Diffuse Tortuosity and Lengthening of the Arteries

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SUMMARY
This article describes the case of a 10-year-old girl with generalized tortuosity and lengthening of all her major arteries—the carotid arteries, the aorta from the arcus to the bifurcation, and the iliac, femoral, splenic, hepatic, renal, and intercostal arteries. The condition appears to be a new entity. Pertinent abnormalities were as follows: gross pulsation of the arteries in the neck, telangiectasia of both cheeks, high palate, tortuosity of all the arteries, aortic valvular insufficiency, 1+ to 2+ capillary fragility on tourniquet test (lacet), 1+ Wassermann reaction, 4+ cephalin flocculation, and histological fragmentation of the internal elastic membrane of the arteries.

Syphilis, arteriosclerosis, hypertension, mucopolysaccharidosis, and defects of amino acid metabolism were ruled out and the author concludes that the condition was most likely caused by a congenital defect of the elastic tissues of the arterial system.

Additional Indexing Words: Aortic valvular insufficiency Telangiectasis Arterial dysplasia

Tortuosity of a single artery or its collaterals has been well documented in all age groups. An entity in which there is buckling or kinking of the aortic arch, any part of the aorta, or tortuosity of only one or two major arteries has long been recognized. In 1852, Coulson described a patient who apparently had a tumor in the neck, which later proved to be a tortuous carotid artery. Later, in 1898, Balfour also described this entity.

Schneider and Felson reviewed 125 cases of buckling of the innominate artery and described three cases of their own. Most of their patients were elderly women with hypertension, atherosclerosis, and cardiomegaly. Many other authors have described this same entity. Others have reported kinking, elongation, tortuosity, or pseudoacoartation of the aortic arch or a part of the descending aorta. A review of the literature indicates that tortuosity of a single artery is not rare, but involvement of two arteries in the same individual is seldom seen.

Localized tortuosity of individual arteries is seen in a few elderly persons, but generalized tortuosity of the arterial system has not been reported in the literature.

Recently we had occasion to see a 10-year-old girl, all of whose major arteries—the carotids, aorta from the arcus to bifurcation, and the iliac, femoral, splenic, hepatic, renal, and intercostal arteries—were tortuous and lengthening. She also had a fusiform aneurysm at the beginning of the descending aorta with aortic valvular insufficiency. After consulting with several leading centers of cardiology, radiology, and pathology, we found that no such entity had ever been seen or reported before.

Report of Case
S.T., a 10-year-old girl, was admitted to the Hacettepe Medical Center in June 1965 with the following symptoms of 2 years’ duration: pulsations in the anterior part of the neck and both submandibular regions, palpitations and dyspnea on exertion, occasional fever, and abdominal pain. There were no unusual findings.

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in her history concerning birth, infancy, and childhood. She had normal growth and development. She had no history of rheumatic fever but had had the usual childhood diseases.

About 2 years before admission, her family had noticed pulsations in her neck. They were told by a doctor at that time that the child probably had had heart disease for many years.

**Family History**

There was no history of unusual disease, syphilis, or tuberculosis in the family. Three brothers, aged 3, 8, and 19 years, are living and well.

**General Examination**

The patient appeared to be in good condition. Her weight was 26 kg; height, 126 cm; head circumference, 50 cm; blood pressure, 110/10 mm Hg. She was neither orthopneic nor dyspneic. There was a slight capillary pulsation in the nails. Pulsus Corrigan or a water-hammer type of pulse and a pistol shot sound were noted in the peripheral arteries. Both carotid arteries were visible, tortuous, and pulsating vigorously (fig. 1). The brachial and femoral arteries were also tortuous and pulsating. There were a few small telangiectases in both cheeks, but no edema, cyanosis, or clubbing of the fingers or toes. Slight microadenopathy was noted in the submandibular, axillary, and inguinal areas. The arch of the palate was slightly higher than normal. There was no dislocation of the eye lens nor any other findings which might suggest Marfan's disease. The skin was not hyperelastic. The respiratory system was within normal limits. There were no abnormal psychological or neurological findings. In the ophthalmologic examination, pulsations of the arteries and veins were visible. X-ray studies of the gastrointestinal system revealed a filling defect in the lower part of the esophagus caused by pressure from an extrinsic mass which proved to be the tortuous aorta.

**Circulatory System**

The apex of the heart was located at the eighth intercostal space on the midsagittal line. A 1+ systolic thrill could be felt at the first intercostal space on the left side of the sternum and a 4+ diastolic thrill was felt over the rest of the precordium and from the right clavicle down to the right costal margin on the anterior side of the chest. The thrill was very harsh and rough, especially on the right side. At the first, second, and third intercostal spaces, there was a soft, grade II/VI systolic murmur which ended in the middle of systole. The second heart sound was considerably increased at the apex, pulmonary, and aortic positions. A rough decrescendo-type, grade IV/VI diastolic murmur started with the second sound and covered almost three fourths of the diastole. This murmur was most clearly heard over the right anterior part of the chest; it decreased on the left side of the sternum and disappeared completely 2 cm from the left border of the sternum. Blood pressure in both arms was 100/10 mm Hg, and both legs, 110 systolic mm Hg by palpation. The edge of the liver was sharp and palpable 2 cm below the right costal margin in the midsagittal line. The spleen was not palpable.

The electrocardiogram showed left ventricular hypertrophy with strain, but sinus rhythm was normal. X-ray examination of the heart was made with a barium swallow. A large mass could be seen at the right supracharic area in the anteroposterior view. The left border of the heart was visible below the diaphragm and was consistent with left ventricular hypertrophy. Vascularity of the lungs was within normal limits. The upper part of the esophagus was pushed toward the right; the lower part toward the left. The left anterior oblique view showed a large

**Figure 1**

Carotid arteries should be noted.

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dense area, which was the continuation of the heart shadow, filling all of the anterosuperior part of the chest and looking like an enlarged aorta. The left ventricular shadow was obviously behind the vertebral column. The right anterior oblique view showed the lower part of the esophagus to be pushed anteriorly and to the left (fig. 2).

Cardiac Catheterization

The right brachial artery, which proved to be very tortuous, and the right median basilic vein were isolated. Although catheters of different sizes were tried in the vein, none could be passed as far as the superior vena cava. The tip of the catheter always entered the right jugular vein. In the artery, also, the catheter could not be introduced farther than the subclavian artery, and took a spiral course. The catheters were removed and the incision closed. Next, the right saphenous vein and femoral artery were exposed. A no. 7 French catheter was introduced through the saphenous vein to the right atrium and right ventricle but could not be passed into the pulmonary artery. From the right atrium, the catheter slipped into the left atrium and left superior pulmonary vein, probably through a patent foramen ovale. Oxygen saturation and pressures recorded at various levels are shown in table 1.

The results of catheterization did not indicate any left-to-right or right-to-left shunt at the atrial and ventricular levels. Systolic pressure in the right ventricle was slightly elevated. The femoral artery was tortuous and soft, but the lumen seemed normal and the color of the intima was a normal creamy gray. A no. 7 Lehman catheter (125 cm long) was introduced through the right femoral artery into the ascending aorta, but because of the extreme length of the tortuous vessel despite the introduction of the entire catheter, the tip remained above the aortic valve. Lengthening was estimated as three times that normal for the child’s age. The tortuosity of the catheter in the iliac arteries and in the abdominal and thoracic aorta could be clearly seen on fluoroscopic examination.

Aortography

Forty milliliters of 76% Urografin (sodium and meglumine diatrizoate) was injected into the ascending aorta and three exposures per second for 3 seconds were made.

The aortogram revealed a much enlarged ascending aorta (fig. 3) which looked like a fusiform type of aneurysm, located just beyond the aortic valve cusp. The dye was regurgitated into the left ventricle. (The tip of the catheter was 15 cm above the aortic valve because of the tortuous path through the artery, even though the catheter was 125 cm long.)

Six days later aortography was repeated in order to visualize the abdominal aorta and its branches. The aortic arch, thoracic and abdominal aorta, and all the arteries (iliac, intercostal, splenic, hepatic, mesenteric superior and inferior, celiac, and renal) were tortuous, some of them much resembling a telephone cord (fig. 4).

Laboratory Examinations

Extensive laboratory tests were carried out with normal results. Renal function was normal;

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Oxygen Saturation and Blood Pressure at Different Levels</th>
</tr>
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<tbody>
<tr>
<td>Levels</td>
<td>Oxygen saturation (%)</td>
</tr>
<tr>
<td>Superior vena cava</td>
<td>58</td>
</tr>
<tr>
<td>Right atrium, high</td>
<td>56</td>
</tr>
<tr>
<td>Right atrium, middle</td>
<td>59</td>
</tr>
<tr>
<td>Right atrium, low</td>
<td>65</td>
</tr>
<tr>
<td>Inferior vena cava</td>
<td>70</td>
</tr>
<tr>
<td>Inferior vena cava, 8 cm. below</td>
<td>69</td>
</tr>
<tr>
<td>Right ventricle, middle</td>
<td>59</td>
</tr>
<tr>
<td>Left atrium (3 samples)</td>
<td>94</td>
</tr>
<tr>
<td>Left superior pulmonary vein</td>
<td>94</td>
</tr>
<tr>
<td>Femoral artery</td>
<td>93</td>
</tr>
</tbody>
</table>

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the specific gravity of the urine was 1.010 to 1.030. Hemoglobin averaged 12 g/100 ml, and the white and differential counts were normal. Capillary fragility, as determined by the tourniquet test, was 1 to 2+; bleeding time was 3.5 minutes; and prothrombin time, 25 seconds (control, 13 seconds).

The Venereal Disease Research Laboratories (VDRL) test for syphilis and the Kahn test were negative; the Wassermann reaction was 1+; the Treponema fixation test (Nelson Mayor) was specific fixation before meal, 43%; after meal, 39%. After 2 days of treatment with vitamin K, the prothrombin time was 13 seconds and the tourniquet test was 1+.

The results of serum electrophoresis and various other tests are given in table 2. Chromosome studies of the patient and her father were within normal limits.

**Amino Acids**

The total amino acids found in the urine were 7 taurine units, using the two-dimension paper chromatography method. On another occasion it was 20 units. Total amino acids in the patient’s plasma was 53 taurine units. Amino acids detected in the patient’s urine and blood are given in table 3.

**Biopsies**

Liver, skin, and muscle biopsies revealed normal conditions.

The arterial specimen was a piece of tubular, pale gray tissue resembling a vessel. Microscopic examination of sections stained with hematoxylin and eosin showed no remarkable abnormality. Sections stained with Verhoeff’s stain, however, showed a decrease in elastic fibers in the media. The internal elastic membrane was intact in some areas but not in others (fig. 5). No inflammatory cell collections could be seen above the arterioles in the adventitia. Sections studied for toluidine blue metachromasia showed areas of pinkish changes. However, this was not considered to be abnormal.
Relevant Findings in This Case

These were dance of the arteries, telangiectasis of both cheeks, high palate, tortuosity of all the arteries, aortic valvular insufficiency, 1+ to 2+ tourniquet test for capillary fragility (lacet), 1+ Wassermann reaction, 4+ cephalin flocculation, decreased elastic fibers of the external membrane, and fragmentation of the internal elastic membrane of the arteries.

Discussion

Of paramount interest in this case is the possible etiological factor or factors responsible for such diffuse tortuosity and lengthening of the arteries in a 10-year-old girl.

The most common etiological factor in cases of single tortuosity is arteriosclerosis. The coincidence of generalized spiral arteries with Marfan's syndrome has not been reported in the literature. There was no arachnodactyly in our patient; the length of the extremities, fingers, and toes were all within normal limits. Furthermore, the absence of hyperextensibility of the joints and the presence of normal eyes and external ears were all inconsistent with a diagnosis of Marfan's syndrome. Our patient had only a slightly higher than normal arch of the palate.

Syphilis has seldom been considered an etiological factor in arterial tortuosity. Although our patient had 1+ Wassermann reaction, VDRL and Kahn tests were negative. Parents and siblings gave negative results for all these tests. The Treponema fixation test was inconclusive. Because there were no clinical or radiological signs of syphilis, it was ruled out as an etiological factor.

Open and needle biopsy specimens from the liver were normal despite the fact that gamma globulin was slightly elevated, a sharp
Considerable decrease in elastic tissue fibers in the media. The internal elastic membrane was not intact in most areas. Verhoeff's stain for elastic tissue; × 40.

Table 2

Results of Serum Electrophoresis and Other Tests on Blood and Urine

<table>
<thead>
<tr>
<th>Serum electrophoresis</th>
<th>Albumin</th>
<th>37.63%</th>
<th>(54.25% control)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>a1-globulin</td>
<td>6.82%</td>
<td>(1.58% control)</td>
</tr>
<tr>
<td></td>
<td>a2-globulin</td>
<td>19.00%</td>
<td>(7.78% control)</td>
</tr>
<tr>
<td></td>
<td>β-globulin</td>
<td>11.99%</td>
<td>(14.11% control)</td>
</tr>
<tr>
<td></td>
<td>γ-globulin</td>
<td>24.55%</td>
<td>(22.66% control)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Additional findings</th>
<th>Thymol turbidity</th>
<th>1 unit</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sia test</td>
<td>Negative</td>
</tr>
<tr>
<td></td>
<td>Nonprotein nitrogen</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Blood</td>
<td>35 mg*</td>
</tr>
<tr>
<td></td>
<td>Urine</td>
<td>18.2 mg*</td>
</tr>
<tr>
<td></td>
<td>Blood sugar</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CO₂</td>
<td>25.36 mEq†</td>
</tr>
<tr>
<td></td>
<td>Chlorides</td>
<td>104 mg*</td>
</tr>
<tr>
<td></td>
<td>Cholesterol</td>
<td>128 mg*</td>
</tr>
<tr>
<td></td>
<td>Free</td>
<td>44</td>
</tr>
<tr>
<td></td>
<td>Ester</td>
<td>84</td>
</tr>
<tr>
<td></td>
<td>Mucopolysaccharides in urine in 24 hr (Control, 30 mg) 36 mg</td>
<td></td>
</tr>
</tbody>
</table>

*Per 100 ml
†Per liter
liver edge and 4+ cephalin floculation were noted.

The only relevant findings of the arterial biopsy were a decrease of the external elastic membrane and fragmentation of the internal elastic membrane. The breakdown of the elastic lamellae with age and the fragmentation and calcification of the arterial elastic tissue have been described. In addition, it has been demonstrated that calcification of the medial elastic tissue does not depend on a pre-existing arteriosclerosis. There was no detectable calcium in the arterial biopsy specimen of our patient, and we were unable to determine the cause of the fragmentation of the internal elastic membrane.

Wolff reported an unusual case of diffuse destruction of elastic tissue with mucoid accumulations in the aortic media of a 12-day-old infant. The lesions were associated with somatic defects including cardiac hypertrophy and widening of the aortic and pulmonary valve cusps. Similar lesions in association with coarctation of the aorta have been reported in young people. Such lesions apparently are not as rare as was supposed and are not limited to the older age group but may occur in young persons with rapid development of signs and symptoms.

The possibility of an amino acid defect in our patient was raised because of the condition of the arteries, decreased and fragmented elastic tissue, the 4+ cephalin-floculation reaction, and the slightly increased globulin fraction. Fragmentation of lysis of the elastic framework of the aorta has been produced in rats by feeding them a diet containing 50% Lathyrus odoratus seeds. Further, Odiette in 1932 reported the interesting but unconfirmed observation that the formation of elastic fibers in tissue cultures is enhanced by the addition of certain amino acids, including glycine, glutamic acid, phenylalanine, and tryptophane. Administration of elastase to animals has been shown to alter the incorporation of labeled glycine into elastin. Glycine was incorporated only very slowly into elastin and disappeared very slowly. This finding provides some biochemical basis for the view, long held by histologists, that elastin is formed only during growth and is limited in its ability to repair and regenerate. Our patient, however, had normal concentration of amino acids in urine and serum.

We concluded that syphilis, arteriosclerosis, hypertension, mucopolysaccharidosis, and defects of amino acid metabolism were not, per se, responsible for the diffuse tortuosity and lengthening of the arterial system in our patient. It seemed more likely that the condition was caused by a congenital defect of the elastic tissues of the arterial system.

Acknowledgment

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