Scleroderma:
Beyond Corrine's Skin

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Corrine's Condition

- Corrine, 42, presents with blanching of her fingers in the cold, dyspnea, dry cough and dysphagia

On exam:

- There are Velcro crackles at the lung bases
- A few telangiectasia and discrete bands of skin thickening and hyperpigmentation on her forearms are found
- There is a very slight thickening of the skin on her fingers and hands

What is the most likely diagnosis?

The most likely diagnosis is systemic sclerosis (scleroderma). All patients with scleroderma present with Raynaud's disease. Although Raynaud's disease is common in the normal population, the clues in Corrine's case are:

- Dyspnea, dry cough and Velcro rales: All suggestive of underlying interstitial fibrosis, a common finding in scleroderma
- Telangiectasia, skin tightening and hyperpigmentation: Also all common in scleroderma
- Dysphagia: Suggestive of esophageal motility disturbance—a classic feature of scleroderma

For Corrine's baseline test results, go to page 30.

Systemic sclerosis, or scleroderma, is a multisystem disorder of connective tissue characterized by fibrosis of the skin and internal organs, microvascular disease and activation of the immune system.

What tests should you order for Corrine?

There is no one test that will make the diagnosis of scleroderma. However, most patients will have a positive antinuclear antibody (ANA), and a negative ANA almost rules out the diagnosis. Therefore, in Corrine's case, this test should be ordered to see if scleroderma is a possibility. However, Corrine's diagnosis is clinical and her presentation is enough to convince us that she has scleroderma.

Next, tests should be ordered to evaluate the extent and severity of the disease:

- **Pulmonary involvement:** Chest X-ray, pulmonary function tests and, if we suspect active alveolitis, a high-resolution computed tomography scan (HRCT) of the lungs.[1]
- **Pulmonary hypertension:** Another aspect of pulmonary disease is pulmonary hypertension.[2] An echocardiogram should be done to rule out pulmonary hypertension as a cause of her dyspnea. Don't forget that she could have both interstitial disease and pulmonary hypertension—they are not necessarily related to each other.
- **Esophageal disease:** Radionuclide esophageal transit study—esophageal scintigraphy can detect esophageal involvement in patients with asymptomatic disease, showing a typical pattern of retention of radioactivity in the lower esophagus, with clearing after the patient is upright or drinks a glass of water. This is an excellent indicator of dysmotility in both early and advanced disease.[3]
- **Myopathy:** This can sometimes be part of scleroderma, therefore, a creatinine kinase should be ordered to rule it out.

Corrine's Results

- ANA: Positive at a dilution of 1/640; anti-topoisomerase (anti-ScL 70) antibodies were present. (This antibody is typical of diffuse scleroderma as distinct from the more benign limited disease in which the skin involvement usually remains in the hands and feet)
- Chest X-ray: Bilateral basal interstitial changes
- Pulmonary function tests: FVC 58% predicted, TLC 58% predicted and DLCO 45% predicted
- Echocardiogram: Normal
- Radionuclide esophageal transit study: Thirty-five per cent of retention of the bolus at 20 seconds and 15% at 10 minutes. These are moderately abnormal values. By 10 minutes, a normal person has almost none of the bolus still in the esophagus.
- CK: Normal
- HRCT lung: Significant bilateral basal fine interstitial lung disease with increased interstitial and septal markings; ground glass attenuation involving the posterior aspect of both lower lobes. (The ground glass abnormality is important—it suggests not only scarring in her lungs, but "active" alveolitis.)

ANA: Antinuclear antibody
FVC: Forced vital capacity for carbon monoxide
TLC: Total lung compliance
DLCO: Diffuse capacity of the lung
CK: Creatinine kerase
HRCT: High-resolution computed tomography

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What about treatment?

Unfortunately, no medication has ever been shown to affect the overall course of the scleroderma. Therefore, therapy should be based on the organ systems involved.

- **Skin:** Several drugs, such as penicillamine, methotrexate and even colchicines have been tried. None have been scientifically proven to be of any benefit.
- **Raynaud's disease:** It is not necessary to treat this unless it is particularly disturbing. We offered Corrine a calcium channel blocker, which she declined.
- **Esophagus:** Heartburn from reflux is important because esophagitis may heal with strictures that will require mechanical dilatation for the ensuing dysphagia. The heartburn was treated with a proton pump inhibitor and, as Corrine's dysphagia was due to a motility disorder, we tried domperidone.
- **Lung:** This seemed to be the most serious manifestation of her illness. The fact that she had alveolitis on her HRCT suggested that she had a component of lung disease that might respond to therapy, which might prevent further pulmonary fibrosis from developing. Studies of the role of cyclophosphamide for alveolitis are ongoing and the full results are not yet reported. However, most rheumatologists are using cyclophosphamide, as did we, for this situation.[4,5]

What happened to Corrine?

Corrine did not do well. Her pulmonary function tests eventually worsened; she developed pulmonary hypertension and both stomach and small bowel disease with symptoms of delayed gastric emptying and small bowel bacterial overgrowth. Erythromycin was used as a pro-motility agent and did provide some relief for her early satiety and vomiting.[6] Intermittent antibiotics helped her diarrhea. She has been referred to the transplant service to consider a lung transplant, but because of the severity of her gastrointestinal disease, Corrine's chances of being accepted are poor.

Luckily, Corrine's case is not representative of the average patient with scleroderma, who has a much better prognosis. However, her story does serve to emphasize the multi-system nature of scleroderma and the need to break down both the evaluation and the treatment into organ-specific components.

References

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