At thoracotomy, the parietal pericardium was normal. Two liters of straw colored fluid were recovered from the pericardial cavity. The heart was encased within thick, white, glistening epicardium. In addition, there was a constricting band of fibrous tissue at the base of right atrial appendage which was aneurysmal. Epicardium was peeled from the anterior and the lateral surfaces of the ventricles, and the right atrial appendage was resected without using cardiopulmonary bypass. Following surgery, the patient made an uneventful recovery. Three weeks postoperatively, repeat hemodynamic study showed that the mean right atrial pressure had come down to 5 mm Hg (a = 8, v = 6). Equalization of pressures was no longer seen. Histopathologic examination of the epicardium revealed marked hyaline thickening with sparse mononuclear infiltration. There was no evidence of granuloma or malignancy.

DISCUSSION

The localized, constricting epicardial band in our case was at an unusual site, between the right atrial appendage and body. This resulted in aneurysmal dilatation of the right atrial appendage mimicking an intramural tumor on computerized tomography with evidence of “tumor blush” on right coronary angiogram. Although the two-dimensional echocardiogram was highly suggestive, the diagnosis could be established with certainty only at surgery.

It is not uncommon for cardiac and pericardial tumors to present with ventricular diastolic restriction. However, diastolic restriction due to constrictive epicarditis masquerading as a cardiac mass, as seen in our patient, is extremely unusual and to the best of our knowledge, has not been reported in the literature.

In summary, localized epicarditis is as much of an entity as localized pericardial constriction. Fibrous epicardial bands can produce a clinical and hemodynamic picture resembling a cardiac tumor. Exploratory thoracotomy can be diagnostic, and resection of the epicardium may result in complete recovery.

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Nifedipine and Prazosin in the Management of Pulmonary Hypertension in CREST Syndrome*

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A 62-year-old woman with CREST syndrome and isolated pulmonary hypertension (without evidence of interstitial lung disease) underwent right heart catheterization to evaluate the effect of steroid and vasodilator treatment on hemodynamic parameters. During 12 weeks of prednisone treatment in a dosage of 40 mg daily, her condition markedly deteriorated clinically and hemodynamically as manifested by pulmonary artery pressure (PAP), pulmonary vascular resistance (PVR), cardiac output (CO), mixed venous O2 saturation, and systemic vascular resistance (SVR). Successful trials with various vasodilators demonstrated ineffectiveness of isosorbide dinitrate and phenoxycbenzamine, whereas nifedipine was effective in a 15-mg single dose, and prazosin 1 mg was partially effective in reducing PVR, SVR, and increasing CO and mixed venous O2 saturation. The combination of nifedipine 10 mg and prazosin 0.5 mg given alternately every four hours for 48 hours was the most effective in reducing PVR and PAP. Clinical response was favorable as well until treatment with medications was discontinued due to gastrointestinal side effects one month later.

(Chest 1990; 98:759-61)

Pulmonary hypertension occurs frequently in patients with progressive systemic sclerosis (PSS) and in its CREST variant and is a major cause of mortality and morbidity. Most commonly it follows interstitial pulmonary disease but may be observed as a primary abnormality of the vasculature (isolated pulmonary hypertension), especially in patients with the CREST variant of the disease. Management of this problem is very difficult and although various treatment regimens have been tried, most results are inconsistent.

Recently, we observed a favorable hemodynamic and clinical response to a combination of nifedipine and prazosin in a patient with systemic sclerosis and pulmonary hypertension.

CASE REPORT

A 62-year-old woman was admitted to the hospital for evaluation of severe shortness of breath and peripheral edema of six months' duration. Despite vigorous diuretic treatment she was in New York Heart Association class IV. She had a history of CREST syndrome, with long-standing Raynaud's phenomenon, and one year of sclerodactyly, multiple telangiectasia, esophageal hypomotility, and gastroesophageal reflux. Serologic studies revealed a weakly positive

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titer for antinuclear antibodies and a latex fixation titer of 1:1280. There was no evidence of renal involvement.

Examination revealed a woman with overt right heart failure and signs of severe pulmonary hypertension, including right ventricular uplift, markedly accentuated pulmonic second heart sound, and a murmur consistent with tricuspid regurgitation. Lungs were clear by auscultation. Electrocardiogram showed right ventricular hypertrophy and strain with right axis deviation, and chest roentgenogram demonstrated pulmonary arterial hypertension without signs of left heart failure or parenchymal involvement of lungs.

Pulmonary function tests revealed arterial blood gas levels of PaO₂ of 59 mm Hg and PCO₂ of 24 mm Hg in room air, forced vital capacity of 2.34 L (84 percent of predicted), FEV₁/FVC of 75 percent (103 percent of predicted) with slight decrease of mid and terminal flows (FEF₂₅-₇₅% was 1.32 L, which was 55 percent of predicted). There was marked decrease in diffusion capacity (31 percent of predicted).

Right heart catheterization was performed with a Swan-Ganz catheter, pressures were measured in the right atrium (RAP), pulmonary artery (PAP) and pulmonary capillary wedge (PCWP), and oxygen saturations were measured in the pulmonary artery (mixed venous blood) and in the radial artery. Cardiac output (CO) was calculated according to Fick's oxygen method assuming oxygen consumption according to Crocker et al. Measurements were done at room air and were repeated after 30 minutes of oxygen administration by a 40 percent mask. Pulmonary vascular resistance (PVR) and systemic vascular resistance (SVR) were calculated. There was markedly increased pulmonary resistance (almost ten times the normal values) and somewhat increased SVR with depressed CO and pulmonary arterial hypertension, with normal wedge pressure. All parameters showed only minimal response to oxygen administration (Table 1).

The patient was diagnosed as having isolated pulmonary hypertension due to CREST syndrome, without parenchymal lung disease. A trial of steroid treatment was begun with prednisone 40 mg daily. With this treatment no subjective improvement was noted, and right ventricular failure signs worsened with marked peripheral edema and weight gain, necessitating an increase in diuretic dosage.

Twelve weeks later she was catheterized again to see whether any hemodynamic improvement occurred after steroid therapy and to assess the hemodynamic effect of various vasodilators. After obtaining baseline measurements on room air and after 40 percent O₂ administration, the patient received a single dose of each of the following medications: oral phenytoin (10 mg), sublingual isosorbide dinitrate 5 mg and 10 mg, oral nifedipine 15 mg, and prazosin 1 mg. Measurements were taken at intervals of 30 minutes until 120 minutes and at 240 minutes following each administration.

All measurements were performed with the patient breathing 100 percent oxygen by mask. At least 24 hours were allowed between each drug to ensure its complete clearance. Baseline measurements were repeated before each administration.

Following the single drug studies, a 48-hour protocol using combined nifedipine 10 mg every 8 hours and prazosin 0.5 mg every 8 hours was given alternately every 4 hours. Hemodynamic measurements were taken after 48 hours.

The following observations were made (Table 1):

1. There was marked deterioration of all hemodynamic parameters during 12 weeks of steroid treatment, with more than doubling of the pulmonary as well as systemic resistances. The PVR increased from 1,045 to 2,126 dyn·sec·cm⁻¹ and SVR increased from 1,805 to 3,380 dyn·sec·cm⁻¹. Hemodynamic parameters were not influenced by oxygen administration.

2. Phenytoin and isosorbide dinitrate were ineffective and failed to reduce pulmonary resistance and pressures at all.

3. Nifedipine (single oral dose of 15 mg) was effective in reducing PVR (from 2,105 to 1,629 dyn·sec·cm⁻¹) and SVR (from 4,304 to 2,679 dyn·sec·cm⁻¹) with resultant increase in CO (from 1.71 to 2.21 L/min) and mixed venous O₂ saturation. Maximal effect was achieved 45

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<th>Table 1 — Hemodynamic Measurements*</th>
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<td><strong>BP, mm Hg</strong></td>
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<td>Normal Range</td>
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<td>Nifedipine 15 mg (after 45 min)‡</td>
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<td>Prazosin 1.0 mg (after 120 min)‡</td>
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*BP = arterial blood pressure—systolic/diastolic (mean); PAP = pulmonary artery pressure—systolic/diastolic (mean); PCWP = mean pulmonary capillary wedge pressure; RAP = mean right arterial pressure; CO = cardiac output; SVR = systemic vascular resistance; PVR = pulmonary vascular resistance.
†After oxygen = at least 30 minutes of oxygen 40 percent by face mask.
‡These are maximal effect values, out of multiple measurements. Time of peak effect is given in parentheses.
§Nifedipine 10 mg and prazosin 0.5 mg were given alternately every four hours, for 48 hours.

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minutes after administration.

(4) Prazosin 1 mg was only minimally effective in reducing PVR (1,843 to 1,799 dyn·cm⁻²). It was effective (but less than nifedipine) in reducing SVR (from 3,686 to 2,794 dyn·cm⁻²) and increasing CO (from 1.91 to 2.09 L/min). The effect on mixed venous O₂ saturation was similar. Maximal effect was achieved 120 minutes after administration.

(5) The combination of nifedipine 10 mg and prazosin 0.5 mg alternately for 48 hours was more effective than each of the single drugs in reducing PVR (from 1,843 to 1,376 dyn·cm⁻²) and PAP (from 54 to 49 mm Hg), with only a small decrease in systemic blood pressure. The SVR (from 3,686 to 2,462 dyn·cm⁻²) and CO (from 1.91 to 2.21 L/min) were affected less than with nifedipine 15 mg alone, but more than with prazosin 1.0 mg alone. Mixed venous O₂ saturation increased as with both medications alone (52 to 59 percent).

Table 1 shows the maximal effect of each of the effective medications (nifedipine, prazosin, and their combination) and the time of maximal effect.

The patient was discharged from the hospital with the combination (nifedipine 10 mg and prazosin 0.5 mg alternately every four hours), home oxygen, and diuretics. Steroid therapy was tapered off over three weeks. Over one month she lost 5 kg in weight with less diuretic therapy than before. After one month she stopped both medications due to severe gastrointestinal upset that was attributed to the medications. She was therefore kept on a regimen of prazosin 0.5 mg three times a day only with diuretics, with continuous deterioration and a 6-kg weight gain until her death a few months later.

**DISCUSSION**

The problem of pulmonary involvement in systemic sclerosis and its CREST variant is becoming the major cause of mortality and morbidity since remarkable advances have been made in antihypertensive treatment of renal disease of PSS. There are few reports concerning treatment of pulmonary hypertension in these patients. Steroid therapy is suggested following uncontrolled observations by Enson et al. In our patient, marked deterioration occurred with steroid treatment.

Only few reports are available about vasodilator treatment of pulmonary hypertension in PSS and CREST. Nitroprusside, phentolamine, diazoxide, dinoprostone (PGE₂), and hydralazine were not helpful. Results with captopril and verapamil were contradictory. Single-dose studies with nifedipine demonstrated success in reduction of PVR and PAP. Yet, in some of these reports the effect was transient and there was no long-term benefit. We are not aware of any reports of the use of prazosin in pulmonary hypertension of systemic sclerosis. Its effect in primary pulmonary hypertension is not sustained, as measured in two patients only.

In our case, a favorable response of the pulmonary vasculature to nifedipine 15 mg was found, as well as an effect on the systemic vascular bed, without significant hypotension. Prazosin 1 mg had only minimal effect on pulmonary vasculature, but it improved CO and mixed venous O₂ saturation, mainly through its action of peripheral vasculature. The combination of nifedipine and prazosin in prolonged (48 hours) administration in smaller doses resulted in even further reduction of PVR and PAP, whereas the peripheral effects and effect on CO were similar to or less than the effect of nifedipine 15 mg alone, but more than with prazosin 1 mg alone.

The clinical response was impressive and the effect was sustained for a month, with rapid deterioration after discontinuation of treatment with the combination. Unfortunately, severe gastrointestinal side effects precluded the continuation of this combination, so that we do not have long-term results.

Whereas a beneficial response was noted in our patient, there is a considerable risk in such therapy with nonselective pulmonary and systemic vasodilatory effect. It can result in a profound hypotension in patients with severe pulmonary vascular disease. It should therefore be started under close hemodynamic monitoring.

Our preliminary results suggest that the combination of nifedipine and prazosin should be studied in a controlled trial in patients with systemic sclerosis and pulmonary hypertension.

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