January 30, 2019

CTS INSPIRATIONS

CTS NEWS

President's Message

Dear members and friends of the California Thoracic Society,

I am incredibly honored to be serving as the President of CTS for the next year during such an exciting time of growth for our society. Our membership and our educational conferences are now thriving, and we remain one of the strongest chapters of the American Thoracic Society. I would like to personally thank **Dr. Philippe Montgrain** for his strong leadership and guidance of the society over the past year.

Having just returned from another remarkable CTS conference in Monterey with very useful hands-on sessions and world-renowned speakers, I was reflecting back to that same conference 16 years ago when I presented a case at this conference as a fellow. These conferences with their great educational programs and opportunities for networking are one of the highlights of my year. Thank you to **Drs. Michelle Cao, George Su,** and **William Stringer** for volunteering so many hours over the past year to assemble this year's amazing conference! Congratulations to **Ana Carolina Costa Monteiro**, **Janelle Pugashetti** and **Michelle Quan,** the winners of our 5th annual CTS Fellow / Multidisciplinary Poster Competition.

CTS has impressed me with the collegiality of its members, the amazing educational programs that are now offered twice a year, and the advocacy for advancing the respiratory health of our patients and our communities. Over the next year, we will be expanding our efforts to support our members who are early in their careers with our newly formed Career Development Committee to be chaired by Dr. Nicholas Kolaitis.

I would like to invite all of you to become more involved in CTS this year. One way to do that is to help CTS as we advocate for our patients with lung disease. We are currently trying to remedy the under-funding for COPD research by the NIH, and we are collaborating with the American Lung Association of California to raise awareness about the effects of air pollution and climate on health.

I hope that you will join with me in inviting other members of our community to join the California Thoracic Society and moving forward issues that are of most interest to our patients and their health. Please feel free to contact me if you would like to become more involved in CTS or if you have ideas for advancing our mission!

Respectfully,

Lorriana Leard, MD
President, California Thoracic Society

Editor's Note:

This month, we feature the first in a short series of clinical articles on *Restless Legs Syndrome* by Dr. Buchfuhrer at Stanford University. In addition, Dr. Sunwoo from UCSD contributes a clinical article on *Cystic Lung Diseases*. CTS Inspirations features succinct scholarly overviews of topics in pulmonary, critical care and sleep medicine. If you are interested in contributing a piece, or have an announcement regarding educational or advocacy events that would be of interest to California's respiratory health community, please contact me at wang.angela@scrippshealth.org.

Diagnosing and Treating Restless Legs Syndrome (RLS)

Mark J. Buchfuhrer, M.D.
FRCP(C), FCCP, FASSM
Stanford School of Medicine, Sleep Disorders Center

Key Points:

1) Every patient with insomnia should be questioned about possible RLS symptoms as it is a common cause of insomnia and patients usually do not mention their symptoms since they have difficulty describing them.

2) RLS patients do not need a sleep study (unless superimposed sleep apnea is suspected) to make a diagnosis but RLS patients should have serum ferritin and iron levels and if below 50-100 mcg/L, iron supplementation should be considered.

3) When choosing a dopamine agonist for first line therapy, consider using a long acting drug such as the rotigotine patch and do not exceed the recommended FDA approved maximum doses (.5 mg for pramipexole, 4 mg for ropinirole and 3 mg for the rotigotine patch). Even better would be to keep the short acting dopamine drugs at much lower than approved doses. Lower doses of the dopamine agonists also decrease the risk of ICDs **(**Impulse Control Disorders).

4) Consider augmentation (worsening of RLS symptoms after starting a medication) to treat RLS whenever a patient who has been on stable dopamine agonist treatment for at least 6 months requests more medication. Try to avoid increasing the dopamine agonist dose to treat worsening symptoms.

5) Initiate treatment for new RLS patients with an alpha-2-delta ligand (gabapentin, gabapentin enacarbil or pregabalin) unless there are concerns with the side effects of these drugs (sedation, weight gain, depression/suicidal ideation).

Despite being frequently underdiagnosed and misdiagnosed, RLS is a very common disorder affecting about 10% of the adult Caucasian population and about 2% of the population with RLS severe enough to require treatment. The diagnosis is established solely by identifying and fulfilling all the 5 clinical criteria (no tests including sleep studies are required) which can be remembered easily by the acronym URGES:

1. ***U**rge* to move the legs associated with unpleasant leg sensations.
2. ***R**est* induces symptoms
3. ***G**ets* better with activity
4. ***E**vening* and nighttime worsening.
5. ***S**olely* not accounted by another medical or behavioral condition

When treatment is required for patients with more severe disease that occurs for 2 or more days per week, therapy choices may be based on the algorithm detailed in the Mayo Clinic Proceedings in 2013. The drugs of choice include dopamine agonists (pramipexole, ropinirole and the rotigotine patch) or alpha-2-delta ligands (gabapentin, gabapentin enacarbil or pregabalin). However, there are more recent concerns with using the dopamine agonists which include **ICDs** and augmentation. ICDs (compulsive gambling, shopping, eating, internet use or hypersexuality) may occur in about 5-10% of RLS patients on dopamine agonists and often result in disastrous consequences such as the loss of hundreds of thousands of dollars. Augmentation is a worsening of RLS symptoms due to taking a dopamine agonist drug and occurs at a rate of 7-8% per year with the short acting dopamine agonists (pramipexole and ropinirole). Since these drugs have been available for over 20 years and prescribed for over 90% of RLS patients for the past 10 years, augmentation with marked worsening of RLS symptoms requiring very high doses of the dopamine agonists has become a very common treatment emergent issue requiring significant expertise to resolve. Since the occurrence of augmentation is dose related, patients needing a dopamine agonist should be kept on the lowest dose possible and a better choice may be the longer acting rotigotine patch which is associated with less augmentation problems.

Because of the above treatment emergent problems with dopamine agonists, many experts suggest starting patients on an alpha-2-delta ligand. However, CNS depressive side effects such as sedation, confusion and dizziness may limit their use. Therefore, combining lower doses of a dopamine agonist and an alpha-2-delta may relieve RLS symptoms while limiting side effects.

In more severe cases, opioids may be very helpful (especially in cases of augmentation) as add on or solo therapy for RLS. All RLS patients should have serum iron and ferritin levels checked as many RLS patients are iron deficient and respond to iron supplementation. Patients with ferritin levels below 50-100 mcg/L may improve with iron supplementation which often is best achieved with intravenous administration.

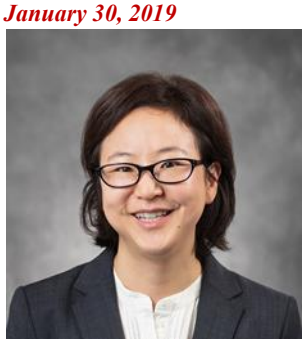
REFERENCES:

Silber MH, Becker PM, Earley C, et al. Medical Advisory Board of the Willis-Ekbom Disease Foundation. Willis-Ekbom Disease Foundation revised consensus statement on the management of restless legs syndrome. Mayo Clin Proc. 2013 Sep;88(9):977-86.

Garcia-Borreguero D, Silber M, Winkelman J, et.al. Guidelines for the first-line treatment of restless legs syndrome/Willis–Ekbom disease, prevention and treatment of dopaminergic augmentation: a combined task force of the IRLSSG, EURLSSG, and the RLS-foundation. Sleep Med. 2016; 21:1–11.

Allen RP, Picchietti DL, Auerbach M, et al. International Restless Legs Syndrome Study Group (IRLSSG). Evidence-based and consensus clinical practice guidelines for the iron treatment of restless legs syndrome/Willis-Ekbom disease in adults and children: an IRLSSG task force report. Sleep Med. 2018 Jan;41:27-44.

Silber MH, Becker PM, Buchfuhrer MJ, et al. Scientific and Medical Advisory Board, Restless Legs Syndrome Foundation. The Appropriate Use of Opioids in the Treatment of Refractory Restless Legs Syndrome. Mayo Clin Proc. 2018 Jan;93(1):59-67.



Cystic Lung Diseases
Bernie Y. Sunwoo, MBBS
Associate Professor of Clinical Medicine
Medical Director, Pulmonary and Sleep Medicine
University of California San Diego

Cysts are commonly seen on chest computed tomography (CT). Pathologically, a cyst is any round circumscribed space surrounded by an epithelial or fibrous outer wall. Radiographically, a cyst is a round parenchymal lucency or low attenuation area with a well-defined, typically thin-walled interface with normal lung, usually containing air [1]. As the use of CT increases, cystic lung disease is being more frequently encountered in clinical practice, necessitating an awareness of the range of pulmonary and systemic disorders that can manifest with pulmonary cysts.

When approaching cystic lung disease the first step is to discriminate pulmonary cysts from potential radiographic mimickers including cavities, emphysema, bronchiectasis and honeycombing [2]. Cavities typically have a wall thickness >4 mm within pulmonary consolidation, a mass or a nodule. Emphysema, unlike cysts, lack distinct walls. Cystic bronchiectasis or irreversible dilation of the bronchi is differentiated from cysts based on continuity with the airways on continuous CT sections. Honeycombing is characterized by clustered, thicker walled airspaces, typically 3 to 10 mm in diameter stacked on each other, and is seen in pulmonary fibrosis.

The differential diagnosis for cystic lung disease is broad and can be narrowed depending on whether cysts are solitary or diffuse. Solitary cysts are often congenital or sequelae of prior infections or chest trauma. Diffuse cystic lung diseases (DCLDs) can be caused by low-grade or high-grade metastasizing neoplasms, polyclonal or monoclonal lymphoproliferative disorders, infections, interstitial lung diseases, smoking, and congenital or developmental defects, but more common causes include lymphangioleiomyomatosis, pulmonary Langerhans cell histiocytosis, Birt-Hogg-Dube syndrome and cystic diseases associated with lymphoproliferative disorders including lymphocytic interstitial pneumonia and light-chain deposition disease [3, 4].

Critical review of chest high-resolution CT by an expert radiologist is essential in accurately diagnosing DCLDs. Expert radiologists were able to accurately diagnose DCLDs in approximately 80% of cases based on review of HRCT features alone [5]. The number, distribution and morphology of the cysts and associated CT findings in the right clinical context can help narrow the differential diagnosis.

Lymphangioleieomyomatosis (LAM) is a cause of diffuse cystic lung disease characterized by proliferation of abnormal smooth-muscle like cells. LAM can be associated with tuberous sclerosis or occur sporadically. Sporadic LAM is almost exclusively seen in women of childbearing age. It is characterized by pulmonary cysts, lymphatic abnormalities including chylothorax and renal angiomyolipomas. The cysts in LAM are typically multiple, diffusely distributed, thin walled, 0.2 to 2 cm and round. Clinically pulmonary cysts can manifest as progressive dyspnea and hypoxemia due to loss of lung parenchyma or as a pneumothorax, often recurrent.

Pulmonary Langerhans Cell Histiocytosis (PLCH) is an inflammatory bronchiolitis with loosely formed nodules of dendritic cells aggregating around small airways, resulting in varying degrees of interstitial inflammation, alveolar macrophage infiltration and proliferative vasculopathy [6]. In children LCH is part of a multisystem disorder while in adults it is generally isolated to the lungs and almost universally seen in young adult smokers. Chest CT reveals nodules and cysts that can be irregular, bizarre-shaped and thick walled with relative sparing of the lung bases and costophrenic angles. In the appropriate clinical context, a typical chest CT can be highly suggestive of the diagnosis.

Birt-Hogg-Dube (BHD) syndrome is a rare, autosomal dominant disorder caused by mutations in the Folliculin gene, and is characterized by the formation of fibrofolliculomas (small, dome-shaped, papules), renal cancers and pulmonary cysts. There is great phenotypic variability in the clinical features of BHD. Multiple and bilateral pulmonary cysts are seen in greater than 80% of BHD patient. Cysts associated with BHD are typically basilar predominant, round-lentiform in shape and usually encompass less than 30% of the total lung field. The surrounding pulmonary parenchyma is largely normal and patients are typically asymptomatic from a pulmonary perspective until the development of a pneumothorax.

The benign end of a spectrum of pulmonary lymphoproliferative disorders including follicular bronchiolitis (FB) and lymphocytic interstitial pneumonia (LIP) can be associated with pulmonary cysts. FB is characterized by peribronchial and peribronchiolar lymphoid follicles with reactive germinal centers while in LIP dense interstitial lymphocyte infiltrates are seen. The cysts in FB/LIP are typically thin-walled, usually affecting <10% of lung field and may be bordered by an eccentric vessel. It can be associated with areas of ground-glass opacities, centrilobular and subpleural nodules, thickened bronchovascular bundles, interlobular septal thickening and lymphadenopathy. LIP can be idiopathic but it is more commonly associated with various systemic and infectious disorders that are associated with dysgammaglobulinemia and lymphocytic infiltration including Sjogren syndrome and HIV [7].

REFERENCES

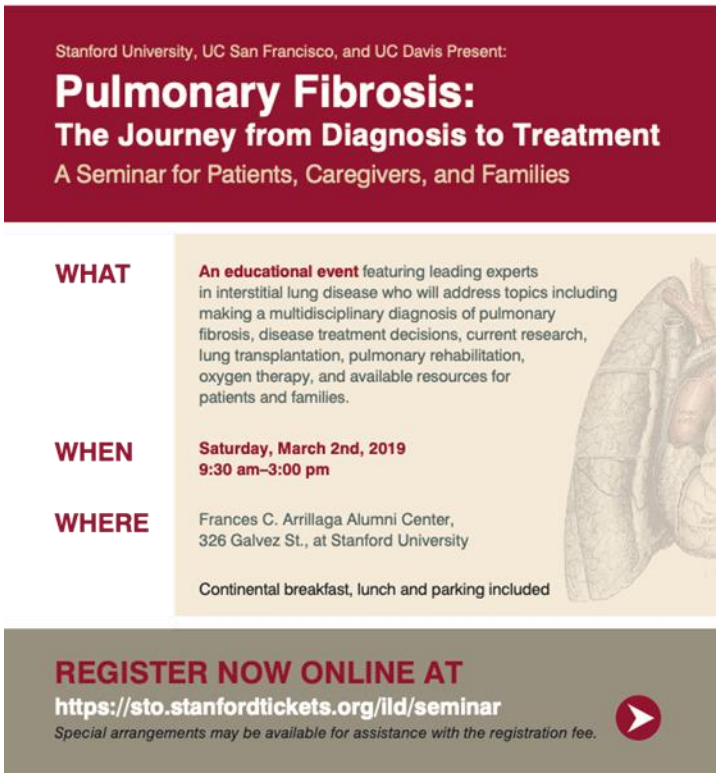
1. Hansell, D.M., et al., Fleischner Society: glossary of terms for thoracic imaging. Radiology, 2008. 246 (3): p. 697-722.
2. Jawad, H., et al., Cystic interstitial lung diseases: recognizing the common and uncommon entities. Curr Probl Diagn Radiol, 2014. 43(3): p. 115-27.
3. Gupta, N., et al., Diffuse Cystic Lung Disease. Part II. Am J Respir Crit Care Med, 2015. 192(1): p. 17 -29.
4. Gupta, N., et al., Diffuse Cystic Lung Disease. Part I. Am J Respir Crit Care Med, 2015. 191(12): p. 1354-66.
5. Gupta, N., et al., Accuracy of chest high-resolution computed tomography in diagnosing diffuse cystic lung diseases. Eur Respir J, 2015. 46(4): p. 1196-9.
6. DeMartino, E., R.S. Go, and R. Vassallo, Langerhans Cell Histiocytosis and Other Histiocytic Diseases of the Lung. Clin Chest Med, 2016. 37(3): p. 421-30.
7. Panchabhai, T.S., C. Farver, and K.B. Highland, Lymphocytic Interstitial Pneumonia. Clin Chest Med, 2016. 37(3): p. 463-74.

ANNOUNCEMENTS:

Stanford University, in collaboration with UC San Francisco and UC Davis, presents an Interstitial Lung Disease educational event for patients, families, and caregivers featuring leading experts who will address topics including making a multidisciplinary diagnosis of pulmonary fibrosis, disease treatment decisions, current research, lung transplantation, pulmonary rehabilitation, oxygen therapy, and available resources. The event will be held on the beautiful Stanford campus at the Frances C. Arrilaga Alumni Center on March 2, 2019.

For the full program, directions, and online registration information please go to:

https://tickets.stanford.edu/sites/default/files/pulmonary_fibrosis_seminar_directions_and_program.pdf



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California Thoracic Society
18 Bartol St. #1054 | San Francisco, CA, 94133 | 415-536-0287
Connect with CTS at https://calthoracic.org/

CTS Editors:
Angela Wang, MD
Chris Garvey, NP
Laren Tan, MD