Dear colleagues:

July 1st ushers a new academic and fiscal year. As usual, a new crop of trainees are joining the Department. The academic credentials of this group are impeccable. This new residents have a mean Step 1 score on USMLE of 92. These extraordinary high scores have been common place for our trainees in the last two years. These exceptional young physicians are also engaged in innovative research.

On this year’s Research Day, one third of platform and poster presentations of fellows and residents were made by the members of the Department. Of the platform presentations Dr. Senan Sultan was the fourth place prize winner and Dr. Thomas Walsh received the fifth place prize. In addition among the poster presentations Dr. Aasita Patel received the second place prize and Dr. Abdul-Razzak Alamir received the 5th place prize. I am very happy to see that the research productivity of the house staff is excellent. The challenge for all of us is to maintain this excellence.

The exceptional performance of our residents would not have been possible without the dedication and commitment of our faculty members. Indeed year after year our faculty members continue to receive the highest honors for teaching. This year fourteen faculty members of the Department were recognized for their exceptional contributions to the teaching mission of the University of Florida.

In parallel to the stellar performance of our residents and faculty members, the Department had an exceptionally good financial year despite the economic challenges. This unprecedented outcome was the result of the sacrifices and the hard work of many outstanding faculty members and their support personnel.

The past year has certainly been a very productive academic year and we are looking forward for another year full of academic accomplishments.

Arshag D. Mooradian, M.D.
Professor of Medicine
Chairman, Department of Medicine
Atrial Fibrillation: Current Update

Atrial fibrillation (AF) is an electrical disorder affecting primarily the left atrium (LA) of the heart. The atria fail to conduct the electrical impulses properly and beat very rapidly in a totally irregular and chaotic manner, resulting in atrial contractile dysfunction. It is a progressive disease which, if left untreated, will lead to tissue fibrosis, cellular electrical perturbation and adverse structural remodeling of the heart chamber.

AF poses a major public health problem in the United States and Europe. Prevalence increases from 0.1% among adults younger than 55 years to 9.0% in persons aged 80 years or older. Currently, more than 2.3 million US adults are afflicted. With the growing older population, these numbers are only expected to increase. The common risk factors for developing AF include age, high blood pressure, coronary artery disease, congestive heart failure and hyperactive thyroid. Other less well recognized risk factors such as positive family history will become better characterized in the future through genetic studies.

There are many treatment options for AF. They can be divided into two general categories. The so-called “rhythm-control approach” strives to keep the patient out of AF by the maintenance of sinus rhythm (the normal rhythm of a healthy heart). The so-called “rate-control approach” lets the patient remain in AF while only the heart rate is kept under control. The former approach is used for patients who experience adverse symptoms when they are in AF. The latter approach is generally reserved for older patients with heart disease who are not necessarily symptomatic while in AF. Rhythm control can be achieved by anti-arrhythmic drugs (AADS), electrical cardioversion, catheter ablation (CA) or a combination thereof. Rate control is primarily achieved with heart rate-controlling medications. Each of these modalities has its own advantages and disadvantages.

One of the popular controversies is whether one of the two approaches is superior to the other. Several large randomized trials performed in the past 10 years have demonstrated the comparable clinical outcomes (cardiovascular morbidity and mortality) of two strategies. Clinicians often point to the toxicities of AADS used to maintain sinus rhythm as a potential reason for the observed lack of superiority of rhythm-control in these trials. As a result, the rhythm-control strategy has been accepted with less enthusiasm than it probably deserves to be. There are two important limitations of such trials. First, the relatively young and healthy patients with symptomatic AF for which the rhythm-control approach would have been ideal are underrepresented in these studies. Second, the rhythm-control strategy taken as a whole is not capable yet of keeping all patients in sinus rhythm all the time, making the comparison of the outcomes of two strategies somewhat unfair. Physicians have been concentrating their effort in recent years to develop a better way of maintaining sinus rhythm in patients with AF.

A very important treatment aspect of AF is systemic anticoagulation. The risk of ischemic stroke in patients with AF who are not adequately anticoagulated is approximately 5% per year. This value is incrementally higher for patients with cardiovascular risk factors. Thus, for patients with one or more cardiovascular risk factors, systemic anticoagulation with warfarin is strongly recommended. Other options for anticoagulation (e.g. plavix), although not firmly established, exist for those who cannot tolerate warfarin.

Catheter ablation is a special means of achieving a cure (rhythm control) of AF in a select group of patients who are experiencing frequent symptomatic episodes of AF. This is a highly complex procedure lasting approximately 5-6 hours during which the four pulmonary veins are electrically isolated from the LA. This is performed by the use of a thin catheter that delivers radiofrequency (a form of heat) energy at its tip. It has been demonstrated in a landmark study 10 years ago that a vast majority of the electrical triggers initiating AF episode reside within the muscular cuffs of pulmonary veins, a vascular structure that drains oxygenated blood from the lungs into LA. This procedure aims to eliminate such triggers by pinpoint tissue destruction. Patients undergoing this procedure can expect up to 70% cure rate at one year follow-up. Appropriate patient selection is critical to success and patients with AF are encouraged to contact our Section of Cardiac Electrophysiology to see whether they would be an appropriate candidate to undergo this procedure.

REFERENCES:
Almost all bronchoscopic procedures are performed with the flexible fiberoptic bronchoscope (the rigid bronchoscope was used in the past). Flexible fiberoptic bronchoscopy allows detailed inspection of the first several divisions of the tracheobronchial tree. Numerous instruments can be passed through the working channel of the scope for a variety of diagnostic and therapeutic indications.

Common Indications for Bronchoscopy
- Hemoptyis
- Suspicion of Lung Cancer
- Staging of Lung Cancer
- Atelectasis
- Pulmonary Infections
- Refractory Wheezing
- Esophageal Cancer
- Foreign Body
- Interstitial Lung Disease
- Lung mass
- Bronchial Strictures, Stenosis

Almost always these procedures are done after the application of topical lidocaine for anesthesia and then after the administration of Fentanyl and Versed to achieve conscious sedation. This results in a very low risk to the patient of either harm or significant discomfort which allows these procedures to generally be outpatient procedures. The procedure itself takes 10-15 minutes and most patients have no memory of the procedure.

Biopsy of visible airway lesions is diagnostic 95% of the time with less than a 5% complication rate. Transbronchial lung biopsies coupled with bronchoalveolar lavage yield diagnoses of 50% - 90% in diffuse parenchymal lung disease depending on the etiology of the process, usually with the same low likelihood of complication.

More specialized bronchoscopic procedures using a flexible ultrasound bronchoscope coupled with transtracheal needle aspiration can give a specific tissue diagnosis of mediastinal disease processes such as malignant or infectious adenopathy. These procedures can prevent the need for more invasive surgical procedures such as mediastinoscopy. This diagnostic modality has become a mainstay in the staging of lung cancer.

Bronchoscopy is performed daily on an elective basis after a patient has been evaluated by one of our four pulmonary physicians.
A CLINICAL CASE

Robert Zaiden, MD, Assistant Professor, Oncology
Taren Ohman, MD, Internal Medicine Resident
Jeffery House, DO, Assistant Professor, GIM
Bruce Villas, MD, Associate Professor, Pathology
Fauzia Rana, MD, Assistant Professor, Oncology

Angioimmunoblastic T-cell lymphoma presenting as extensive psoriasis: a case report and discussion

CASE PRESENTATION

A 38-year-old woman was admitted with bilateral inguinal lymphadenopathy and suspected right hip abscess. She had experienced a full body, dry scaly rash a month earlier, and a skin biopsy by a dermatologist at an outside facility was suggestive of psoriasis. A CT scan of the right lower extremity obtained after admission was negative for abscess but revealed marked superficial lymphadenopathy. Blood and urine cultures were positive for methicillin-resistant Staphylococcus aureus (MRSA).

The patient was treated with IV and oral antibiotics, and discharged home to continue antibiotic therapy. She remained febrile despite having completed her IV antibiotic regimen, and noted increasing pain and swelling bilaterally in her axillary and inguinal regions. The extensive pruritic, scaly rash noted on previous admission persisted, and the patient was readmitted for further workup.

Physical examination showed dry and tight-appearing skin with nodular, hyperkeratotic lesions that were actively pruritic. Excoriations and open lesions with minimal weeping involved the entire body. Examination of the extremities revealed multiple tender right inguinal lymph nodes measuring 1–2 cm and a tender rubbery left inguinal lymph node measuring 5–6 cm. A right cervical lymph node measuring 2–3 cm was also noted.

Laboratory data revealed a white-cell count of 27,000 and a hemoglobin concentration of 8.8 mg/dL. Peripheral smear showed a few smudge cells, with 46% lymphocytes and 32% granulocytes. Tests for HIV, HBV, and HCV were negative. Serum protein electrophoresis showed a diffuse hypergammaglobulinemia. A PET scan revealed bilateral axillary and inguinal areas of increased metabolic activity. Histologic examination of an excised hypermetabolic left inguinal lymph node showed partial effacement of its architecture, with polymorphous lymphocytes, eosinophils, plasma cells, histiocytes, vascular proliferation, and clusters of atypical large lymphoid cells with pale “clear” cytoplasm (Figure 1). Immunostains revealed the atypical large lymphoid cells to be CD3+, CD20–, CD15–, CD30–, and ALK-1–, consistent with T-cell immunoblasts. Flow cytometric analysis of the lymph node also revealed an atypical CD4+ T-cell population. These findings supported the pathologic diagnosis of angioimmunoblastic T-cell lym-
phoma (AITL). The patient was started on standard CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone) chemotherapy and received 2 cycles of this regimen, but declined to continue treatment and was lost to follow-up. Two months after her last cycle, she was admitted to the medical intensive care unit with fulminant MRSA septic shock and died within 24 hours.

**Figure 1:** Lymph node biopsy showing a polymorphous lymphoid infiltrate with clusters of immunoblasts having abundant pale cytoplasm, increased mitotic figures, eosinophil infiltrate, and prominent vascularity (hematoxylin and eosin stain; magnification, 40x).

**Figure 2:** Lymph node biopsy showing positive CD3 staining of large lymphoid cells consistent with angioimmunoblastic T-cell lymphoma (immunoperoxidase stain; magnification, 60x).

**DISCUSSION**

AITL, also referred to as angioimmunoblastic lymphadenopathy with dysproteinemia (AILD), is a relatively rare disease, accounting for only 1%–2% of non-Hodgkin lymphoma and about 15% of peripheral T cell lymphoma. It is a typically a disease of middle aged to elderly adults, with a median age of 64 at presentation and a slight male predominance.

Although many patients have an initial remission, most will experience a relapse and die of infectious complications, with mean survival being 15–36 months. Many patients also eventually experience evolution into high-grade aggressive lymphomas. High-dose chemotherapy followed by autologous stem cell transplant remains the best chance for long-term remission.

**REFERENCES**

Vancomycin–induced Oto- and Nephrotoxicity.

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The arsenal of antimicrobials available to clinicians was significantly increased in number and strength in 1958. Within one year’s time, vancomycin, methicillin, and cephalothin entered the market largely due to the urgency created by emerging Staphylococcal resistance patterns.

Vancomycin, a glycopeptide antibiotic, was originally discovered in a sample of dirt containing Amycolatopsis Orientals. Isolates from A. orientalis were found to inhibit the late stages of cell wall synthesis in dividing gram-positive bacteria, even in the presence of laboratory-induced resistance.

The original formulation of vancomycin distributed from the laboratory and tested in patients was unpurified and responsible for many of the otic and renal adverse reactions observed in patients. The formulation was also responsible for the original nickname “Mississippi Mud.” Although vancomycin was the first FDA-approved agent able to successfully treat infections from highly resistant bacteria, the perceived toxic effects ultimately relegated its use to that of a second-line option for patients with serious β-lactam allergies or treatment-resistant infections.

ADVERSE EFFECT PROFILE

Beginning in the 1980s, clinicians began to demonstrate a renewed interest in vancomycin as an effective and relatively tolerable therapeutic agent for serious infections. The lingering concern of adverse renal and otic effects was met with increased monitoring of vancomycin serum concentrations (a practice that remains in place today).

The adverse effect profile observed in patients treated with early formulations of vancomycin included irritation, chills, and rash. While the purification process and slower infusion rates minimized these reactions, vancomycin continued to be associated with otic (e.g., cochlear toxicity, vestibular toxicity) and renal adverse effects (e.g., nephrotoxicity, interstitial nephritis).

OTOTOXICITY

After sixty years of vancomycin use in clinical practice, only low-grade evidence (i.e., case reports) hints to a correlation between the two events. Moreover, the majority of the cases of ototoxicity occurred in an era when vancomycin was associated with a high level of impurities.

In 2009, the American Academy of Audiology released a position statement and clinical practice guidelines for monitoring ototoxicity. The guidelines do not provide agent-specific recommendations, but do focus on appropriate auditory assessments and monitoring programs. Detection of ototoxicity in the absence of easily recognizable signs and symptoms is an arduous task considering hearing loss typically occurs at high frequencies (>4000 Hz). Studies reporting vancomycin-induced ototoxicity should be carefully scrutinized to determine how and when audiologic assessment occurred.

The analysis of eighty-nine patients receiving vancomycin therapy (average treatment duration of 27 days) showed a 12% rate of high-frequency hearing loss, with a significant increase in incidence in patients aged 53 years and older. Although the data observed in the study may suggest an association between age and incidence of ototoxicity, key limitations prevent a general acceptance of the authors’ conclusion: total daily vancomycin dose for all patients did not reflect use of high-dose vancomycin, the temporal relationship of trough measurement and vancomycin administration was not assessed, and the authors used an inaccurate level of measurement when assessing hearing loss.

The most recent guidelines from the Infectious Disease Society of America (IDSA) and the American Society of Health-System Pharmacists (ASHP) recommend monitoring of serum vancomycin levels when other ototoxic agents are used concomitantly. However, routine monitoring of monotherapy is not recommended as a necessary method to prevent ototoxicity (Level III/Grade B recommendation) due to the rare occurrence and lack of correlation with serum drug concentrations. Treatment should be discontinued if symptoms of toxicity occur.

NEPHROTOXICITY

The IDSA/ASHP define vancomycin-induced nephrotoxicity as multiple increases in serum creatinine concentration greater than 0.5 mg/dL (or ≥50%) from baseline after several days of vancomycin therapy without an alternative explanation (Level II/Grade B). Interstitial nephritis is a serious and rare adverse event that generally presents when vancomycin is used in combination with an aminoglycoside. In contrast to vancomycin-induced ototoxicity, vancomycin-induced nephrotoxicity is typically reversible upon discontinuation of vancomycin.

In the 1980s, vancomycin quickly became the drug of choice in patients requiring treatment for MRSA. Because vancomycin use rapidly increased over a relatively short period of time, changes in the resistance pattern and minimal inhibitory concentration (MIC) of typically susceptible organisms was observed. Interestingly, it has been speculated that the increased incidence of vancomycin–induced nephrotoxicity is indirectly related to resistance patterns and high MICs necessitating the need for higher vancomycin doses.

Although popular medical and pharmacy textbooks continue to list nephrotoxicity in vancomycin’s adverse effect profile, the medical literature is unclear and limited in its ability to support an association. A comprehensive review of the medical literature can be found in the February 2010 issue of The American Journal of Medicine.

DOSING

Vancomycin is dosed according to actual body weight (ABW). Although data is limited in obese patients, initial doses should be calculated using an ABW, with subsequent doses adjusted based on serum vancomycin concentrations. Vancomycin dosages of 15 to 20 mg/kg (based on ABW) given every 8 to 12 hours are required for most patients with normal renal function to achieve the suggested serum concentrations when the MIC is ≤1 mg/L.

MONITORING

While some investigators have found vancomycin therapeutic drug monitoring to be associated with decreased nephrotoxicity, the IDSA/ASHP guidelines do not support monitoring peak concentrations to decrease the frequency of nephrotoxicity (Level 1/Grade A). The most recent guidelines only recommend monitoring of trough concentrations in patients with a therapeutic vancomycin goal of 15 to 20 mg/dL (Level III/Grade B) or who have a high risk of toxicity (e.g., receiving concurrent nephrotoxins, Level III/Grade B; unstable renal function, Level II/Grade B; treatment duration of >3 to 5 days, Level II/Grade B).

Trough samples should be obtained 30 minutes before the fourth dose in patients with normal renal function to ensure that target con-
concentrations are attained (Level II/Grade B). After concentrations are within the desired range, subsequent monitoring should be based on clinical judgment (Level III/Grade B). However, if a sustained vancomycin trough concentration of 15 to 20 mg/L is desired, at least once-weekly measurements are recommended (Level III/Grade B) or more frequently in hemodynamically unstable patients.

**RELATIONSHIP BETWEEN TROUGH CONCENTRATIONS, RESISTANCE, AND THREATENING FAILURE**

Vancomycin is most effective as a bactericidal antibiotic at concentrations three to five times the organism’s MIC. A low serum vancomycin concentration (<10 mg/L) has been shown to be directly correlated with the emergence of vancomycin-intermediate S. aureus (VISA) and inducible heterogeneous VISA (hVISA), a resistant strain with a seemingly susceptible MIC value of 0.5 to 2 mg/L. Currently, there is no mechanism for determining the presence of hVISA. This is particularly concerning given the risk of treatment failure.

**SUMMARY**

Vancomycin-induced ototoxicity and nephrotoxicity is uncommon. Patients receiving an aminoglycoside are at greatest risk. Monitoring has not been shown to be effective in preventing ototoxicity or nephrotoxicity. However, monitoring of trough concentrations in the prevention of toxicity is recommended in patients with a therapeutic vancomycin goal of 15 to 20 mg/dL or in patients who have a high risk of toxicity. Otherwise, trough concentrations should be monitored only to ensure efficacy.

### NEWS & NOTES

**Exemplary Teachers Awards**

Fourteen faculty members in the Department of Medicine were chosen to receive the 2010 University of Florida College of Medicine Exemplary Teachers Award.

The awardees include (arranged alphabetically): Drs. Irene Alexandraki, Doug B. Chapman, Donald A. Conetta, Malcolm T. Foster, Jeffrey G House, Robert J. Kim, Steven J. Lavine, Ghania Masri, Senthil R. Meenrajan, Alan B Miller, Juan C Munoz, Pramod K. Reddy, Manish Relan, and Elisa M. Sottile.

This award is given in recognition of outstanding teaching contributions of individual faculty members. The awardees will receive a plaque, a lapel pin and a financial award determined by the compensation plan’s incentive for outstanding teaching.

Congratulations to the awardees.

**Our residents shine at the American College of Physicians Florida Chapter 2010 Associates Meeting in Orlando**

Atman Shah had an oral presentation entitled, “Comparative Study of the Clinical and Tumor Characteristics in Women with Breast Cancer of Different Age Groups.”

Sudha Koduru also had an oral presentation entitled, “Abiotrophia Spp. Endocarditis Presenting as Non-ST Elevation Myocardial Infarction.”

Hasan Riaz presented a poster titled “Auto-immune hemolytic anemia and Hodgkin’s disease.”

### References


At this meeting our all-intern Doctor’s Dilemma Team received a silver medal for their performance. The team included Reshma Ramlal, Chandrika Chandrasekharaan, and Rohan Samson.

**Golden Apple Award**

At the College of Medicine Senior Awards Banquet, the Golden Apple Award for the most outstanding clinical rotation was presented to the Department of Medicine by the Class of 2010.

Congratulations and thanks to all the Department’s Jacksonville faculty, whose teaching efforts clearly contributed to the receipt of this award, which will be recognized on our campus on the perpetual Golden Apple plaque located in the LRC Atrium.

**Faculty appointed as Editors**

Dr. Charles Heilig (Nephrology) and Dr. Arshag D. Mooradian (Endocrinology) were recently appointed as section editors of the American Journal of Therapeutics. The journal is an indispensable resource for all prescribing physicians who want to access pharmacological developments in cardiology, infectious disease, oncology, anesthesiology, nephrology, toxicology, and psychotropics without having to sift through stacks of medical journals. The journal features original articles on the latest therapeutic approaches as well as critical articles on the drug approval process and therapeutic reviews covering pharmacokinetics, regulatory affairs, pediatric clinical pharmacology, hypertension, metabolism, and drug delivery systems.
University of Florida physicians know that in some cases, it may take more than one expert opinion to get the best results. Working in collaboration with the Shands Jacksonville Imaging Center at Emerson, they are able to offer a comprehensive array of radiological services. The best images interpreted by the best minds result in the best treatments. This is how radiology should be.

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