electron microscopy in differentiating PHG from amyloidosis.

Katzenstein and Askin\textsuperscript{5} prefer to consider those cases which histologically resemble PHG, but stain positive for amyloid to be nodular pulmonary amyloidosis. We believe that the light and electron microscopic features of PHG are sufficiently distinctive to warrant separation from nodular pulmonary amyloidosis, despite the fact that the histochemical stains for amyloid are focally positive in some cases of PHG.

The etiology and pathogenesis of PHG are unknown. Engleman et al\textsuperscript{1} postulated that PHG represents an exaggerated immune response, possibly due to chronic granulomatous infections such as tuberculosis or histoplasmosis. This exaggerated immune response may result in deposition of immunoglobulins, fragments of immunoglobulins, or immune complexes in the lung. In support of this hypothesis, Schlosnagle et al\textsuperscript{3} demonstrated autoantibodies (antineuclear antibody, rheumatoid factor, and positive antителoglobulin tests), as well as circulating immune complexes in two patients with PHG. Autoantibodies were not present in our patient. Circulating immune complexes containing IIS IgA were demonstrated in our patient. The perivascular arrangement of the hyaline lamellae and their electron-dense, compact, homogeneous, amorphous ultrastructural appearance also give support to the hypothesis that the hyaline lamellae consist mainly of immune complexes. Immunoperoxidase stains failed to reveal the presence of immunoglobulins in the hyaline lamellae in our patient. It may be that the antigenic determinants of the immunoglobulin were masked when the immune complexes were deposited in the lung.

The clinical course of PHG in most patients is benign, although there may be gradual enlargement of the pulmonary nodules over several to many years.\textsuperscript{1} Three patients with PHG developed sclerosing mediastinitis (which closely resembles PHG histologically) and one patient developed sclerosing mediastinitis and then sclerosing retroperitonitis.\textsuperscript{1} During the one year following the diagnosis of PHG, our patient has remained relatively well, his pulmonary nodules have enlarged, and there is no evidence of sclerosing mediastinitis.

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REFERENCES

Successful Treatment of Fetal Supraventricular Tachycardia with Maternal Digoxin Therapy*

Charles R. King, M.D.; Leone Mattioli, M.D.; Kenneth K. Goertz, M.D.; and Wayne Snodgrass, M.D., Ph.D.

In a fetus with supraventricular tachycardia (SVT) and cardiac failure, normal sinus rhythm (NSR) was restored with maternal digoxin therapy at 26 weeks' gestation. The diagnosis of cardiac failure was based on ultrasound evidence of ascites and scalp edema. Cardiac failure was attributed to the persistent SVT. The infant remained in NSR and was delivered at 36 weeks' gestation because of persistent ascites. Intracardiac anatomy was normal. This case confirms the usefulness of prenatal ultrasound examinations in the diagnosis of fetal SVT and cardiac failure and illustrates the effectiveness and safety of transplacental digoxin therapy in the management of fetal SVT.

Sustained fetal SVT is now a well-recognized cause of cardiac failure in utero and of nonimmune hydrops fetalis. In a series of 13 cases of nonimmune hydrops fetalis, three fetuses had SVT as a sole cause.\textsuperscript{1} Transplacental pharmacologic treatment of fetal SVT has been attempted without success with digoxin\textsuperscript{2} and with digoxin and propranolol.\textsuperscript{3} Successful treatment of fetal SVT has been reported with digoxin,\textsuperscript{1,4,5} digoxin and verapamil,\textsuperscript{6} and propranolol.\textsuperscript{9}

We describe an infant with intrauterine cardiac failure due to SVT in whom normal sinus rhythm was restored by maternal oral digitalis therapy. The infant was delivered by cesarean section at 36 weeks' gestation because of ascites. The heart was structurally normal at birth, and normal sinus rhythm has been maintained with therapy digoxin at 11 months of age.

CASE REPORT

In a 24-year-old, primigravida, a fetal heart rate of 190 to 220 beats per minute (bpm) was first observed at 20 weeks' gestation. At 26 weeks, when the patient was first referred for evaluation, the initial fetal heart rate was 228 bpm, and sonographic evidence of scalp edema, polyhydramnios, and ascites was observed. Within 60 hours of initiation of oral digoxin therapy (0.125 mg/day), the fetal heart rate had normalized. Weekly tests of fetal well-being, i.e., nonstress tests, were performed beginning at 28 weeks' gestation. All of these studies were reactive. In addition, on three occasions, contraction stress tests were performed, and results were negative. Assessment of fetal growth by sonography revealed a normal interval growth between 26 weeks and 29 weeks, when the biparietal diameter was 7.3 cm. Subsequent interval growth at 31 and 34 weeks was normal, with a biparietal diameter of 8.8 cm at 34 weeks. Immediately preceding delivery, the ultrasound evaluation showed a gestational age of 36 to 37 weeks with appropriate interval growth. In addition, there was evidence of decreased fetal scalp edema and normal cardiac anatomy, but persistence of ascites. This was thought to be an ominous sign, which prompted the delivery by cesarean section. Amniocentesis for fetal lung maturity was not obtained. Results of examinations

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including maternal serology, SGPD screen, rubella titer, thyroxine level, antibody screening, torch screen, hemoglobin electrophoresis, routine blood chemistry studies, CBC, and urinalysis all were normal.

At 36 weeks gestation, the mother was delivered by cesarean section of a 2,750 g male infant with an Apgar score of 8 at one minute and 8 at five minutes. Marked ascites with an abdominal girth of 38 cm was present. The infant’s respirations were labored. The heart rate was 130 bpm. The rhythm was sinus, and the ECG was normal. An M-mode echocardiogram showed normal cardiac anatomy with an increased ratio of left atrium to aortic root. Right and left ventricular systolic time indices and left ventricular shortening fraction were in the normal range. The chest roentgenogram showed hazy lung fields and an increased cardiothoracic ratio. The cord venous blood digoxin level was 0.4 ng/ml, while the maternal digoxin blood level was 3.6 ng/ml.

Shortly after birth, a paracentesis yielded 270 ml of clear, sterile, ascitic fluid. Digoxin, at a maintenance dose of 10 μg/kg/day, was begun. The infant had an uneventful recovery and, at the last visit at 11 months of age, was thriving well in normal sinus rhythm.

**Discussion**

This report describes the successful pharmacologic treatment of fetal SVT by maternal oral digoxin therapy. To the best of our knowledge, to date there are six cases in the literature (Table 1) of successful transplacental digoxin treatment of fetal SVT. Lingman et al.\(^6\) having reported the first case. At variance with the other reported cases, our patient, despite normal sinus rhythm, had only partial resolution of the fetal edema and ascites, which prompted the delivery by cesarean section. Reasons accounting for the persistent edema and ascites in our case may be the early onset of SVT (20 weeks’ gestation) and its duration prior to the initiation of digoxin therapy (six weeks).

Factors determining fetal outcome in fetal SVT are uncertain. Experimentally, Rudolph and Heyman\(^5\) have shown that when the paced heart rate in fetal lambs was increased, the cardiac output increased to 2500 bpm. Beyond 300 bpm, there was a precipitous fall in cardiac output. Thus, acutely, fetal heart rate is an important determinant of cardiac output. In a recently reported series, however, Newberg and Keane\(^2\) observed that neither the duration of fetal SVT nor the heart rate was predictive of the condition of the fetus at birth. Furthermore, at least in one case reported by Hilrich and Evrard,\(^6\) fetal SVT, first detected at 26 weeks’ gestation, was present at birth (heart rate, 300 bpm) without evidence of cardiac failure. In contrast, in infants and children, the duration of SVT is an important cause of congestive heart failure. Cardiac failure developed in one half of the infants and children in whom the paroxysmal tachycardia lasted 48 hours in a series reported by Nadas et al.\(^3\)

It is now well recognized that when fetal SVT is detected, sonographic evidence of cardiac failure should be sought,\(^5,6\) and the examination should include echocardiography to exclude cardiac anatomic defects.\(^1,7\) Transplacental treatment should be begun at the first evidence of cardiac failure indicated by scalp edema and or ascites.\(^1,5,7\)

We chose digoxin therapy because the drug readily crosses the placenta, reaches high concentration in the fetal myocardium, and is effective both in termination of fetal SVT and in maintenance of normal sinus rhythm (Table 1). Experimentally, Berman et al.\(^5\) have shown that the fetal lamb myocardium is far less sensitive to digitalis-induced arrhythmias than that of the ewes. Chan and Wong\(^4\) have observed that none of the newborn infants whose mothers received digoxin therapy for rheumatic heart disease showed signs of digoxin-induced arrhythmia. Thus, from these data and the experience obtained thus far, it appears that digoxin may be the drug of choice in the transplacental treatment of SVT.

In pregnant women receiving digoxin therapy, Rogers et al.\(^12\) found equal digoxin levels in cord blood and in maternal blood, which was also observed by Lingman et al.\(^3\) However, in our case, in the case reported by Kerenyi et al.,\(^4\) and in those reported by Chan and Wong\(^4\) the cord blood digoxin concentration was lower than the maternal serum digoxin concentration.

Digoxin and verapamil in combination were used by Wolff et al.\(^12\) to treat successfully fetal SVT in one case. Normal sinus

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**Table 1—Successful Transplacental Treatment of Fetal Supraventricular Tachycardia (SVT) With Digoxin**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Age of Detection of SVT</th>
<th>Dose and Mode of Therapy</th>
<th>Termination of SVT After Therapy</th>
<th>Mode of Delivery and Gestational Age</th>
<th>Fetal Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lingman et al.(^6)</td>
<td>29 wk</td>
<td>IV 0.5 mg, then</td>
<td>24 hr</td>
<td>38 wk, vaginal</td>
<td>Healthy newborn, normal sinus rhythm</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.25 mg p.o. daily</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Kerenyi et al.(^4)</td>
<td>29 wk</td>
<td>0.25 mg q6h p.o., then</td>
<td>48 hr</td>
<td>31-33 wk, cesarean section</td>
<td>WPW with short bursts of SVT</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.25 q12h</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Harrigan et al.(^4)</td>
<td>26 wk</td>
<td>1.5 mg p.o. over 14 hr, then 0.25 mg/day</td>
<td>15 hr</td>
<td>38 wk, vaginal</td>
<td>Healthy, normal sinus rhythm</td>
</tr>
<tr>
<td>Kleinman et al.(^4)</td>
<td>27-28 wk</td>
<td>Unknown</td>
<td>1 wk*</td>
<td>39 wk, unknown</td>
<td>Chaotic atrial rhythm, requiring digoxin and propranolol</td>
</tr>
<tr>
<td>Wiggins et al.(^7)</td>
<td>24 wk</td>
<td>1 mg over 24 hr, then 375 μg p.o. daily</td>
<td>6 days</td>
<td>Term, unknown</td>
<td>Normal sinus rhythm</td>
</tr>
<tr>
<td></td>
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</tr>
<tr>
<td>Present case</td>
<td>20 wk</td>
<td>0.125 mg p.o. daily</td>
<td>60 hr</td>
<td>36 wk, cesarean section</td>
<td>Normal sinus rhythm, ascites</td>
</tr>
</tbody>
</table>

* Mother stopped taking digoxin at 38 weeks gestation. Atrial ectopy and SVT recurred at 39 weeks and persisted through birth.

† Personal communication

574 Fetal Supraventricular Tachycardia (King et al)
rhythm was restored after five days of therapy. Propranolol also has been used successfully to treat SVT in a fetus with Wolff-Parkinson-White syndrome by Teuscher et al. Hypoglycemia and bradycardia have been observed by Habib and McCarthy in four neonates with good Apgar scores whose mothers had received propranolol during pregnancy. Cottrill et al. have also reported marked bradycardia and hypoglycemia in a neonate whose mother had received 160 mg of propranolol daily. These authors have considered propranolol therapy during pregnancy as a risk factor for the neonate. However, Rubin, on the basis of current available information on β-blockers in pregnancy, has cast doubts on the adverse effects of propranolol on the fetus.

In conclusion, this case confirms the usefulness of ultrasound examination in the diagnosis of fetal cardiac failure and the effectiveness and safety of translacental digoxin therapy for SVT.

REFERENCES

Pulmonary Arteriovenous Fistula Showing a Fall in Shunt Fraction During Exercise*  

Hajime Maeda, M.D.; Yasunawa Monani, M.D.; Kazuya Nakahara, M.D.; Shinichiro Miyoshi, M.D.; and Yasunaru Kawashima, M.D., F.C.C.P.

A 23-year-old man with pulmonary arteriovenous fistulas of the right middle lobe is described. During the incremental exercise test, the shunt fraction dropped from 19 percent to 12 percent as the cardiac output increased. We discuss the mechanism of this fall in shunt fraction in this patient during exercise.

Exertional dyspnea is the most common symptom in patients with a pulmonary arteriovenous (AV) fistula, and the arterial oxygen tension has been reported to decrease during exercise in about half the patients. The patient described herein showed a fall in shunt fraction during the incremental exercise test. His arterial oxygen tension first increased and then decreased. The purpose of this report is to describe the behavior of the fistulas and the other pulmonary capillaries of this patient in response to increased cardiac output during exercise.

CASE REPORT

A 23-year-old man was referred to our hospital for evaluation of occasional mild dyspnea while sleeping. He had never felt dyspnea on exertion. There was no history of pulmonary disease or congenital malformations in the patient's family, and he had no history of smoking.

The patient was a well-developed young man with normal vital signs and no cyanosis or digital clubbing. There were no hemangiommas or telangiectasias. The heart sound was normal and auscultation of the lungs revealed no rales or bruits.

The hemoglobin level was 17.9. The ECG findings were normal. The chest x-ray film showed two rounded densities in the right lung. Pulmonary angiographic studies (Fig 1) demonstrated two pulmonary AV fistulas originating from the vessels of the right middle lobe. The pulmonary function tests were normal.

He underwent the incremental exercise test on a cycle ergometer (Mijnhardt Medical Instrument, Model FEMS) one week before and four months after surgery. Minute ventilation (Ve), oxygen consumption (Vo2), and carbon dioxide production (Vco2) were measured by an on-line microcomputer combined with a hot-wire respiratory flow meter, a zirconia solid electrolyte oxygen analyzer, and an infrared carbon dioxide analyzer (Minato Medical Science, System RM-200). The radial artery was cannulated, and a Swan-Ganz catheter was inserted for arterial and mixed venous blood sampling. The cardiac output and right-to-left shunt fraction were calculated according to the following formulas:

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