Systemic Arterial Disease with Myocardial Infarction

Report on Two Infants

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SUMMARY

This report deals with two cases of infants who died of myocardial infarction. Autopsy revealed an occlusive, diffuse, generalized lesion in medium and small-sized arteries, with particular involvement of the heart, skin, gastrointestinal tract, kidneys, pancreas, and liver. It showed a fibrous thickening of the intima; the internal lamina elastica, the media, and the adventitia remained unchanged. A pathogenic interpretation of the vascular lesions is attempted, and their asynchrony in the most seriously involved organs is pointed out. The vascular lesions have a great resemblance to those seen in progressive arterial occlusive disease. Despite the antecedent of chronic arsenic poisoning through drinking water, no demonstrable etiologic evidence was found in the vascular lesions; nevertheless, its connection with arsenic, as in blackfoot disease, should be considered.

Additional Indexing Words: Blackfoot disease Arsenic poisoning Arteriosclerosis

The purpose of this paper is to present a form of generalized arteriosclerosis found in the autopsies of two infants who died of myocardial infarction. Both of them were born and lived in Antofagasta, Chile. These two infants were not related to each other. They were seen over a period of 4 months.

Similar cases were not found in the medical literature. However, there are two conditions which bear a certain resemblance: progressive arterial occlusive disease, because of the arterial lesions, and the blackfoot disease of Taiwan, because of the coexistence of a generalized arterial disease with chronic arsenic poisoning through drinking water.

In both cases, chronic arsenic intake from drinking water was elicited, based on the rise of arsenic contents in the water to toxic levels in certain sectors of the city. Arsenic tests in hair and tissues revealed traces of this element.

Report of Cases

Case 1

A 2½-year-old white boy, with diarrhea, fever spells, and bronchitis since he was 3 months old, showed white spots surrounded by a dark halo on the skin. Three months before death, there was dyspnea and fatigue, cardiomegaly and hepatomegaly, and the ECG (fig. 1) showed an apical myocardial infarction. He died suddenly with great precordial pain.

Pathologic Findings. The heart weighed 135 g (normal, 65 g), and it was diffusely enlarged. At the apex of the left ventricle there was a transmural infarct scar, 1 sq cm, with a central necrotic area surrounded by a hemorrhagic zone 5 x 3.5 cm looking like an infarct of approximately 3-weeks' duration. No signs of recent infarction were found. The distribution of the coronary arteries was normal and showed severe stenosis of the lumen, especially in the anterior descending branch. Microscopic examination showed a loose fibrous thickening of the intima, predominantly eccentric and continuous as demonstrated through serial sections (fig. 2); the internal elastic lamina and medial layer were generally undamaged; there was a slight fibrosis of the adventitia. In the kidneys the arciform and interlobular arteries showed a fibrous thickening of the intima; about 10% of the glomeruli were fibrous with signs of relative arterial ischemia. In the skin there was atrophy of the epidermis with slight hyperkeratosis. The dermis showed fibrosis; the elastic fibers were thick and fragmented; the small hypodermic arteries showed a fibrous thickening of the intima. The liver showed slight fibrosis, predominantly of the portal spaces, with occasional fine fibrous septa between these spaces. The arteries in the portal triads showed slight eosinophilia and fibrillary thickening of the intima (fig. 3). The lungs had a nonspecific chronic peribronchitis, and in some areas numerous desquamated cells in alveolar spaces were seen.
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Case 2

A 2-year-old white boy, with clinical symptoms very similar to those of case 1, had a diagnosis of myocardial infarction before death.

Pathologic Findings. The heart weighed 115 g and was diffusely increased in size with hypertrophy and dilatation of the left ventricle. An old transmural infarct was present in the posterior wall; the septum and apex of the left ventricle showed small areas of recent infarction in the vicinity. The coronary arteries and their main branches showed severe stenosis, the lumen being practically occluded in the anterior descending branch (figs. 4-6). The microscopic lesions were very similar to those of case 1. In addition, in larger arteries, the internal lamina elastica showed interruptions as well as slight neoformation of elastic fibrils in the thickened intima. One of the sections of the anterior descending artery showed scant accumulation of foam cells with a few cholesterol crystals. In the pericardium, the small arteries had their lumen occluded by fibrous tissue without hemosiderin. The skin (fig. 7) and liver showed lesions similar to those seen in case 1. In the omentum and large intestine the medium and small-sized arteries showed a fibrous thickening of the intima and considerable luminal stenosis; there was a moderate increase of collagen fibers in the serosa and submucosa of the large bowel (fig. 8).

Samples of both cases were tested with Castel's method for identifying arsenites (presence of precipitates in the form of copper arsenites) with negative results. Skin samples from both cases did not include the already described whitish spots.

Discussion

Similar cases have not, to our knowledge, been published. There is, however, a great resemblance to the arterial lesions described in progressive arterial occlusive disease. This condition, also known as atrophic papulosquamous dermatitis,
malignant atrophic papulosis, or Köhlmeier-Degos disease, is infrequent; it generally affects young men and begins with a characteristic papulosquamous skin eruption. After weeks or years other viscera become involved. It consists basically of a progressive fibrous thickening between the endothelium and the internal lamina elastica in medium and small-sized arteries and arterioles throughout the body, particularly in the gastrointestinal tract, brain, heart, and kidneys; sometimes the arterial lesion resembles an endarteritis or a thrombosis undergoing organization. Its etiology is unknown. There does not seem to be any connection with any exogenous toxic agent. Most of the patients die of intestinal vascular complications, peritonitis, or cerebral infarction. None has died of myocardial infarction. On the other hand, our cases had no comparable skin lesions, arteritis, nor recent arterial thrombosis.

Experimental vascular lesions in arsenic poisoning show lipoid deposits in the intima, swelling and proliferation of the endothelium, thickening and hyalinization of the wall, and thrombosis of large veins and endocardium following toxic alteration of the endothelium and vascular wall.4

A more recently described disease supports the possibility of arsenic participation in the vascular alterations already described. This is “blackfoot disease,” endemic in the South Coast area of the

Figure 2
Case 1. Anterior descending coronary artery, cross section. Severe fibrous thickening on the inner aspect of the internal lamina elastica becoming looser toward the lumen. Scant elastic delamination and neof ormation of elastic fibers. (Verhöff-van Gieson; × 32.)

Figure 3
Case 1. Liver. Artery in portal triad with granular eosinophilic thickening of the intima. In this area some vacuoles or spaces as well as altered and degenerating nuclei are seen. (Verhöff-van Gieson; × 1250.)
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island of Taiwan (China). Gangrene of hands and feet, to which it owes its name, would be explained by arteriosclerosis obliterans or thromboangiitis obliterans. It is closely related to chronic arsenic poisoning from drinking water. More recent studies tend to demonstrate that it would be a generalized arterial disease, thus explaining the greater number of cardiovascular diseases as the cause of death.

The differential diagnosis of our cases with periarteritis nodosa, Leo Bürger's disease, and infantile arteriosclerosis presented no difficulties, nor with the rapid form of progressive systemic sclerosis.

In the search for an explanation of the pathogenesis of the lesion of the intima, I feel that it is obvious that the severity of vascular stenosis varies even within the same organ, and that initially, judging from the vessels that were found to be less damaged, there would be a sequence of the following lesions: swelling and vacuolization of the intima (neutral lipids and fibrin stains being negative), proliferation of the endothelium, edema, and presence of granular and eosinophilic fibrillary substance in the spongy space. The fibroblastic proliferation in this space would develop later, maturing to the point of collagen transformation and final hyaline degeneration. I have not found inflammation nor giant cells in these areas. In apparently older lesions I found neoformation of scant collagen and elastic fibrils.

The observed visceral involvement would be brought about by a relative or absolute arterial ischemia. This would explain the cardiac hypertrophy, the diffuse or partial fibrosis and/or atrophy, and the infarct in the most damaged areas.

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References

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Figure 4
Case 2. Anterior descending coronary artery, cross section. Great fibrous thickening on the luminal aspect of the internal lamina elastica, very similar to that seen in the same type of artery in case 1 (fig. 2). (Verhoff-van Gieson; X 32.)
Case 2. Small branch of coronary artery in the myocardium. Fibrous and cellular thickening on the inner aspect of the internal lamina elastica. (Verhöff-van Gieson; × 200.)


Figure 5
Case 2. Anterior descending coronary artery, longitudinal oblique section. The lumen is seen at the top and at the bottom of the photomicrograph. The continuous and uniform thickening shows focal fine elastic fibrils, close to the lumen (top left). (Verhöff-van Gieson; × 80.)

Figure 6
Case 2. Skin. Fibrosis of the dermis and hypodermis with thickening and increase and fragmentation of elastic fibers. At the bottom, an almost occluded hypodermal artery. (Verhöff-van Giesen; × 32.)

Case 2. Large bowel. At the bottom, a highly stenotic artery in the peritoneal subserosa; toward the top, both muscular layers with their myenteric plexus can be seen. (Verhöff-van Giesen; × 80.)
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