Higher Index of Suspicion for PAH Is Warranted

Hospitalizations for the condition have tripled since 1980 and the incidence is continuing to rise.

BY ALICIA AULT
Associate Editor, Practice Trends

BALTIMORE — The incidence of pulmonary arterial hypertension is widely underestimated, but with better diagnostic tools and more treatments, rheumatologists and others can intervene earlier in the disease process, said Dr. Hunter Champion at a cardiovascular conference sponsored by Johns Hopkins University, Baltimore.

There are 1-2 million cases of pulmonary arterial hypertension (PAH) a year, primarily affecting women and usually striking people in their 40s. But PAH is on the rise, said Dr. Champion of the university.

Hospitalizations for PAH tripled from 1980 to 2002, when they hit 260,000, according to the National Hospital Discharge Survey (www.cdc.gov/mmwr/preview/mmwrhtml/ss5405a1.htm#tab10). New data is being assembled that will show that PAH is more common than thought.

Suspect PAH if there is a loud pulmonic closure, right ventricular lift, systolic murmur (tricuspid regurgitation), diastolic murmur (pulmonary regurgitation), or right ventricular presystolic gallop. A family history of PAH, connective tissue disease, congenital heart disease, portal hypertension, a history of deep vein thrombosis or pulmonary embolism, human immunodeficiency virus, and appetite-suppressant use are all risk factors, Dr. Champion said.

Symptoms usually include dyspnea, angina, syncope, edema, and Raynaud's phenomenon. PAH is often misdiagnosed as coronary artery disease (CAD), heart rhythm disorder, asthma, or, sometimes, a psychiatric condition such as panic disorder, he said.

Diagnostics should be done to rule out HIV, emphysema, sleep disorder, CAD, and autoantibody disorders such as systemic lupus erythematosus.

A right heart catheterization is critical, he said. "Until you have that, you don't really have a handle on what's going on."

The catheterization also will give a reading on pulmonary artery pressure and response to vasodilators, both of which help determine a therapeutic strategy.

PAH arises through the endothelin, nitric oxide, and prostacyclin pathways. Three prostacyclin analogues are the most commonly used therapies: epoprostenol (Flolan), treprostinil (Remodulin), and iloprost (Ventavis). The drugs are expensive—$60,000-$100,000 a year—and have drawbacks, including jaw, leg, and site pain (for epoprostenol, which is delivered through an in-dwelling catheter), and risk of infection and thrombocytopenia. With epoprostenol, rebound PAH is common, he said.

Bosentan (Tracleer) acts on the endothelin pathway. The oral medication has been shown to delay PAH progression, although it is still considered palliative. It has a high risk of teratogenicity, which is important to consider because many PAH patients are women in their childbearing years.

Liver damage is also a continuing concern. The Food and Drug Administration recently strengthened hepatotoxicity warnings and emphasized the need to conduct monthly liver function tests. Bosentan is also expensive: $36,000 a year.

Two new therapies are considered promising for treating PAH, they include Sitaxsentan, which was recently designated as approvable by the FDA, and ambrisentan, which is close to market. Both are type-A selective endothelin receptor antagonists.

Sildenafil (Viagra) has been shown to improve patient functioning, as demonstrated by the 6-minute walking test. Dr. Champion said he was impressed with the drug's ability to convert patients from class IV to class III status or from class III to class II. The phosphodiesterase 5 inhibitor is marketed as Revatio for PAH. It is the lowest-priced therapy, at about $9,800 a year.

Lung transplantation is a possibility for advanced PAH, but a recent change in United Network for Organ Sharing rules has lengthened patients' wait, Dr. Champion said. "It is the option of last resort but certainly is necessary," he said. ■

Search Medical History for Neuropsychiatric Lupus Clues

BY NANCY WALSH
New York Bureau

GLASGOW, SCOTLAND — When acute nonspecific symptoms might represent neuropsychiatric lupus, it is necessary to carefully review a patient's past medical history, because the presenting symptoms of systemic lupus erythematosus are manifold, may mimic other disorders, and can evolve over time, Dr. Hala Y. Sadik reported in a poster.

This is particularly the case when the onset is acute, as happened in a case treated by Dr. Sadik of the Academic Rheumatology Unit, University Hospital Aintree, Liverpool, England.

In August 2005, a 57-year-old woman presented with hypothermia, bradycardia, confusion, a low score on the Glasgow Coma Scale, and hyponatremia.

The patient's plasma sodium level was low (120 mmol/L), as well as her plasma osmolality (235 mOsm/kg), while urinary sodium and osmolality levels were both high. A diagnosis of inappropriate antidiuretic hormone secretion was made, Dr. Sadik reported in a poster session at the annual meeting of the British Society for Rheumatology.

Initial management included fluid restriction and administration of double-strength normal saline, which normalized the plasma sodium level, reported Dr. Sadik.

Initial MRI of the head raised the possibility of neurosarcoidosis, but serum angiotensin-converting enzyme levels and chest x-ray were normal.

A repeat MRI with gadolinium suggested demyelinating disease or systemic lupus erythematosus. Immunology profile findings included positive antinuclear antibody (ANA) and double-stranded DNA antibody. Thrombocytopenia and lymphopenia also were present.

Upon review, her previous case records from another hospital revealed that she had been admitted in 1992 with a 2-week history of arthralgias, Raynaud's phenomenon, thrombocytopenia, lymphopenia, and positive ANA.

A diagnosis of lupus had been considered at that time, and she was followed for several years as an outpatient, but ANA remained weakly positive and double-stranded DNA was persistently negative, so the diagnosis had been dismissed, Dr. Sadik wrote.

With improvements on the Glasgow Coma Scale during her current admission, it became apparent that the patient was profoundly depressed, so she was treated with mirtazapine.

Following a diagnosis of neuropsychiatric lupus, the patient began treatment with intravenous methylprednisolone and cyclophosphamide.

Significant improvements were seen in her disabling depression, and her hematologic parameters normalized, reported Dr. Sadik. ■

Next Step: Digitization of Images

Videocapillaroscopy *from page 1*

neously and irregularly enlarged microvascular loops are among the earliest and most striking features of Raynaud's phenomenon as a result of connective tissue disease.

The peculiar looped shape of the enlarged capillaries is distinctive. The presence of even a single loop with a circumscribed or homogeneous diameter exceeding 50 µm should be considered as a potential marker of microangiopathy related to an early scleroderma-spectrum disorder, he said. In a recent study, giant capillaries were observed in 100% of patients with systemic sclerosis.

► **Local microhemorrhages.** These are also signs of microvascular damage in early disease. Local trauma must be excluded before the finding can be attributed to secondary Raynaud's phenomenon.

► **Edema.** This is frequently observed at the level of the dermal papillae, mainly in active cases of systemic sclerosis.

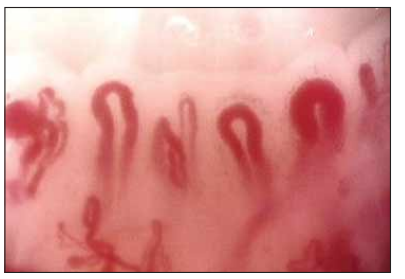
► **Angiogenesis.** The appearance of capillary neoformation, a sign of late disease, can widely vary. One characteristic form of angiogenesis includes highly tortuous and arborized capillary loop clusters, often surrounded by dropout of normal capillary loops.

The main morphologic hallmark in angiogenesis is the clustering of tortuous capillaries with pronounced heterogeneity, including thin or large meandering and bushy capillaries. In distinction, coiled capillaries are the morphologic hallmark of angiogenesis in the elongated papillae of psoriatic plaque.

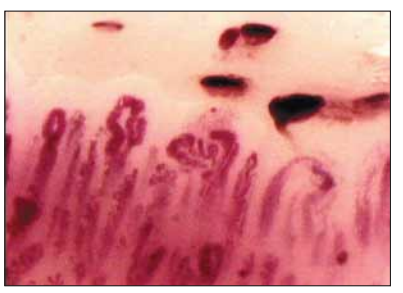
► **Loss of capillaries and avascular areas.** A reduced number of capillary loops—less than 30 observed in 5 mm in the distal row of the nailfold—should be considered highly specific for secondary Raynaud's phenomenon. In advanced systemic sclerosis, only 20% of the capillaries may have a normal appearance on nailfold videocapillaroscopy. Extensive loss of capillaries may result in large avascular areas. Rapidly progressive nail bed capillary loss is a strong indicator of systemic sclerosis even in new-onset Raynaud's.

Both Dr. Herrick and Dr. Cutolo are investigating more advanced methods of capillaroscopy that involve digitization of the images.

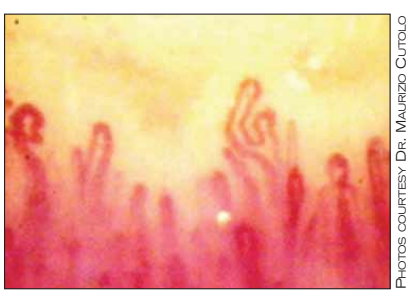
"We hope that the new modifications and developments in capillaroscopy will allow us to track changes in the capillaries over time," they said. ■



Giant capillaries are an early sign of secondary Raynaud's phenomenon.



Also, in early disease, hemorrhages mark microvascular damage.



PHOTOS COURTESY DR. MAURIZIO CUTOLO

Loss of capillaries are shown in the nailfold of a Raynaud's patient.