LETTERS TO THE EDITOR

Refractory Autoimmune Pancreatitis: Azathioprine or Steroid Pulse Therapy?

TO THE EDITOR: We read with interest the article by Church et al. (1) on autoimmune pancreatitis (AIP) in the first series from the United Kingdom. They diagnosed 11 patients with AIP and treated them with oral steroid. Although initial response to steroid therapy was excellent in all patients, six patients (55%) relapsed on steroid reduction or withdrawal, and four of them responded to azathioprine and increased steroid. Because azathioprine therapy may cause acute pancreatitis and requires frequent blood tests for early detection of side effects (2–4), a safe and simple alternative for refractory AIP is needed.

AIP is a recently described unique form of chronic pancreatitis characterized by sausage-like diffuse swelling of the pancreas, a diffusely irregular narrowing of the main pancreatic duct, a high serum IgG4 concentration, and a response to oral steroid therapy (5, 6). In unresponsive patients with the biliary stenosis caused by AIP, surgery may be necessary for the relief of symptoms and for differentiation from malignancy (5). Because oral steroid therapy requires a long period for the drug tapering, the biliary stenosis suspected to be caused by AIP but cannot be distinguished from malignancy is not indicated for the therapy (5, 6). Steroid pulse therapy is a well-recognized alternative for refractory autoimmune disorders without steroid tapering. We, therefore, applied the therapy for refractory AIP, resulting in dramatic response for a short period (5, 6).

Azathioprine is an effective drug as a maintenance and steroid-sparing agent in autoimmune disorders and organ transplants (2–4). Although azathioprine is widely used in Crohn’s disease, a major drawback is the frequent occurrence of side effects, especially acute pancreatitis (2). A large population-based case-control study found an eight-fold increased relative risk of acute pancreatitis in all users of azathioprine (3). In animal models, azathioprine involves activation of circulating vasoactive mediators, formation of microthrombi, or direct injury of the capillary endothelium, and then deteriorates pancreatic microcirculation, thereby increasing ischemia and acinar cell injury (4). Although further comparative studies are needed, we believe that azathioprine therapy should be avoided in pancreatic diseases such as AIP, whereas steroid pulse therapy is a more effective alternative for refractory AIP.

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REFERENCES


Autoimmune Pancreatitis: Optimal Therapy Has Not Been Determined

TO THE EDITOR: We would like to thank Matsushita et al. for their interest in our article. They raise specific points concerning the type of steroid therapy for acute autoimmune pancreatitis (AIP) and the use of azathioprine in disease relapse. These points are part of the broader question: What is the optimum therapy for autoimmune pancreatitis (AIP)? This question remains unanswered, as published data include only small case series and case reports. No randomized controlled data exist.

Treatment options for acute AIP include observation only, a tapering regimen of oral steroids without maintenance therapy, tapering oral steroids followed by low-dose maintenance therapy, and intermittent steroid pulse therapy. Disease relapse may be treated by further steroid therapy with or without second line therapy in the form of immunosuppressive drugs such as azathioprine or 6-mercaptopurine.

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Although a proportion of patients with AIP appear to improve spontaneously, it is increasingly apparent that steroid therapy is effective in resolving symptoms, improving imaging, and possibly in reducing the longer-term consequences of the disease (1). The usual approach is to use oral prednisolone 30–40 mg daily for 2–4 wk with a dose reduction of 5 mg per week thereafter. This approach results in a rapid clinical and radiological improvement, usually evident within 2–4 wk, as reported by a number of authors (2–5) and also demonstrated in our series. Matsushita et al. report a single case of AIP recurrence after surgery for biliary stricture (6). The authors state that in cases of biliary stricturing disease, which are difficult to differentiate from malignancy, oral steroid therapy should not be used. They treated their patient with two courses of intravenous methylprednisolone over 3 days each, and assessed response after 2 wk. The biliary stricture improved and the patient was then managed with a tapering course of oral prednisolone. From our own experience we would argue that a similar response would be expected with oral prednisolone from the outset. Therefore, we question the need for intravenous therapy. We would agree that when there is a strong suspicion that a patient has a resectable malignancy, surgery should not be delayed. However, in cases of AIP, there are usually features in the patient’s history, imaging, and serology which make AIP at least as likely, and in such cases a trial of steroids with regular review would be a reasonable approach that would be likely to save these patients from undergoing unnecessary surgery.

Our patient series currently includes 26 patients, of whom 11 (42%) have experienced a disease relapse (unpublished data), a rate similar to that reported by other authors (1). Perhaps the lessons of autoimmune hepatitis will ultimately apply to AIP: that good responses to initial steroid therapy are seen, but disease relapse is common in the absence of longer-term maintenance immunosuppression (7). Relapses in AIP usually respond to reintroduction or an increased dose of steroids. In order to prevent further relapse, most authors have reported either the use of low-dose maintenance steroids (prednisolone 2.5–10 mg daily), or immunomodulators (e.g., azathioprine, or mycophenolate mofetil). The use of low-dose maintenance steroids is associated with two main problems. First, there is a significant relapse rate: the study by Hirano et al. reported a 32% relapse in patients on low-dose steroids (4). Second, there is a risk of developing steroid side effects in this generally elderly population. Vertebral fractures, osteonecrosis of the femoral head, and diabetes have all been reported in AIP patients (4) with steroid effects perhaps accentuated by associated pancreaticobiliary disease. While the side effects of immunosuppressants may also be severe, none of the eight azathioprine-treated patients in our series experienced severe side effects, although one patient required dose reduction due to nausea. Similar results have been reported by other groups (1). The risk of acute pancreatitis secondary to azathioprine is low, occurring in 2–3.8% of inflammatory bowel disease patients treated with the drug (8, 9). The actual risk in AIP patients is unknown. The analogy with autoimmune hepatitis may again be appropriate in that azathioprine may rarely cause significant liver function derangement but has a proven role in maintaining disease remission (10). We believe that AIP is a chronic, multisystem inflammatory condition that is likely to require long-term maintenance therapy in a significant proportion of patients. We feel that the current evidence supports the use of azathioprine as a steroid-sparing agent in those patients who relapse on withdrawal of steroid therapy. Further studies are required to define the optimum dose and duration of therapy in these patients and also to obtain safety data.

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REFERENCES


Comparison of Seven Staging Systems in Cirrhotic Patients with Hepatocellular Carcinoma in a Cohort of Patients Who Underwent Radiofrequency Ablation with Complete Response

TO THE EDITOR: I read with great interest the article by Guglielmi et al. (1), where the authors compared seven
staging systems for patients with hepatocellular carcinoma (HCC) undergoing radiofrequency ablation (RFA). The authors reported that the Barcelona Clinic Liver Cancer (BCLC) system showed the best discrimination ability and monotonicity of gradients for the patients, as compared to the other six staging systems (1, 2). The investigators demonstrated that the BCLC system had the potential to be the most predictive model in nonsurgical patients, as well as in surgical patients. The investigators must be congratulated for their difficult work. However, I have some comments on this article. First, an early censor rate was not mentioned in the text. Any cohort study with a rate of loss to follow-up greater than 20% is regarded as low quality (3). Early censor rates can be different between each stage, and I think it can affect the discriminatory ability of each staging system. I would like to know the author's opinion concerning the effect of the early censor rate on the staging systems. Second, five patients with portal vein thrombosis were included in the study. I think that patients with portal vein thrombosis are usually contraindicated for RFA. I am curious what the rationale was for the inclusion of these patients in the study.

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REFERENCES


Comparison of Seven Staging Systems in Cirrhotic Patients with Hepatocellular Carcinoma in a Cohort of Patients who Underwent Radiofrequency Ablation with Complete Response—Response to Dr. Yun Ku Cho

TO THE EDITOR: We appreciate the commentary on our paper “Comparison of seven staging systems in cirrhotic patients with hepatocellular carcinoma in a cohort of patients who underwent radiofrequency ablation with complete response” by Dr. Yun Ku Cho (1). He underlined the problem of early censor rate. In our study we retrospectively analyzed patients who underwent radiofrequency ablation (RFA) from 1998 to 2005. The 6 and 12 months censor rates were 7 and 16%, respectively, and we did not identify significant differences of early censor rate among categories of different staging systems. In particular in Barcelona Clinic Liver Cancer (BCLC) staging system the 12-month censor rate was 18% for class A1, 14% for A2, 9% for A4, and 15% for B, respectively. The BCLC classes A3 and C (3 patients in each group) did not have 12-months censored patients. RFA was introduced around 1990s as a palliative treatment of hepatocellular carcinoma (HCC) and the follow-up time of published studies are still short (2). It should be underlined that the prognosis of HCC is dismal and the 5-yr survival after RFA is lower than 30% (2). For this reason in our experience, as others in the literature, a mean follow-up time of almost 2 yr is considered adequate for survival analysis. Our mean follow-up time of 26 months is comparable to other studies in the literature.

Dr. Yun Ku Cho also observed the inclusion in our study of seven patients with portal vein thrombosis. The presence of portal vein thrombosis is a major prognostic factor in HCC after surgical and nonsurgical therapies. In our study, patients with main portal vein thrombosis were not included, whereas a small group of patients (less than 10% of patients) with segmental portal vein involvement has been treated with RFA. The prognostic significance of portal vein involvement has been demonstrated also in our study with 57% of patients who died within 3 yr compared to a lower rate (39%) for patients without vascular involvement; however, it should be noted that two out of seven patients survived more than 3 yr. In this group of patients, RFA showed its safety with no patients who experienced major complication. Also in other studies in literature, RFA has proved its safety in patients with portal vein thrombosis, and the authors stated that portal vein thrombosis should not be considered a contraindication for RFA (4, 5). Obviously, the long-term efficacy of RFA in these patients needs further validation.

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Meta-Analyses on the Prophylactic Use of Antibiotics in Acute Pancreatitis: Many Are Called but Few Are Chosen

TO THE EDITOR: I read with interest the article by Bai et al. that was published in the recent issue of the Journal (1). The authors conducted a meta-analysis of seven randomized controlled trials (RCTs) on the prophylactic use of antibiotics versus placebo/no antibiotics in acute pancreatitis patients with necrosis proven by computed tomography (CT). Bai and colleagues concluded that the prophylactic administration of antibiotics did not reduce the risk of infected pancreatic necrosis and mortality in patients with acute necrotizing pancreatitis, as well as encouraged other researchers to conduct further top-quality trials to investigate this question. However, I have some comments with regard to this publication.

My first concern regards the selection of studies for this meta-analysis. Although the authors aimed to derive a summary estimate of antibiotics effect exclusively from patients with CT-proven necrosis, this was not the case in some of the included trials. In particular, some patients were included in the individual trials on the basis of ultrasound diagnosis (2) or the level of serum C-reactive protein (3). On the other hand, the authors excluded the study by Spicak et al. (4) because of “no data of pancreatic necrosis.” Awkwardly enough, their colleagues from the same research institution, who conducted a meta-analysis on the same topic less than 2 yr ago, did find the required data and included that study in their meta-analysis (5).

The second point is that Bai et al. recommended enrolling only patients with CT-verified pancreatic necrosis in a future large-scale RCT. However, it is known that CT is of limited use within the first days of the disease and has a good diagnostic performance only by day 3 after admission (6). Thereby, this recommendation would lead to a delayed institution of antibiotics, the possible potential of which as a prophylactic treatment might be exhausted by the time of diagnosis of pancreatic necrosis by CT. Furthermore, one should be aware that a future adequately powered RCT should recruit 400 patients with acute necrotizing pancreatitis to show a significant reduction in infected pancreatic necrosis from 20% to 10% (7). As the recent RCT in 32 centers (many of which are highly dedicated to the studies on acute pancreatitis) in North America and Europe was able to recruit only 100 patients over 2 yr (8), the recommendation with regard to a new large-scale trial seems fairly formal and unrealistic at the present time.

Third, it is interesting to know that, apart from the two meta-analyses from China mentioned above (1, 5), eight more attempts were undertaken to statistically aggregate the data on the same research question. While only two new RCTs were published in 2006–2007 (3, 8), it seems paradoxical that 7 of the 10 meta-analyses were published within the same time period (1, 5, 9–13). Notably, a total of 13 different RCTs were included in those seven meta-analyses, all of which purported to define the role of antibiotic prophylaxis in acute pancreatitis. However, as a result of employing different inclusion criteria, the authors alternately came to ambivalent conclusions and provided opposite recommendations regarding the prophylactic effect of antibiotics on the risk of pancreatic infectious complications (Table 1).

In the setting of this looming deadlock, some authorities recommended to leave the decision on the use of prophylactic antibiotics to the discretion of single institutions (7). However, I believe that such an approach may contravene the essence of evidence-based medicine. To my mind, the contradictory findings of different authors indicate that the exploited standard methodology of meta-analysis is inapt in addressing such complex question as the prophylactic effect of antibiotics in patients with acute pancreatitis because of the marked heterogeneity among the conducted RCTs. Thereby, an application of advanced statistical techniques (e.g., α-spending function and stochastic curtailment (14)) should be used to provide a sound and unbiased estimation of the antibiotics as a prophylactic modality in acute pancreatitis. With this aim in mind, a close collaboration among the physicians, statisticians, and clinical epidemiologists should be established to answer one of the most controversial questions in the modern pancreatology.

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Table 1. Characteristics of the Meta-Analyses Published in 2006–2007.

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Prophylactic Antibiotics in Acute Pancreatitis: Further High-Quality Trials Are Still Warranted

TO THE EDITOR: We wish to thank Dr. Maxim S. Petrov for showing interest in our article (1); however, some issues need to be clarified.

First, we are not awkward at all because, if the addresses and affiliations of the authors of the two different articles were reviewed carefully, it is quite clear that the institution of the authors (Renji Hospital, Shanghai Second Medical University) mentioned (2) is NOT the same institution as ours (Changhai Hospital, Second Military Medical University).

Second, though the authors (2) included an article by Spicak et al. (3) in their meta-analysis, the focus of their research was on the role of prophylactic antibiotics in severe acute pancreatitis, and not computerized tomography (CT)-verified acute necrotizing pancreatitis; consequently, the subgroup patients with CT-verified acute necrotizing pancreatitis were not analyzed.

During the process of selection of relevant trials, we found three, and not one, articles by Spicak et al. (3–5), but, unfortunately, the data for the subgroup of patients with CT-verified pancreatic necrosis in the first two studies (3, 4) were not available. Additionally, the third study (5) seems to be a kind of combination of the previous two studies; therefore, we decided it would be more appropriate to wait for the full-text publication to evaluate the methodological quality of the study.

With regard to one of the included trials (6), due to our oversight, we did not notice that not all the enrolled patients received CT scan examination; nonetheless, after personal communication with Dr. Ola Røkke, we retrieved the correct subgroup data of mortality and pancreatic necrosis infection rate in patients with CT-documented necrotizing pancreatitis (imipenem group 12 patients, control group 16 patients), that is, 2 patients in the imipenem group and 2 patients in the control group died, while 2 patients in the imipenem group and 4 patients in the control group developed pancreatic necrosis infection. Therefore, we reanalyzed the seven trials, and the overall effect of antibiotics on mortality (risk ratio [RR] 0.73, 95% confidence interval [CI] 0.43–1.23, P = 0.24) and pancreatic necrosis infection (RR 0.85, 95% CI 0.58–1.26, P = 0.42) did not change much. We believe these analyses defended the results of our study.

Dr. Maxim S. Petrov doubted why only 7 of 15 trials were included in our study. The selection of trials was not cherry-picking; by contrast, as stated in the method section, the aim of our study was to evaluate the effect of prophylactic intravenous antibiotics on infected pancreatic necrosis and mortality in acute necrotizing pancreatitis, and thus we chose relevant trials according to the predetermined protocol. We had comprehensively reviewed all the relevant trials, including the 15 trials mentioned by Dr. Maxim S. Petrov, before conducting this present meta-analysis, and revealed that there was substantial clinical heterogeneity among all these trials. In view of this, it is impossible to combine the results of these trials, and based on these greatly heterogeneous trials, it is also impossible to produce meaningful conclusion. We suggest it may be appropriate to include all these trials in a systematic review but not in a meta-analysis.

From these trials that we analyzed, we may conclude that within the past two decades significant progress has been made in the medical approach to pancreatic necrosis, but the evidence for the recommendations for or against the use of...
antibiotics remains inconclusive. It is clear that the most important limitation to an evidence-based approach of use of antibiotics lies in the difficulty for any single medical center to enroll sufficient number of patients with pancreatic necrosis to satisfy the requirements for statistical power. We believe future multicenter or multinational trials or individual patient data analysis would be mandatory to answer current and future critical problems in necrotizing pancreatitis. Although advanced statistical methods are important for data analysis, without well-designed and executed trials, no statistical method can close the book on the prophylactic effect of antibiotics.

Finally, we sincerely appreciate the help from Dr. Ola Røkke for kindly providing the necessary data in their study (6).

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Disparities in Liver Transplantation for Localized Hepatocellular Carcinoma: Race or Socioeconomic Class?

TO THE EDITOR: Race has been identified as a variable for liver transplant in localized hepatocellular cancer. However, socio-economic class may adversely affect certain races. That is why the socioeconomic status of an individual may be the predominant factor in variable transplant rates and will require different kinds of intervention.

Siegel et al. (1) studied the patients with nonmetastatic hepatocellular cancer (HCC) using the population-based cancer registries using the US National Cancer Institute’s Surveillance, Epidemiology and End Results (SEER) database.

Forty-five percent of the final study population was Non-Hispanic Whites, 29% Asians, 17% Hispanics and 9% African American, showing disproportionately more Asians affected by HCC (Asians comprise only 3.6% of US population). Only 21% of the analyzed population received transplant despite having high survival benefit. Married, young age group, whites were more likely to receive liver transplant. African Americans and Asians were half as likely to receive liver transplant as the Non-Hispanic Whites (13% and 17% vs. 25% whites).

The study did not address why, despite having significant survival advantage, only 21% (25% of whites) of the localized HCC population received a liver transplant. Are there referral bias, insurance limitations, lack of social support, comorbidities, substance/alcohol abuse, etc., issues? African Americans (even belonging to younger age groups) and Asians received proportionately lower transplants. If this is true, it is definitely not a good sign more than four decades after the Civil Rights Act was passed in the U.S. Congress in 1964. How valid is the above statement? Are we really giving preference to one race over the other? Is there any other confounding variable that is being projected as a racial factor?

Noteworthy, unlike other cancer surgeries such as esophageal cancer or lung cancer, liver transplant requires long-term follow-up, has strict selection criteria, requires strict psycho-social scrutiny in terms of compliance potentiality, family support for post transplant follow-up and care, assessment of personal habits, i.e., substance abuse, alcohol abuse, and, of course, the financial factor with valid health insurance. It is in that area that some of the minority ethnic groups may not do favorably well and may act as confounding variables. Mentionable here, race/ethnicity and social/economic class are very closely inter-linked to affect the lifestyle, mortality and morbidity of an individual (2). Lower income groups have higher morbidity (3) as well as mortality (4) even after the race factors are taken into consideration. Likewise, socioeconomic classes could have a stronger influence on low proportion of liver transplant and also lower transplant rates in African Americans and Asians.

Like all national data-based programs on health mortality, the SEER program also does not have any data on the class characteristics (i.e., income, education or profession). In fact, United States is one of the few developed countries where mortality statistics are not collected by class. (2) As a consequence, we may be overemphasizing the racial factors. This major flaw in the data was duly acknowledged by the authors. A prospective population-based study will be able
to address this issue as well as the 21% overall low transplant rate and focus our attention to the problem of socio-economic disparity contributing to variable liver transplant rates. This type of analysis in liver transplant and health care delivery will have broader policy implications (5).

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Response to Haque

TO THE EDITOR: Haque and Zariat correctly point out that race/ethnicity is probably an indicator for other factors, including socioeconomic status. SEER does not allow us to distinguish issues related to class and education, as we acknowledge in our manuscript. SEER also does not give information related to underlying comorbidities. This may explain to some extent why the vast majority of those with localized hepatocellular cancer (HCC) in our study did not receive a transplant for their HCC. However, we have also shown both overuse and underuse of transplant for HCC in a cohort of older patients, pointing out that other biases may play a role (1).

While selection for receipt of a liver transplant for HCC may be more involved than for some other types of cancer surgeries, underuse of potentially curative surgery has been noted in many other cancer types, including esophageal and lung (2, 3). All of these issues support the need for further research in this area.

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REFERENCES

The Cell Phone Camera Enters the Gastroenterologist’s Office

TO THE EDITOR: Cell phones have become ubiquitous. Arranging for appointments and sick calls have been handled by the telephone for decades. Newer technology allows the automated refilling of prescriptions and notification of laboratory results. Newer Internet-enabled phones permit research of the disease pathophysiology, local and national support groups, and even a comparison of physicians’ qualifications. I recently had two experiences illustrating new ways in which patients are using technology to change the practice of medicine and, particularly, gastroenterology.

A 30-yr-old man presented with an 8-yr history of bowel problems. He often has 2–3 days between bowel movements and then will have 2–5 stools over a few hours. The stool consistency can vary from hard pellets to loose brown water with mucus. Often there is an aching pain in the left lower quadrant, which is relieved after the bowel movement (BM). Problems at work or with his family often precipitate these distressing episodes. There is no bleeding, fevers, or weight loss. Evaluation by his primary care physician, including laboratory work, was unremarkable. There are dietary changes with decreased fat intake improved his problem for a short while. Coincident with visa issues, his symptoms worsened. At the patient’s insistence, he was referred to a gastroenterologist. To be sure that his concerns were fully appreciated, he used his cell phone to take photos of each BM for 10 days with annotations of date and time. He also prepared pictures of his commode at home and work so that the place could be identified. His cell phone model was capable of producing a slideshow presentation.

A 74-yr-old woman had a near syncopal episode at home.

The Cell Phone Camera Enters the Gastroenterologist’s Office
These two cases illustrate patients’ increasing ability to provide historical information with a visual impact that was not easily accessible prior to cell phone cameras. Of particular note, both instances were initiated by the patients. Cell phone cameras have proven useful in providing visual information to dermatologists (1) and primary care physicians (2). There is now also a niche for gastroenterology.

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Rupture of Pancreaticoduodenal Artery Aneurysm Caused by Superior Mesenteric Artery Embolism

TO THE EDITOR: True pancreaticoduodenal artery (PDA) aneurysms are highly associated with celiac artery (CA) stenosis or occlusion, about 60–75% (1), and pancreaticoduodenal arcades ordinarily function as collateral pathways from the superior mesenteric artery (SMA) to the celiac branches in this situation (1, 2). Sutton and Lawton postulated, with the phrase “aneurysm of collateral supply,” that development of PDA aneurysm was a direct consequence of increased blood flow (3). In fact, the aneurysms disappear with recovery of normal blood flow by revascularization of the CA (4). We report an interesting case in which a high flow by an SMA embolism at the distal portion of the PDA inflow contributed to the rupture of the PDA aneurysm with CA stenosis; in this case, angiographic findings clearly indicated the critical participation of a rapid rise in PDA flow in the aneurysm rupture.

A 65-yr-old man was referred to our hospital because of epigastralgia and diarrhea for 2 days. His body temperature was 37.2°C, blood pressure was 126/100 mmHg, and he had an irregular pulse rate of 103 beats/min. Hemoglobin was 15.6 g/dL, white blood cell count was 15,310/mm³, C-reactive protein was 19.4 mg/dL, and serum amylase was 63 IU/L. Other laboratory tests were within normal limits. Electrocardiography showed atrial fibrillation.

Computed tomography (CT) scan of the abdomen showed a retroperitoneal hematoma (Fig. 1A, white arrow) between the duodenum and the pancreas with PDA aneurysm (Fig. 1A, white arrowhead) and the thickened wall of the terminal ileum and cecum (Fig. 1B, white arrow) consistent with ischemic changes (Figure 1B). Three-dimensional CT angiography (Fig. 2A) revealed the inferior PDA aneurysm (Fig. 2A, yellow arrow) with CA stenosis (Fig. 2A, red arrow) and the embolism at the distal portion of the PDA inflow in the SMA (Fig. 2A, white arrow), respectively. Selective CA and SMA angiography also showed these findings (Fig. 2B). Selective microcoil embolization for aneurysm was undertaken and the patient has been on a good clinical course. Ischemic colitis due to SMA embolism was also confirmed by colonoscopy.

In the present case, it seems to be likely that the PDA aneurysm originally developed by increased PDA flow due to CA stenosis and was followed by the embolism at the distal portion of the PDA inflow in the SMA due to atrial fibrillation. These events brought ischemic colitis and a rapid rise in PDA blood flow and, finally, the rupture. To our knowledge, this is the first case of PDA aneurysm rupture by SMA embolism, and it also supports the hypothesis that hemodynamic changes participate in both formation and rupture of PDA aneurysms.

The management of not only ruptured but also nonruptured PDA aneurysms is important because the size of PDA aneurysms is not related to the risk of rupture (1). In embolization, new aneurysm formation due to increased blood flow in

![Figure 1](image_url). Computed tomography (CT) scan of the abdomen showed a retroperitoneal hematoma (A, white arrow) between the duodenum and the pancreas with PDA aneurysm (white arrowhead) and the thickened wall of the terminal ileum and cecum (B, white arrow) consistent with ischemic changes.
the other PDA was reported (5). And thus, a revascularization procedure is recommended for either nonruptured or ruptured cases with CA stenosis. However, it was not performed at the patient’s request. Careful follow-up for aneurysm recurrence will be required.

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Hepatic Splenosis Diagnosed by Spleen Scintigraphy

TO THE EDITOR: A 59-yr-old gentleman had a splenectomy in his childhood after trauma to the abdomen. He underwent a physical check-up at our hospital and denied any abdominal discomfort. There was no personal or family history of neoplasm. Physical examination was unremarkable. Blood serological tests revealed positive hepatitis B virus surface antigen, but antibody against hepatitis C virus was negative. As well, both alpha-fetoprotein (4.8 ng/mL, normal <20 ng/mL) and carcinoembryonic antigen (2.4 ng/mL, normal <6 ng/mL) levels were within normal limits. Abdomen ultrasound (US) disclosed absence of spleen and a 0.9-cm-sized hypoechoic nodule abutting the anterior surface of left lateral hepatic segment. Abdomen computed tomography (CT) without contrast medium administration revealed two hypodense nodules in hepatic segment VII, 2.2 cm and 1.5 cm in size, respectively. There was also a 1.2-cm-sized hypodense nodule at the left lateral hepatic segment. All of these lesions were located near the liver capsule. After contrast administration, the lesions became homogeneously hyperdense in the arterial phase, isodense in the portal venous phase, and slightly hypodense in the equilibrium phase. The main portal trunk and its branches were patent. Magnetic resonance imaging (MRI) of the abdomen without contrast medium injection showed that the lesions were homogeneously hypointense on T1-weighted imaging (Fig. 1A) and hyperintense on T2-weighted imaging (Fig. 1B). After intravenous administration of gadolinium-diethylenetriaminepentaacetic acid (Gd-DTPA), global enhancement of the lesions was found in the arterial phase (Fig. 1C) and the lesions became isointense in the portal phase (Fig. 1D). With reference to the history of splenectomy, hepatic splenosis was strongly suspected. However, with only these US, CT, and MRI features, it was difficult to distinguish splenosis from other hepatic masses such as adenoma, focal nodular hyperplasia, and hepatocellular carcinoma (HCC). We then arranged 99m technetium (Tc)-labeled heat-denatured red blood cell scintigraphy, which disclosed uptake of the labeled cells in areas corresponding to the nodules seen on other image studies (Fig. 2) and confirmed the diagnosis of hepatic splenosis.
Figure 1. (A) T1-weighted MR image before the administration of Gd-DTPA delineated the lesions as hypointense nodules. (B) T2-weighted MR image showed the lesions as hypointense nodules. (C) T1-weighted MR image after the administration of Gd-DTPA revealed global enhancement of the lesions in the arterial phase. (D) T1-weighted MR image after the administration of Gd-DTPA disclosed that the lesions became isointense in the portal phase.

Figure 2. 99m Tc-labeled heat-denatured red blood cell scintigraphy showed uptake of the labeled cells in areas corresponding to the MRI.
In 1939, Buchbinder and Lipkoff introduced the term “splenosis” to describe the first case in a young woman (1). Splenosis represents heterotopic autotransplantation and seeding of splenic tissue, usually occurring after splenic trauma or operation. Splenic vein emboli or a hematogenous spread of splenic pulp has also been described as a possible mechanism of seeding into the liver (2). The implants are rarely clinically important and are incidental findings (3). Some lesions, however, can cause abdominal pain by twisting of a long pedicle attached to the splenic nodule (4). In splenosis, US, CT, and MRI findings are not specific and almost indistinguishable from those of other hepatic neoplasms, especially HCC. As Taiwan is in an endemic area for HCC, and the patient was a case of chronic hepatitis B, it was a difficult task to make an accurate diagnosis of hepatic splenosis by abovementioned image modalities in such a patient. When splenosis is suspected, although histology is the gold standard for the diagnosis, scintigraphy with sensitive 99mTc-labeled heat-denatured red blood cells represents a diagnostic technique of high specificity (5).

This case report demonstrates that hepatic splenosis should be considered in the differential diagnosis of hepatic nodules in a patient with splenectomy, particularly when the lesions are located at the periphery of the liver. In addition, the 99mTc-labeled heat-denatured red blood cell scintigraphy can confirm the diagnosis of hepatic splenosis, and preclude unnecessary interventions such as biopsy, angiography, and operation.

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**Mediastinal Mycobacterium avium-intracellulare Infection Diagnosed by Transesophageal Endoscopic Ultrasound-Guided Fine-Needle Biopsy**

TO THE EDITOR: As a relatively recently implemented modality for sampling mediastinal lesions, the diagnostic spectrum of transesophageal endoscopic ultrasound (EUS)-guided fine-needle aspiration/biopsy (FNAB) is yet to be fully defined at this anatomic site.

While studies have documented the effectiveness of EUS-FNAB sampling of mediastinal lymph nodes for staging of lung carcinoma, few reports have described the utility of EUS-FNAB in infectious processes of the mediastinum. We report the case of a 46-yr-old African-American male patient who presented to our institution with the chief complaint of shortness of breath. His medical history was significant for stage C3 human immunodeficiency virus (HIV) infection, and an immunodeficiency panel revealed a CD4 lymphocyte count of 24. A computed tomography scan of the chest showed a mediastinal mass that was felt to represent adenopathy (Fig. 1). Due to the patient’s dyspnea, bronchial washing was performed.

**Figure 1.** Computed tomography scan showing the posterior mediastinal mass.
Microscopic examination of the bronchial fluid revealed sparse squamous cells, and the specimen was considered insufficient for cytologic diagnosis. The remainder of the fluid was submitted for bacterial, viral, and mycobacterial cultures. At that time, a transbronchial biopsy of the enlarged subcarinal lymph nodes was attempted.

Microscopic review of the sampled tissue proved it to be insufficient for diagnosis.

With culture results pending, the patient underwent transesophageal EUS-FNAB of the mediastinal mass. During the procedure, a mass was identified in the area of the distal left atrium and extended superiorly to the subcarina. By ultrasonography, the mediastinal mass was felt to consist of multiple enlarged lymph nodes, the largest measuring 3.5 × 1.7 cm. Three core biopsies were obtained by EUS-FNAB, and as the differential diagnosis included lymphoma, one biopsy was submitted for flow cytometric immunophenotypic analysis, but was insufficiently cellular for diagnosis. Microscopic examination of the remaining core biopsies revealed sheets of spindle cells that had relatively bland, elongated nuclei (Fig. 2). Based upon the histologic appearance, the differential diagnosis included a benign fibrous proliferative lesion, a low-grade sarcoma, and a proliferation of epithelioid histiocytes. Immunohistochemical stains for cytokeratin, smooth muscle actin, S-100 protein, and CD34 performed to investigate the histogenesis of the lesion were negative. Special stains for acid-fast and fungal organisms, however, highlighted numerous elongated acid-fast organisms in the spindle cells, confirming the spindle cells as histiocytes filled with mycobacterial organisms. Subsequently, the pending respiratory and blood cultures speciated the organisms as *Mycobacterium avium-intracellulare* (MAI).

While EUS-FNAB was initially described for the diagnosis of gastrointestinal lesions, its diagnostic utility has been expanded for the sampling of mediastinal lesions, particularly at lymph node stations 4 (lower paratracheal), 5 (subaortic/anterosuperior window), 7 (subcarinal), 8 (parasophageal below the carina), and 9 (pulmonary ligament) in the Mountain/Dresler classification (1). The utility of EUS-FNAB for staging of non-small cell carcinoma of the lung has been described (2), but its use in the diagnosis of infectious mediastinal lesions has rarely been documented. Sampling of the mediastinal lymph nodes using this technology has documented infection with *Nocardia spp.*, *Histoplasma capsulatum*, *Candida spp.*, and the mycobacterial organisms *M. tuberculosis* and *M. kansasii* (3–5), but to our knowledge, this is the first case in which MAI has been isolated. While other sampling modalities such as transbronchial ultrasound-guided needle aspiration have well-established utility in the diagnosis of both neoplastic and infectious mediastinal lesions at lymph node stations 2 (upper paratracheal), 4 (prevascular and retrotracheal), 7 (subcarinal), 10 (hilus), and 11 (interlobar), lower subcarinal and parasophageal lesions frequently exceed the possible range of samplings available with these modalities. Even in the present case, a transbronchial biopsy of the subcarinal lymph node was unsatisfactory. The current case is a valuable example of the utility of EUS-FNAB in sampling infectious lesions of the mediastinum.

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