



HEART'S MICROVESSELS RESEARCH AT ISCHEMIC DISEASE AT HEART OPEN SURGERY

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ABSTRACT

Heart ischemic disease is the main global cause of the mortality and morbidity in the world. The interaction of macrovessels atherosclerosis with microvessel ischemia is fundamental to the effective diagnosis and management of disease. Studies of myocardial tissue's microvessels at open heart surgery using special method of tissue treatment give us a new opportunity to study this disease, which can be useful in clinic as well.

KEYWORDS: Microvessels, heart ischemic disease, light optical microscopy, epoxy resins.

INTRODUCTION

Ischemic heart disease (IHD) is the main global cause of the mortality and morbidity in the world.

IHD can be acute (heart attack), as well as chronicle (stenocardia). In the base of IHD lays ischemia and the alterations of myocardium leaded by it, provoked by lack or complete cessation of blood supply.

One of causes is the plaque buildup in the coronary arterial wall (CAD) that narrows the vessel lumen over time.^[13]

One of the methods of CAD treatment is cardiosurgical correction of coronary vessels (stenting, in more difficult cases coronary artery bypass grafting) lead to improving of myocardium blood supply.

Myocardium vascular supply is achieved through an extensive vascular network that includes larger arteries, also known as a coronary arteries, smaller arteries (arterioles) and capillaries. The set of arterioles and capillaries is known as microcirculation.

CAD is usually associated with larger epicardial coronary arteries. However studies have shown an important role of coronary microvascular dysfunction.^[2,8]

Abnormal dilatory responses of coronary microvessels, microvascular spasm,^[20] and extravascular compensative forces have been identified as pathogenic mechanisms in both chronic and acute forms.^[12]

MATERIALS AND METHODS

Reagents and chemicals: powdered paraformaldehyde, osmium tetroxide, sodium cacodylate trihydrate; 96% ethyl alcohol, acetone, Epon 812, Epon Hardener MNA, Epon Hardener DDSA, Epon accelerator DNP-30, Azur II and sodium borate were of analytical grade and purchased from Sigma Chemical Co. (USA).

In current study small peaces of auricular right atria of patients with coronary artery disease,^[7] as well as other diseases,^[5] were taken at routine cardiosurgical procedures.

All procedures involved human subject were approved by the institutional review board/ bioethical committee (Yerevan State Medical University, RA) conformed to the Legal Aspects of Research Ethics and Science in European Community directive (2001/20/EC).

In this research small pieces of auricular right atria of patients with coronary artery disease (CAD, 7 patients), with pulmonary artery valve stenosis (PAVS, 3 patients, control tissue), with heart chronic ischemic disease (3 patients) were taken at routine cardiosurgical procedures. The archived pics had gotten at 90th years of 20th century in Institute of Michaelyan had not been published earlier.

Small pieces of investigated tissue have immediately put in a cold mix of paraformaldehyde in a sodium cacodylate buffer and glutaraldehyde for 12 hours at 40 C with following post-fixation in 1% OsO₄ solution for 2hr, then dehydration is ascending series of spirits;

saturation in a mixture of acetone and Epon resins of different proportions to make gelatinous capsules were performed.

Observation under a light microscope: semithin epoxy slices with up to 1 micrometer thickness were made using ultra cut Reichert (Austria), stained with Azur II (patent 2844 RA) and studied under light microscope supplied 40 x 10 ocular lens.

The interaction of macrovessels atherosclerosis with microvessel ischemia is fundamental to the effective diagnosis and management of disease.^[22]

Structural microvascular alteration, including arteriolar remodeling and capillary reperfection difficult to access in clinical studies.^[20]

Deregulatory types of hemodynamics of patients with IHD, suffered myocardial infarction revascularization of blood circulatory bed take place more often, compare with patients who haven't cardiovascular disease in anamnesis.^[24]

According to the dates of ultrasound computer doplerography used for investigation of blood flow, patients with arterial hypertonia have breach in all links of circulatory bed, compare to control group patients.

At the same time increase necessity to evaluate and test the status of coronary microvascular bed at IHD.

In humans, coronary microcirculation is not visualized with routine invasive and noninvasive imaging tools.^[6,10,11]

Study of coronary microcirculation alterations at IHD become possible at heart aorta coronary artery bypass graffiti surgery. A little piece of right atrial appendage routinely cut during surgery is very important for visualization and evaluation of the status of microcirculatory bed. It is possible to study the byoptate fixed in epoxy resins on semithin epoxy slices under light optical microscope at appropriate method of staining,^[14] which was proved by results obtained in previous studies.^[18,19]

Goals of Study

Visualization and evaluation of microvessels at aorta coronary artery bypass graffiti.

RESULTS

As have shown the results of our study the images of myocardium microcirculatory bed at heart ischemic disease were obtained using semithin epoxy slices stained by Azur II. The main accent was made on investigation of profiles of small arteries (arterioles). In 90th years of 20th century we have gotten interesting images of myocardium microcirculatory bed at pulmonary artery stenosis depend on stage of disease. This was the main point lead us study this direction.

In this study we use these images as control ones.

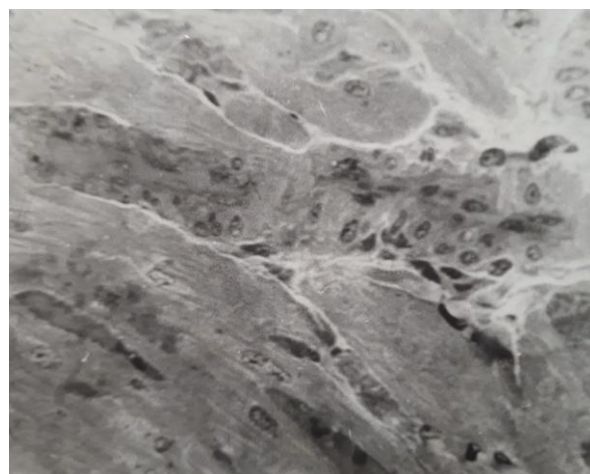


Fig. 1: PAVS. Increasing of wall's cell elements. X 400.



Fig. 2: PAVS. Presence of 2 lumen with the same wall in the vessel profile. X 400.



Fig. 3: PAVS Presence of vessels with small profiles close to each other. X 400.

As well as on control images independent of heart ischemic disease type take place irregular thickness of vessel wall by proliferation of cellular elements. At the same time defer from control take place visible other growth of vessels profiles, extension of profile lumen, as well as its twisting lead in some case to isolation of some

cardiomyocytes. In other way, in some part of vessels the slit and much widened lumen could be presented.

The presence of a big quantity of vessels with slit lumen is typical for chronically form of IHD.

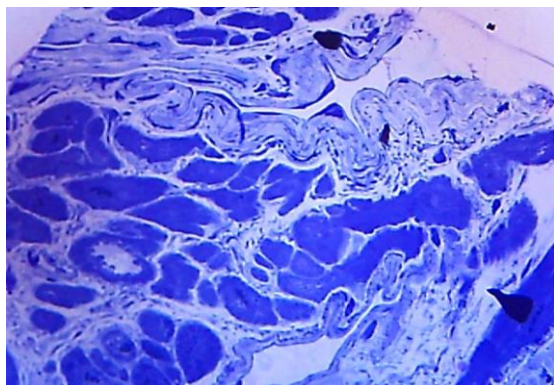


Fig. 4: Chronically form of IHD. Stenocardium of tension and relaxation. The parts of slip lumen are observed.

Pay attention the conjunction of opposite walls of profile of such over growth vessel and forming the new lumen in the wall.

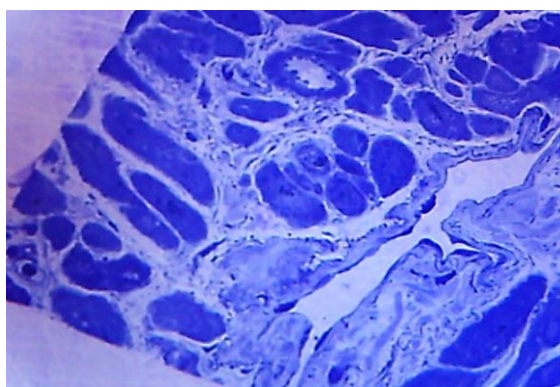


Fig. 5: Stenocardium of tension and relaxation. Forming of new lumen in the wall. X 400

Very important moment for CAD is presence of vessels with a big quantity of profile lumen formed in the vessels walls. They are different by lumen size and are partly full of blood.

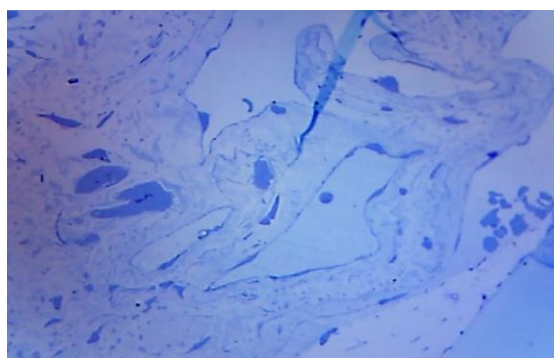


Fig. 6: Presence of several lumen of profile in the vessel wall at CAD. X 400.

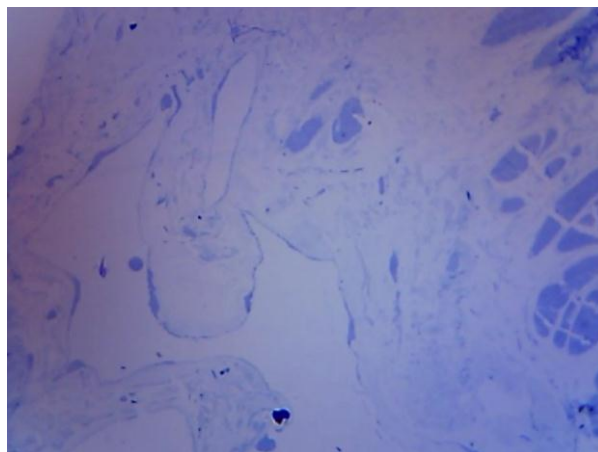


Fig. 7: Increasing of profiles lumens quantity in the vessels wall at CAD. X400.

It must be noted that during all study as well as on all control images was similar presence of small vessels located close to each other with small lumen of profile, still have same parts of walls, indicate to neogenesis of vessels. In some vessels the presence of lumen crossing was obtained.

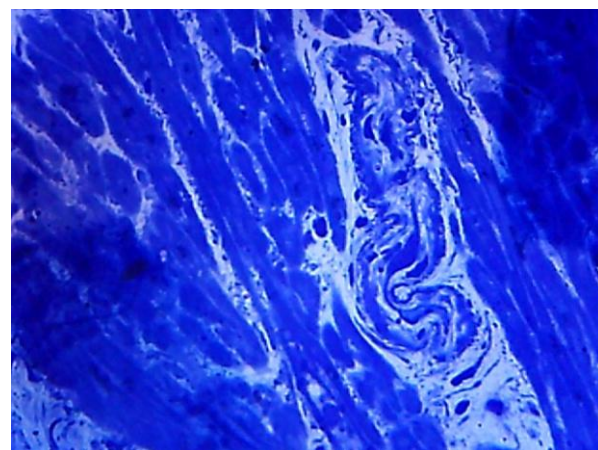


Fig. 8: Crossing of arterioles lumen and creation of 2 lumens at IHD.

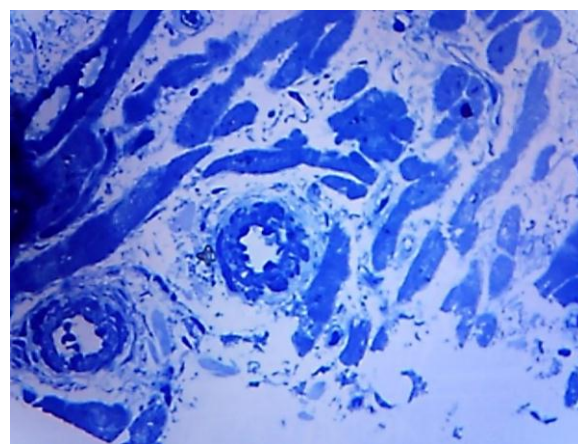


Fig. 9: Presence of two vessels with small profile diameter, located close to each other at CAD. X 400.

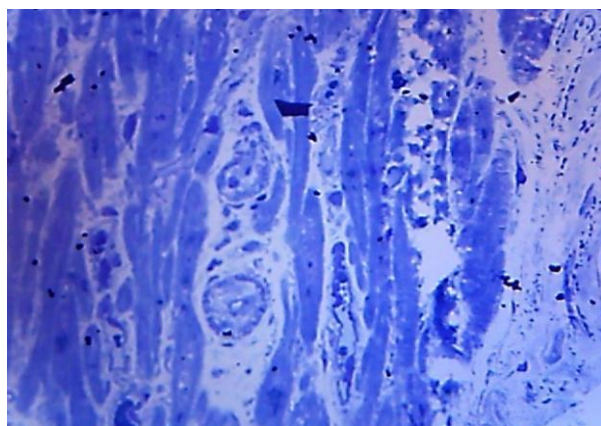


Fig. 10: Presence of two vessels with small profile diameter, located close to each other at CAD. X 400

DISCUSSION

The coronary arterial system represents a continuous network of functionally distinct vessel segments of decreasing size.^[22]

Heterogeneity is a characteristic of microvascular networks and affects structural and functional parameters such as vessel diameter, length and connection pattern, flow velocity wall shear stress and oxidation.^[3,23] Several theories are suggested to explain the pathophysiology of cardiovascular disease. This involves both pre-arterioles (100-500mk in diameter) and arterioles (100mk), which are the resistance vessels responsible for abnormal coronary artery blood flow. Structural alteration, including smooth muscle hypertrophy around the vascular wall, results in increased vessel resistance. Recently it has become more apparent microvascular dysfunction is responsible for morbidity and mortality in many different cardiovascular diseases.^[1]

The study on semithin epoxy slices stained by Azur II give us opportunity to obtain images and reveal pathomorphological changes taking place in the microcirculatory system, to show the mechanism how it's going on. So in myocardium of right auricular atria of patients with pulmonary arterial valve stenosis on the late stages of disease the arterioles with big amount of cell elements in the wall, contraction or full overlapping of lumen were obtained.^[16]

Similar results were obtained during other heart pathology, which by authors indicate to capillaries emptiness and it's dropping out from the blood circulation system.^[21]

Our study of a small piece of auriculum of right atrium, getting at aortacoronary artery bypass surgery let us visualize arteries of microcirculatory bed of myocardium. Proliferation of cell elements of arterioles lead to thickness and twisting of the wall, extension of vessel profiles lumen as well as increasing of its diameter. It is typical for this process, the tendency to decrease of lumen size, which is indicated by

conjunction of opposite walls. This also led to formation of a new lumen in the vessel wall. One of the specificity of pathomorphology at ACD is presence of 3 and more lumens in the wall of arterioles, which could be indicated as convolutes of arterioles (microvascular formations with many lumens of profiles) looks like convolutes of capillaries known as compensatory processes in the capillaries of brain at arterial hypertonia.^[9] Presence of the process of arteriogenesis by intussusception type is observed. Formation of new arterioles from previous is typical for all types of IHD in this study. The term of intussusception angiogenesis, arteriogenesis indicate the ways of new capillaries, arteries and venous formation from previous ones became known in 90th years of last century and its mechanism were detailed investigated.^[4,7]

The kinetics of new blood vessel formation and the structure and functional capacities of the newly formed vessels induced by VPV /VEGF or other cytokines in ischemic tissues have not been carefully investigated.^[5,23] Knowledge of pathophysiological cause - effect relations involving coronary microcirculation is, however still very limited.^[3] Disturbances of coronary microcirculation are involved in different pathophysiological aspects of reperfusion injury.^[3] The pathophysiological mechanism of post- ischemic coronary microvascular dysfunction is still debated.^[17]

No studies have been done on how to prevent to coronary microvessel disease. Researcher don't get know how or in what way prevently coronary MVD differs from preventing heart disease (American Heart Association 10, February 2012).

Getting clear image of microvessel is very important for clinical tasks. At the same time there is necessity to evaluate pathomorphological changes of small blood vessels at IHD by 5th degree scale.^[15]

CONCLUSION

Using semithin epoxy slices of bioplates of right auriculum getting at ACD make possible to visualize arterioles of MCB and evaluate its condition which will be very actual for clinic.

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