Cor Triloculare Biatriatum

Survival to Adult Life

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A HEART comprised of atria and a single ventricle, cor triloculare biatriatum, represents an unusual congenital defect. In her atlas Abbott described this as the unique defect in only 13 of 1,000 malformed hearts. Fourteen other hearts in her series had some anomaly in addition to a single ventricle. To date almost 100 patients with this defect have been reported in the medical literature but of these only 14 have reached adult life. Our patient is the fifteenth adult with cor triloculare biatriatum to be reported.

Case Report

A 41-year-old woman with cyanotic congenital heart disease was observed at the Hitchcock Clinic and Hospital at intervals for 10 years preceding her death. She had also been seen at various centers in Boston and New York. She had been cyanotic from birth, and a diagnosis of congenital heart disease was made at 2 years of age. Save for influenza at 2 and scarlet fever at 6 years, she had no unusual childhood diseases. Her growth and development were normal. Her activities were moderately restricted by dyspnea and easy fatigability. On graduation from high school she became a medical records' librarian. In 1936, she married an engineer but was divorced within a year. In 1940, 17 years before her death, she had the first of many episodes of hemoptysis. At that time the dyspnea, which had never been severe, gradually increased, though it did not incapacitate her. Despite this and a tempestuous domestic and emotional life, she continued to work effectively until 2 years before her death.

The first attempt to establish the type of anomaly was made in 1944. The following defects were suspected: atrial septal defect, persistent right aortic arch, subaortic stenosis, and right ventricular hypertrophy.

Physical examination in 1947 showed deep cyanosis and marked clubbing of the fingers and toes. The blood pressure was 120/70. The retinal vessels appeared dilated and full. The chest was normal. The heart was not enlarged to percussion. Rhythm was regular and the rate was 100 per minute. P₂ was accentuated but not split and was greater than A₂. M₁ was greater than M₂. A grade-II blowing systolic murmur was loudest in the second left interspace. The lungs were clear to percussion and auscultation, and the liver and spleen were not palpable.

The hematocrit value was 75 and the hemoglobin was 21.3 Gm. per cent. The white blood cells were normal, and the platelets were not increased. The sedimentation rate was normal. Urinalysis was negative.

On fluoroscopy the heart was not enlarged but there was slight fullness of the right ventricular shadow. The main pulmonary artery did not appear enlarged but there was engorgement of the right pulmonary artery and to a lesser degree of the left. Engorgement extended well into the smaller vessels of each lung. There was no hilar dance and no atrial enlargement. The aorta appeared normal. Pulsations were of normal amplitude (fig. 1). The electrocardiogram was consistent with atrial hypertrophy. No specific pattern of ventricular hypertrophy could be determined, though some abnormality of intraventricular conduction was suspected (fig. 2). A tentative diagnosis of Eisenmenger's complex with secondary polycythemia was made. Cardiac catheterization and angiocardiography were refused by the patient at that time.

In June 1954, she again noticed increasing dyspnea and had several bouts of hemoptysis. Her family physician therefore performed a phlebotomy and removed between 150 and 200 ml. of blood without incident. The following week during a second phlebotomy, after approximately 100 ml. had been removed, the patient suddenly felt dizzy and faint and complained of numbness of the roof of her mouth. The procedure was stopped. She then experienced increasing dizziness, weakness, and headache and became more cyanotic than previously. The patient reported sudden weakness of the left arm and leg. The increased cyanosis persisted for a week. The left-sided weakness gradually improved.

In October 1954, cardiac catheterization was performed at Mount Sinai Hospital in New York City (table 1).

These determinations showed that the oxygen
content of the blood rose sharply from the right atrium to the ventricle. The oxygen content of the aorta, however, remained the same as the ventricular samples, indicating complete mixture of ventricular blood. It was concluded that the patient probably had a single ventricle. The possibility of pulmonary stenosis was considered, and angiocardiography was recommended but the patient refused. Surgical intervention was not advised.

Anticoagulants to combat the probable thrombotic episodes and radioactive phosphorus, to decrease the polycythemia, were considered advisable. Phlebotomies were thought contraindicated at the time in view of the neurologic complications following one of these procedures. The importance of adequate hydration was recognized.

In the spring of 1955 she became unable to work and was dyspneic on mild exertion. The syncopeal episodes, vertigo, and hemoptysis persisted and signs of left hemiparesis were noted. The hematocrit value was 75, the hemoglobin was 20.4 Gm. per cent, and the red cell count was 8,650,000.

In October 1956 the syncopeal episodes increased in severity and frequency. They were usually precipitated by physical exertion and emotional stress or fatigue, and were more frequent before menses. On hospitalization 3 months later physical examination showed little change. The heart size and the murmurs were the same. Marked secondary polycythemia persisted. Cardiac fluoroscopy showed prominence of the right ventricle and the right pulmonary artery, though not of the main pulmonary trunk. There were large peripheral divisions in the right lower lung fields. There was displacement of the esophagus posteriorly and to the right, which was thought to be due to a combination of aorta and large pulmonary artery. The lung fields, save for heavy vascular markings particularly on the right, were clear. The electrocardiogram showed no change.

Because of the rapid progression of symptoms and the severe polycythemia, the question of phlebotomy was again reviewed in great detail. Because it was considered essential to reduce the blood viscosity within a short time, it was decided to do phlebotomies, despite the risk and the patient's fear of them.

During the next 8 days 4 phlebotomies of 250 ml. were done cautiously with replacement of the same volume of saline solution. During the second phlebotomy the patient experienced numbness and tingling of the roof of the mouth with thickness of speech. She was subsequently noted to be more short of breath and more deeply cyanotic. On the tenth day, during a fifth phlebotomy she again complained of dry mouth and numb tongue after 75 ml. of blood had been removed. Aphasia, profound cyanosis, increased left-sided weakness, and slurred speech were followed by coma and repeated convulsions that cleared after intramuscular magnesium sulfate. No subsequent seizures occurred, but the speech remained thick and the signs of left hemiparesis persisted.

Her subsequent course was marked by recurring thrombotic episodes involving the brain as well as the left subclavian artery. Her condition deteriorated rapidly. Oral and intravenous fluids were increased to 4,000 ml. in an attempt to expand the plasma volume. No signs of congestive heart failure appeared, the urinary output was satisfactory, and there was gradual improvement with slow
Electrocardiogram.

regression of the neurologic signs. The hematocrit value gradually dropped to 65 and persisted at this level. A left greater saphenous phlebitis, extending from the foot to the upper thigh developed. There were no signs of deep phlebitis, and no further thromboses were noted. Several days later she suddenly became comatose and died.

Autopsy Examination

The heart weighed 324 Gm. and was trilocular, composed of 2 atria, with an intact septum, and a single ventricle. Both venae cavae emptied normally into the right atrium, which was dilated to 2½ times normal size but contained no thrombi. It communicated with the common ventricle through a bicuspid valve 10 cm. in diameter. Dorsally, between the two leaflets, a puckered area of endocardium 1 cm. long appeared to be a rudimentary third leaflet. The great vessels leaving the heart were transposed (figs. 3 and 4). Neither the left atrium nor the pulmonary veins from the left lung, which entered it normally, were dilated. From the right lung a single dilated pulmonary vein, 2.5 cm. in diameter, emptied into the left atrium. Communication of the common ventricle with the left atrium was through a normal bicuspid mitral valve, 2.8 cm. in diameter. The aortic valve was normal, save for several small (0.6 by 0.4 cm.) firm, gray-yellow thrombi on each corpus Arantii. The coronary ostia and vessels were normal. The entrance to the pulmonary valve was small, measuring 1.6 cm. in diameter (fig. 5), and there was no differentiation of the valve into cusps. It was markedly stenotic with only a pinpoint lumen. Perched on its superior surface was a cone-shaped thrombus, 0.8 cm. in diameter, which was red-gray, firm, and granular

with a minute aperture less than 1 mm. in diameter at its tip. When explored with a probe this aperture was found to be continuous with the opening in the valve itself (fig. 6). Immediately distal to the stenotic pulmonary valve the main pulmonary artery was dilated to 6.9 cm. in circumference. The right division was markedly dilated to 4.0 cm. in diameter at its origin. The left measured only 12 cm. in diameter. Neither the pulmonary artery nor its branches showed atherosclerosis or thrombosis.

The ligamentum arteriosum was a fibrous cord. The innominate artery and the left subclavian artery arose normally but the lumen of the latter was occluded at its origin for 2.5 cm. distally by a firm, red-brown adherent thrombus. The left internal and external carotid arteries took separate origin from the aortic arch. The bronchial arteries were not followed. Microscopically the myocardium was normal.

The lungs together weighed 1150 Gm. At the

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<td>Superior vena cava</td>
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hilus of the right lung were two large vascular channels; the dilated right pulmonary artery and vein, the latter 5.0 cm. in diameter (fig. 7). No thrombosis was seen. The bronchi were normal. Microscopically all lobes showed extreme dilatation of bronchial and pulmonary arterioles and alveolar capillaries. This appearance was so striking in places as to give the tissue a “honeycombed” appearance (fig. 8A). There was no medial hypertrophy in bronchial or pulmonary arterioles of any size, but the latter showed slight to moderate fibrous intimal thickening. Many bronchial and pulmonary arterioles contained recanalized thrombi or emboli (fig. 8B). Define anastomoses between bronchial and pulmonary arterioles were present (figs. 8C and 8D). One small recent infarction was present in the right upper lobe. There was no pneumonia.

The spleen contained a small healing infarction. Areas of softening, degeneration, and cyst formation were found grossly in the right side of the brain.

Microscopically the bone marrow showed marked hyperplasia, which was predominantly in the red cell series.

The main anatomic diagnoses were: Cor triloculare biaatriatum with transposition of great vessels; pulmonary stenosis, congenital, with superimposed thrombosis; bicuspid “tricuspid” valve; single pulmonary vein, right; dilatation, moderate, main pulmonary artery and marked, right pulmonary artery; bronchopulmonary arteriolar anastomoses; emboli, recanalized, multiple, bronchial and pulmonary arterioles; thrombosis, organizing, of proximal left subclavian artery; infarcts of cerebrum and pons, spleen, and lung.

Discussion

Even with the sophisticated technics available today, an accurate premortem diagnosis of cor triloculare biaatriatum is unusual. There is no uniform pattern, but variation is considerable in the degree of cyanosis, in the characteristics of the murmurs, in the appearance of the electrocardiogram, and in the

Figure 3
View of anterior surface of the heart showing the common ventricle (CV), and the right and left atria (RA, LA). The transposition of the great vessels is evident with the anteriorly placed aorta (A) and behind it the pulmonary artery (PA). The left internal and external carotid arteries (CA) take separate origin from the aortic arch.

Figure 4
View of the posterior surface of the heart showing superiorly the markedly dilated right main division of the pulmonary artery (RPA), and its small left branch (LPA); below is the normal sized left atrium (LA) with the 2 left pulmonary veins (LPV) entering in the usual fashion while on the right is the single dilated pulmonary vein (RPV). The vertical stick indicates the ostia of the vena cava. The ligamentum arteriosum (L. Art.) is now a fibrous cord.
The heart opened anteriorly shows the thick-walled common ventricle (CV), the aortic valve above (AV), and just below it the small entrance to the pulmonary valve (PV). Still more inferiorly the edge of the bicuspid "tricuspid" valve (TV) is visible. Small thrombi are present on the aortic valve cusps.

Figure 5

An anterior view of the unopened, cone-shaped and markedly stenotic pulmonary valve (PV) shows the firmly adherent thrombus (T) on top of it. The arrow indicates the direction of blood flow through the pinpoint lumen on the superior surface of the thrombus.

Figure 6

Contours of the heart at fluoroscopy. A systolic murmur has been recorded in all cases, but its position has varied from apex to second left interspace. Despite the absence of septal tissue very few of these patients show bundle-branch block or intraventricular conduction defects. Cardiac fluoroscopy often reveals evidence of increased pulmonary blood flow, but there is no characteristic x-ray configuration of the heart shadow or of the great vessels. Those defects presenting most confusion in differential diagnosis are Fallot's tetralogy and the Eisenmenger pattern. The accurate diagnosis of a single ventricle rests upon both angiocardiography and cardiac catheterization. The simultaneous filling of the aorta and pulmonary artery from a common ventricular chamber, as seen on the angiocardiogram, indicates the presence of a single ventricle; the demonstration of identical oxygen contents in the pulmonary artery, the aorta, and the ventricle, confirms the diagnosis.

With rare exceptions a single ventricle is associated with transposition of the great vessels, so that the aorta lies anterior to the pulmonary artery. Often a rudimentary outflow chamber, or persistent bulbus cordis can be recognized, and an anatomic classification has been devised by Rogers and Edwards relating the position of the aorta and pulmonary artery to this outflow chamber. Many hearts with a single ventricle have been found to have an additional anomaly. Among these have been patent ductus arteriosus, subaortic stenosis, atresia of the mitral valve and of the ascending aorta, and atrial septal defect.

As emphasized by Rogers and Edwards, patients with cor triloculare biatriatum rarely live beyond childhood, and, indeed, 14 patients only have been recorded who reached the age of 21 years or more. The oldest of these succumbed at the age of 56. Our patient who died at the age of 41 is the fourth oldest on record.

In relation to the problem of survival in patients with cor triloculare biatriatum, it is
pertinent to review the physiology of one of those animal forms that normally possess only a single ventricle. Why is it, for example, that the frog with its single ventricle does so well when man, with his, does so poorly? The immediate answer is that the frog has other means of separating the pulmonary from the systemic distribution of blood. The frog has only a single large vessel, the truncus arteriosus, arising from its single ventricle (fig. 9). This trunk divides into 2 main branches, each of which immediately subdivide into 3 major arteries. One, the pulmocutaneous artery, carries blood to the organs of respiration, the lung, and the skin. The systemic artery carries blood to the extremities and to the abdominal viscera, and the carotid artery carries blood to the head. The so-called carotid gland, a network of small vascular channels, is interposed in the course of the carotid artery, acting as a segment of high resistance. The truncus arteriosus (fig. 10) at a point beyond the semilunar valves, is divided by a long tongue of tissue, attached along most of its dorsal edge, but free ventrally. This is the longitudinal or spiral valve. The mouth of the truncus is near the right atrioventricular valve, so that blood coming from the right atrium, lowest in oxygen content, is the first to be delivered into the truncus at the onset of ventricular systole. The resistance in the pulmocutaneous circuit is lowest, so that this initial volume of unsaturated blood flows into the organs of gas exchange. As the ventricle approaches midsystole, muscle tissue in the wall of the truncus itself contracts, narrowing this channel and forcing the free end of the spiral valve to close over the orifices of the pulmocutaneous arteries. During the midportion of systole, blood flows into the systemic artery where the next lower level of resistance exists. Finally, as the systemic system is filled and systolic pressure reaches its peak, the resistance of the carotid gland in the carotid artery is overcome, and the last volume of blood, chiefly that which has flowed from the left atrium into the left side of the ventricle, with its higher oxygen content, now moves to the head. The thick wall of the frog ventricle contains many little pits or recesses, and acting like a sponge, absorbs much of the blood as it enters from the atria on either side, reducing the degree of admixture that otherwise might occur in the free cavity.

In man, possessing no spiral valve, no carotid gland, and no myocardial sponge, there must be some other mechanism to permit survival. A review of the case histories of long-term survivors failed to reveal the uniform presence of any single associated anomaly. In searching among these for cases similar to our own, we found only a single report in which a deformity of the pulmonary valve accompanied the single ventricle. Carns et al. described a 44-year-old woman who had a rigid, bicuspid pulmonary valve with poststenotic dilatation of the pulmonary artery. This patient, severely cyanotic, with a red blood count of 8.4 million, died after having developed thrombophlebitis of the right sub-
A representative view of the thin-walled and markedly dilated blood vessels of the lung parenchyma derived from both pulmonary and bronchial arteries.

The clavian vein. A patient reported by Mehta and Hewlett \(^8\) lived until the age of 56, but had a persistent truncus arteriosus. The pathway of her pulmonary blood flow was not recorded. One young man \(^9\) who died at 18 years of a ruptured pulmonary artery was found to have a hypoplastic aorta and a patent ductus arteriosus. At least in terms of gross morphology, there is no consistent pattern among this older-age group. Clinically, the only common denominator has been a fairly severe degree of cyanosis. The only exception is Herndon’s case, \(^12\) a 49-year-old man in whom cyanosis was not prominent.

Unfortunately almost none of the reports of these cases includes a description of the microscopic appearance of the lung and its vasculature, for it is very likely that changes in the intrapulmonary vascular network of these patients are of paramount importance in their survival. \(^6\) In the presence of a single ventricle, the distribution of blood flow between the aorta and the pulmonary artery is determined by the resistance in each circuit. Because of its easy distensibility, the pulmonary vascular tree ordinarily presents much the lesser resistance, and as is the case in most patients with this anomaly, the greater volume of blood flows to the lungs. Although oxygenation of this larger volume of blood may contribute to a higher net saturation of the blood mixed in the single ventricle, the obvious disadvantage is that systemic blood flow may be critically low. This deficit in systemic flow accounts for the meager development and early death of most infants born with a single ventricle.

The introduction of some obstruction to flow in the pulmonary circuit, either at the level of the pulmonary valve or in the small pulmonary arteries, would tend to balance the distribution of blood, so that a more adequate volume could be directed out the aorta. This increase in pulmonary resistance can be produced by vasoconstriction or by structural changes in the pulmonary arteries. The resultant shift of blood away from the pulmonary circuit, as it were, would result in a lower level of saturation of mixed ventricular blood. Hence a more satisfactory systemic flow would be gained at the price of more cyanosis. It is possible, of course, that such pulmonary vascular obstruction would become progressively more severe as the result of medial hypertrophy, intimal proliferation, or mul-

**Figure 8A**

*Figure 8A*

A dilated bronchial artery containing a recanalized thrombus. The lining of the bronchus is indicated by the arrow.
multiple intravascular thromboses. However, under such circumstances, the development of anastomotic channels between branches of bronchial and pulmonary arteries would provide an avenue for continued adequate flow of blood past alveolar spaces. This appeared to have been the case in our patient as well as in one reported by Heath.2

A patient can survive to adult life if he can walk this knife edge between a critically reduced systemic output (when pulmonary resistance is too low) and a critically reduced oxygen uptake (when pulmonary resistance is too high). Our patient, with a severe degree of pulmonary valvular stenosis but with multiple bronchial-pulmonary arteriolar anastomoses, was apparently able to accomplish this balance. It is pertinent here to refer to the case report of a boy15 who, with the mistaken diagnosis of Fallot's tetralogy, underwent surgical correction of pulmonic stenosis. He died 3 hours after a successful valvuloplasty and was discovered to have had a single ventricle rather than the tetralogy pattern. Release of his pulmonary obstruction may very well have been his undoing.

In her later years our patient appears to have sustained multiple pulmonary emboli or thromboses with further increase in the pulmonary resistance and further reduction in oxygen uptake. The increasing erythemia compensated to some extent perhaps, but the attendant increase in blood viscosity brought with it the hazard of cerebral vascular thromboses.

A real dilemma of therapy and management was posed by our patient. On the one hand, her condition was deteriorating and she had already suffered cerebral damage from previous thromboses. The high incidence of thromboembolic phenomena under such circumstances was recognized, and reduction of the blood viscosity was urgently needed. On the other hand, we were aware of the known, though unpublished, high incidence of thromboses in patients with congenital heart disease and polycythemia following phlebotomy. After careful consideration phlebotomies were cautiously performed with the disastrous results reported.

A total of 7 phlebotomies was done. Three of these were followed either immediately or within 24 hours by evidence of cerebral damage. The final phlebotomy appears to have initiated a period of prolonged coma and convulsions, with both left and right hemiplegias. Several observers have stated that experience in patients with congenital heart disease and secondary polycythemia has led them to abandon phlebotomy as a means of lowering the
hematocrit level. Repeated instances of acute neurologic changes, some of them transient, others permanent, have been observed. Sudden death has occurred during or immediately following this procedure. As in our case, the amount of blood withdrawn is not always a factor, since this adverse effect has been noted with as little as 75 to 100 ml. No specific reference to this complication of phlebotomy was found in medical literature.

The mechanism for the occurrence of thrombotic episodes during phlebotomy in patients with congenital heart disease and secondary polycythemia is not understood. There are a number of possible contributing factors that must be considered.

In secondary polycythemia the oxygen saturation of the arterial blood is reduced. This suggests that polycythemia is secondary to hypoxemia. Polycythemia with increased hemoglobin content is a consequence of arterial unsaturation. The increased oxygen-carrying capacity achieved in this way is an extremely useful compensatory mechanism until the polycythemia reaches the hematocrit value of 80 or more. At these levels the benefits derived from the increase in available oxygen are outweighed by the disadvantages.
of high blood viscosity. Rudolph, Nadas, and Borges have shown that when the hematocrit value reaches 65 to 70, further increase entails a considerable rise in blood viscosity resulting in an impediment to blood flow, sludging, and even decreased delivery of oxygen to the tissues. The relationship is in the form of a hyperbolic curve. At lower hematocrit levels a fairly large rise in the hematocrit value is required to produce significant change in viscosity. At higher hematocrit levels, however, only minor increases of the hematocrit value produce marked increases in viscosity.

Multiple thromboembolic phenomena are typical of the late course of patients with well compensated cyanotic congenital heart disease. This patient was in the early menopause and was approaching the age of degenerative vascular disease, which increases the likelihood of thromboembolic phenomena.

Tyler and Clark reported that paroxysmal loss of consciousness or convulsions occurred in approximately 18 per cent of a series of 336 patients with congenital heart disease. Those forms of congenital heart disease that had the highest incidence of loss of consciousness, or convulsions, also were marked by lower systemic arterial oxygen content and oxyhemoglobin saturation. The attacks were most frequently seen in patients whose cardiac defect provided a physiologic potentiality for large and rapid variations in the amount of venous blood reaching the systemic circulation.

Thromboses in relation to periods of stress have been shown to occur with marked reduction in clotting time. Increase in viscosity occurs during painful experience, vigorous effort, and in periods of alarm or anxiety. In
the studies by Schneider it has been shown that when people were subjected to interviews arousing personal conflicts and conscious or unconscious anxiety, there occurred in association with elevation of arterial blood pressure shortening of the clotting time and sedimentation rate, and an increase in the blood viscosity with rise in the hematocrit value.

It is likely that all these factors played a part in this patient's adverse response to phlebotomy.

Summary
The case of a 41-year-old woman with congenital pulmonary stenosis and single ventricle is reported. This is the fifteenth instance recorded of survival to adult life of a patient with cor triloculare biaatriatum. Increased pulmonary resistance may be a reason for her comparative longevity, and the significance of prominent bronchopulmonary anastomoses has been discussed. This patient's course demonstrates the hazards of phlebotomy in congenital heart disease and secondary polycythemia. The mechanism for this adverse effect is not understood and warrants further study. Although others have discussed the problem informally, this appears to be the first documented report of the precipitation of multiple cerebral thromboses following phlebotomies.

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