3 掲載論文の紹介

Retrospective Study of Colposcopy for Precancerous Cervical Lesions and Correlation between Diagnosis and Number of Biopsy Specimens

Takahashi R, Kubushiro K, Murakami I, Kugimiya T, Tanaka K, Morita M

Toho J Med 6 (3): 99—103, 2020

要約：

Introduction: Histological diagnosis is performed in patients with abnormal findings on cervical cytology and macroscopic abnormalities of the cervix. In general, targeted histological diagnosis is performed to extract the specimens from lesions with abnormal findings under a colposcope. In this study, we aim to retrospectively verify the number of specimens from different cervical lesions that are most effective for diagnosis.

Methods: We included women with abnormal findings on cervical cytology who underwent targeted biopsy under a colposcope in our hospital from August 2013 to March 2016. The number of specimens extracted and the number of biopsies required to achieve diagnosis were examined in patients with cervical histopathology showing cervical intraepithelial neoplasia (CIN) 1, CIN2, and CIN3. Furthermore, when cervical histology showed indications for conization and total hysterectomy, these procedures were performed to confirm the ultimate histopathological diagnosis.

Results: The definite diagnosis of CIN was made from one, one and two, and one, two, and three biopsies in 81.6%, 96.1%, and 100% patients, respectively.

Conclusions: All patients with CIN1 to CIN3 were diagnosed with three biopsies. In particular, higher number of biopsies was associated with higher rates of definite diagnosis. However, in no cases, definite CIN diagnosis was made at the four biopsies, suggesting that four or more cervical histological biopsies are generally unnecessary. Furthermore, given that 100% patients were diagnosed by their three biopsies, and at most, only three biopsies should be performed.

KEYWORDS: colposcopy, cervical intraepithelial neoplasia, biopsy, cervical cancer

Antibacterial Effects of Vascular Grafts Treated with Rifampicin, Colistin, Vancomycin, or Daptomycin

Okuma S, Hamada M, Hanai Y, Fujii T, Tateda K, Watanabe Y

Toho J Med 6 (3): 104—110, 2020

要約：

Introduction: Some reports suggest that rifampicin treatment of vascular grafts is useful when surgically treating vascular infections and mycotic aneurysms. However, the experimental evidence is limited, and the antibacterial effects of other antibiotic-treated vascular grafts are unknown.

Methods: Vascular grafts were immersed in several antibiotic solutions (rifampicin, colistin, vancomycin, or daptomycin). After *Pseudomonas aeruginosa* PAO1 or *Staphylococcus aureus* N315 were inoculated into the graft exterior, the number of colony-forming units (CFU) inside and outside the grafts was measured over time. Moreover, bonding of colistin and vancomycin to the grafts was quantified.

Results: For grafts immersed in rifampicin, the CFU values outside the grafts decreased over time and those inside the grafts did not increase when the grafts were exposed to a 10^6 CFU/mL concentration of PAO1 or N315. However, at 10^8 CFU/mL, the CFU values increased over time outside and inside the grafts. In PAO1 testing, grafts treated with colistin resisted pathogens in the tested area, and grafts treated with both colistin and rifampicin had even greater resistance. In N315 testing, vancomycin-treated grafts had some resistance to infection, but daptomycin-treated grafts did not. The bonding of colistin and vancomycin to the grafts depended on the immersion time.

Conclusions: Rifampicin-bonded grafts have a strong antibacterial effect when the concentrations of pathogens are low. Colistin-bonded grafts are effective against *P. aeruginosa* infection, and vancomycin-bonded grafts are effective

against *S. aureus* infection.

KEYWORDS: rifampicin-bonded vascular graft, colistin, vancomycin, *Pseudomonas aeruginosa*, *Staphylococcus aureus*

Stromal Fibroblasts Produce Interleukin-11 in the Colon of TNBS-treated Mice

Takeda W, Nishina T, Deguchi Y, Kawauchi M, Mikami T, Yagita H, Nishiyama C, Nakano H

Toho J Med 6 (3): 111—120, 2020

要約 :

Introduction: Interleukin (IL) -11 is a member of the IL-6 cytokine family and is implicated to play a role in pleiotropic functions such as hematopoiesis, bone development, tissue repair, and tumor development. Although the protective function of IL-11 in trinitrobenzene sulfonic acid (TNBS)-induced colitis has been reported, whether *Il11* expression is induced in the colon of TNBS-treated mice is still unclear.

Methods: After inducing TNBS-induced colitis in C57BL/6 mice, *Il6* and *Il11* expressions in the colon were determined using quantitative PCR. Colonic sections were stained with hematoxylin and eosin (H & E) or immunostained with anti-IL-11 antibody along with antibodies against lineage-specific markers. To assess the contribution of the transforming growth factor (TGF)- β signal or mitogen-activated protein kinase/ERK kinase (MEK)/ERK pathway to upregulation of *Il11* expression, we treated mice with TNBS in the presence of neutralizing antibody against TGF- β or a MEK inhibitor, trametinib. Subsequently, *Il11* expression in the colon was determined using qPCR.

Results: TNBS treatment increased *Il11* expression in the colon. Immunohistochemical analysis revealed that IL-11⁺ cells appeared in the subepithelial tissues of the inflamed colon. IL-11⁺ cells expressed podoplanin, vimentin, and collagen IV but did not express α -smooth muscle actin, suggesting that these cells were fibroblasts, and not myofibroblasts. Moreover, TNBS administration induced ERK activation in the colon, and the blockade of the MEK/ERK pathway abolished *Il11* expression in the colon.

Conclusions: Stromal fibroblasts produced IL-11 in the colon of TNBS-treated mice in a MEK/ERK-dependent manner.

KEYWORDS: colitis, interleukin 11, mitogen-activated protein kinase/ERK kinase, stromal fibroblasts, trinitrobenzene sulfonic acid

Efficacy and Safety of De Novo Everolimus Versus Mycophenolate Mofetil with Tacrolimus in Pediatric Kidney Transplantation: 1-year Follow-up

Takahashi Y, Sakai K, Hamasaki Y, Kawaguchi Y, Kubota M, Hashimoto J, Shishido S

Toho J Med 6 (3): 121—127, 2020

要約 :

Introduction: The efficacy and safety of everolimus (EVE) in pediatric kidney transplantation is unknown. We aimed to evaluate and compare the efficacy and safety of EVE/tacrolimus (TAC) with mycophenolate mofetil (MMF)/TAC.

Methods: This 12-month, nonrandomized single-center, open-labeled retrospective observational casecontrol trial included patients aged <18 years receiving kidney from a living-related or deceased donor between January 2012 and May 2017. Among 49 patients with TAC-based immunosuppression regimen, 13 received EVE/TAC regimen post-transplant, and the remaining 36 received the standard regimen using MMF/TAC. Clinical course was evaluated at 1 year.

Results: Patient characteristics between both groups were not significantly different, except for recipient age (EVE/TAC vs MMF/TAC; median: 12.7 vs 5.8 years, $p < 0.01$). Median estimated glomerular filtration rate was similar in both groups (EVE/TAC vs MMF/TAC; median: 72.3 vs 75.5 ml/min/m²) at 1 year. Incidence of Epstein-Barr virus

infection was not significantly different in both, but incidence of cytomegalovirus viremia was significantly lower with EVE/TAC than with MMF/TAC (2 of 13 [15.4%] vs 19 of 36 [52.8%], $p = 0.03$). Stomatitis rate was higher in EVE/TAC than in MMF/TAC (23.0% vs 0.0%, $p = 0.01$). While neutropenia was not statistically different in both groups, no EVE/TAC regimen did show neutropenia. Acute rejection within 1 year did not differ in both groups. Pathological vascular injury was not significantly different in both groups, despite expected vascular protection by EVE.

Conclusions: The efficacies of EVE/TAC and MMF/TAC in pediatric kidney transplantation for 1 year were comparable. Cytomegalovirus infection rate was significantly lower with EVE/TAC than with MMF/TAC regimen.

KEYWORDS: pediatric kidney transplantation, everolimus, acute rejection, efficacy, safety

Novel Treatment for Atrial Septal Defect without an Inferior Septal Rim and Partial Anomalous Right Lower Pulmonary Venous Connection

Kawada K, Katayama Y, Ozawa T, Fujii T, Shiono N, Watanabe Y

Toho J Med 6 (3): 128—131, 2020

要約 :

There is no consensus regarding the ideal surgical procedure for treatment of combined atrial septal defect without an inferior septal rim and partial anomalous right lower pulmonary venous connection. A 41 year-old woman had previously undergone ineffective surgical closure of an ostium secundum-type atrial septal defect. Intraoperatively, we ascertained the correct diagnosis of partial anomalous right lower pulmonary venous connection combined with a residual defect. Incision of the atrial septal wall up to the superior margin along the previous suture line yielded a flap adequate for the atrial septal wall, and this flap was slid again into the entire opening. The spatially complex intracardiac lesion was repaired by using only autologous tissue.

KEYWORDS: atrial septal defect without an inferior septal rim, partial anomalous right lower pulmonary venous connection, autologous tissue

Laparoscopic Excisional Surgery for Growing Teratoma Syndrome Presenting 19 Years after Initial Treatment: A Case Report

Tagui C, Ishida H, Takashima A, Manrai M, Kinoshita T

Toho J Med 6 (3): 132—135, 2020

要約 :

Growing teratoma syndrome (GTS) is rare. The optimum treatment strategy is complete surgical excision. We describe a 42-year-old woman with GTS who was treated with laparoscopic excisional surgery. Initially, we performed right salpingo-oophorectomy; she was diagnosed with grade 2 immature teratoma, which was treated with four courses of peplomycin, etoposide, and cisplatin chemotherapy. Postoperatively, her tumor marker (alpha-fetoprotein) was not elevated; however, 19 years later, she developed an enlarged mass in her pelvic cavity. Laparoscopic surgery revealed some of the enlarged tumors detected by preoperative magnetic resonance imaging in the pouch of Douglas. We resected the retroperitoneal tumors. The histological diagnosis was mature teratomas. We concluded that these tumors were GTS. No recurrent disease was observed 12 months thereafter. This case represents one of the longest reported interval periods before the development of GTS. Laparoscopic surgery is an effective alternative diagnostic and therapeutic approach in cases suggestive of GTS. Laparoscopic surgery might be feasible in cases of GTS, but further study will be needed, given that only a few reported cases have been managed laparoscopically.

KEYWORDS: Growing teratoma syndrome, Laparoscopy, Immature teratoma, Laparoscopic surgery, Case report
