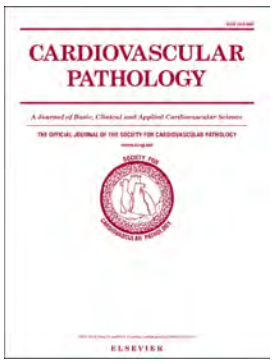

Potential cardiac consequences of thrombocytopenia and thrombocytosis

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Potential Cardiac Consequences of Thrombocytopenia and Thrombocytosis

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Abstract

This report illustrates the heart in three patients with cardiac hemorrhages associated with extreme thrombocytopenia, and the hearts in three patients with rocks speculated to result at least in part from organization of thrombi possibly related to thrombocytosis in one or more cardiac chambers.

Key Words: cardiac hemorrhage; cardiac intrachamber calcified mass; thrombocytopenia; thrombocytosis.

1. Introduction

Nearly 50 years ago an article on morphologic features of the heart in acute leukemia described numerous hemorrhagic lesions (extravasated erythrocytes) in the epicardium, myocardium, and endocardium, and the authors suggested that their cause was severe thrombocytopenia [1]. In subsequent years, numerous other examples of the hemorrhagic lesions have been observed in the heart and in nearly all non-traumatic cases the platelet counts were found to be extremely low (usually about 10,000 per uL). Also, subsequently we encountered several cases of calcified masses in one or more chambers in the heart [2, 3, 4]. The cause of the "rocks in the heart" was not determined but organization of platelet thrombi, as a consequence of thrombocytosis, would appear to be an explanation worthy of serious consideration. This report illustrates a few cases studied at necropsy with severe thrombocytopenia, and a few cases of "rocks in the heart" that may have formed by collections, at least initially, of clumps of platelets (Figures 1 and 2).

2. Material and Methods

For years we have made notes of the platelet counts in many patients in whom hemorrhages were found in the epicardium, myocardium, and/or endocardium at necropsy unrelated to cardiac surgery or other trauma or to coronary heart disease. Shown in figures 3 to 5 are examples of these cardiac hemorrhages, the only cause of which, as far as we could determine, was severe thrombocytopenia. Shown in figures 6 to 8 are illustrations of "rocks in the heart."

3. Results

The findings in this study are represented entirely by the figures and the legends to them (Figures 3-8).

4. Discussion

Illustrated in this report are hearts with hemorrhages and the patients had very low platelet counts (usually about 10,000 per uL), and hearts with calcified masses speculated to be the result of platelet thrombi in patients with thrombocytosis. Search of PubMed for cardiac consequences of thrombocytopenia or thrombocytosis yielded no publications.

The present report of course has major limitations. We do not know what percent of patients with severe thrombocytopenia have hemorrhages in the heart. We suspect that the percent is exceedingly high. Most patients with cardiac hemorrhages associated with thrombocytopenia have no clinical consequences because of the extravasated erythrocytes. The exception might be the patients in whom the hemorrhages interrupted the cardiac conduction system at some point [1]. Whether the "rocks in the heart" were the consequences of thrombocytosis leading to thrombi which eventually calcified is of course an unproven scenario. That platelets were seen within the calcified mass in one of the three patients whose "rocks in the heart" was illustrated suggest that platelets did indeed play a role in producing the calcified masses.

5. Compliance with ethical standard

The authors have no ethical conflicts to disclose.

6. Funding

This research did not receive any specific grant(s) from funding agencies in the public, commercial or not-for-profit sectors.

1. Roberts WC, Bodey GP, Wertlake PT. The heart in acute leukemia. A study of 420 autopsy cases. *Am J Cardiol* 1968; 21:388-412.

2. Dean DC, Pamukcoglu T, Roberts WC. Rocks in the right ventricle. A complication of congenital right ventricular infundibular obstruction associated with chronic pulmonary parenchymal disease. *Am J Cardiol* 1969; 23:744-747.

3. Waller BF, Roberts WC. Systolic clicks caused by rocks in the right heart chambers. *Am Heart J* 1981; 102:459-460.

4. Roberts WC, Rosenblatt RL, Ko JM, Grayburn PA, Kuiper JJ, Guileyardo JM. Cardiac restriction secondary to massive calcific deposits in the left ventricular cavity. *Am J Cardiol* 2014; 113:1442-1446.

Figure 1. This diagram shows the speculated consequences of platelet counts from extremely low to extremely high. With virtually no platelets there is usually massive cardiac hemorrhage and smaller cardiac hemorrhages with a bit higher platelet counts. The very speculative portion of this diagram is the thesis that intracardiac calcified masses are the results at least initially of extremely high platelet counts. This thesis is unproven but there is no explanation currently for why cardiac masses may calcify.

Figure 2. The diagram shown in the *top left* shows large masses of extravasated erythrocytes in the walls of the atria and in the right atrioventricular sulcus. Diagram 2 shows focal mainly endocardial and epicardial hemorrhages, an appearance commonly seen in patients with severe thrombocytopenia. Diagram 3 shows small calcific deposits on the endocardium of right atrium (RA) and right ventricle (RV), and diagram 4 shows much larger calcific masses. This report speculates that these calcific masses are the consequence at least in part of high platelet counts.

Figure 3. Shown here are pictures of the heart in a 23-year-old man who died of acute lymphocytic leukemia. His platelet count was 11,000 per uL and necropsy disclosed a heavy collection of extravasated erythrocytes over the left ventricle both anteriorly and posteriorly as shown in the *left* view. The *right* view is a cross-section of the same heart showing severe intramyocardial hemorrhages in the free wall of left ventricle, ventricular septum, and right ventricular free wall

Figure 4. Shown here is the heart in a 54-year-old woman who died of consequences of adenocarcinoma of the duodenum. The platelet count near death was 10,000 per uL. The *left* is a view of the front of the heart showing extensive hemorrhage into the subepicardial adipose tissue. The *right* view is a cross-section at the ventricles at the level of the tricuspid and mitral

valves showing the subepicardial hemorrhage to also be in the subepicardial region of the left ventricle and the right ventricular aspect of the ventricular septum.

Figure 5. Shown here is the back of the heart (*left*) and a left parasagittal view of the heart on the *right*. The left atrioventricular sulcus contains numerous extravasated erythrocytes, also present in the subepicardial adipose tissue in the posterior portion of the left ventricle. Extensive extravasation of erythrocytes in the atrioventricular sulcus is a common finding in patients with low platelet counts. This 79-year-old man had acute myelocytic leukemia.

Figure 6. Shown here is a radiograph of the heart (*left*) and the opened right-side of the heart (*right)* in an 8-year-old boy who died of acute myelogenous leukemia after a 17-month course. About 10 months before death multiple precordial systolic clicks were heard, loudest along the right sternal border and several calcified masses were visible on a chest radiograph. Necropsy (*right*) showed numerous calcified masses in the right atrium and right ventricle. Sections of the calcified masses disclosed many platelets within them. The calcium was located on the margins (just like an eggshell) and platelets and fibrin were within the calcified wall. One of the calcified masses was analyzed and found to be composed of a mixture of cryptocrystalline tricalcium phosphate and microcrystalline hydroxyl apatite, with some intermixed protein matrix. [Reproduced from Waller BF, Roberts WC. Systolic clicks caused by rocks in the right heart chambers. *Am Heart J* 1981; 102:459-460.]

Figure 7. Shown here is a diagram of the right side of the heart showing many calcified masses within the right ventricular cavity. This heart belonged to a 56-year-old man. These calcified masses were visible on chest radiograph 3 years before death. He died of an acute myocardial infarction. Eleven calcified nodules ranging in diameter from 0.6 to 2.1 cm were present in the right ventricle. Each stone was attached to the right ventricular endocardium by a small fibrous

stalk. The origin of the stones in the right ventricle in this patient is uncertain. That the stones represent the end-stage of organized mural thrombi is possible. Unfortunately, the platelet counts were not done. [Reproduced from Dean DC, Pamukcoglu T, Roberts WC. Rocks in the right ventricle. A complication of congenital right ventricular infundibular obstruction associated with chronic pulmonary parenchymal disease. *Am J Cardiol* 1969; 23:744-747.]

Figure 8. Shown here is a cross-section of the cardiac ventricles (left) and a radiograph of the same section on the (right). The left ventricular cavity is loaded with calcific masses. This patient was a 61-year-old woman who at age 3 had resection of an aortic isthmus coarctation and at age 44, replacement of a stenotic congenitally bicuspid aortic valve. At age 54, she experienced her first episode of acute pulmonary edema. These episodes reoccurred repeatedly during her last 6 years of life. The platelet count was 267,000 per uL 16 hours before death. Serum calcium and serum phosphorus levels were available in her last 3 years of life and all were normal. [Reproduced from Roberts WC, Rosenblatt RL, Ko JM, Grayburn PA, Kuiper JJ, Guileyardo JM. Cardiac restriction secondary to massive calcific deposits in the left ventricular cavity. *Am J Cardiol* 2014; 113:1442-1446.]

Highlights:

Will provide at a later date.

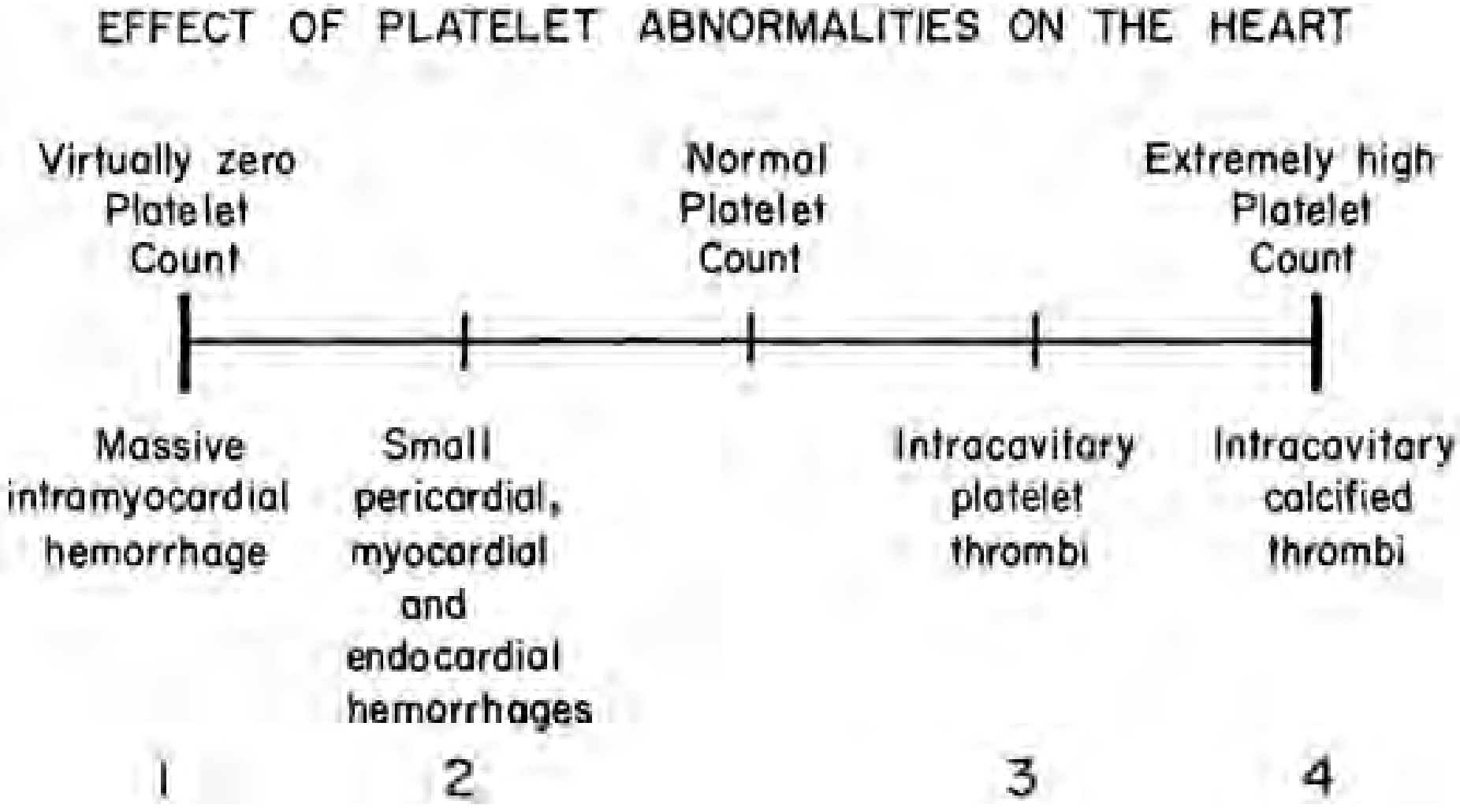
EFFECT OF PLATELET ABNORMALITIES ON THE HEART
Virtually zero Platelet Count
Normal Platelet Count
Extremely high Platelet Count
Massive intramyocardial hemorrhage
Small pericardial, myocardial and endocardial hemorrhages
Intracavitary platelet thrombi
Intracavitary calcified thrombi
1
2
3
4

Figure 1

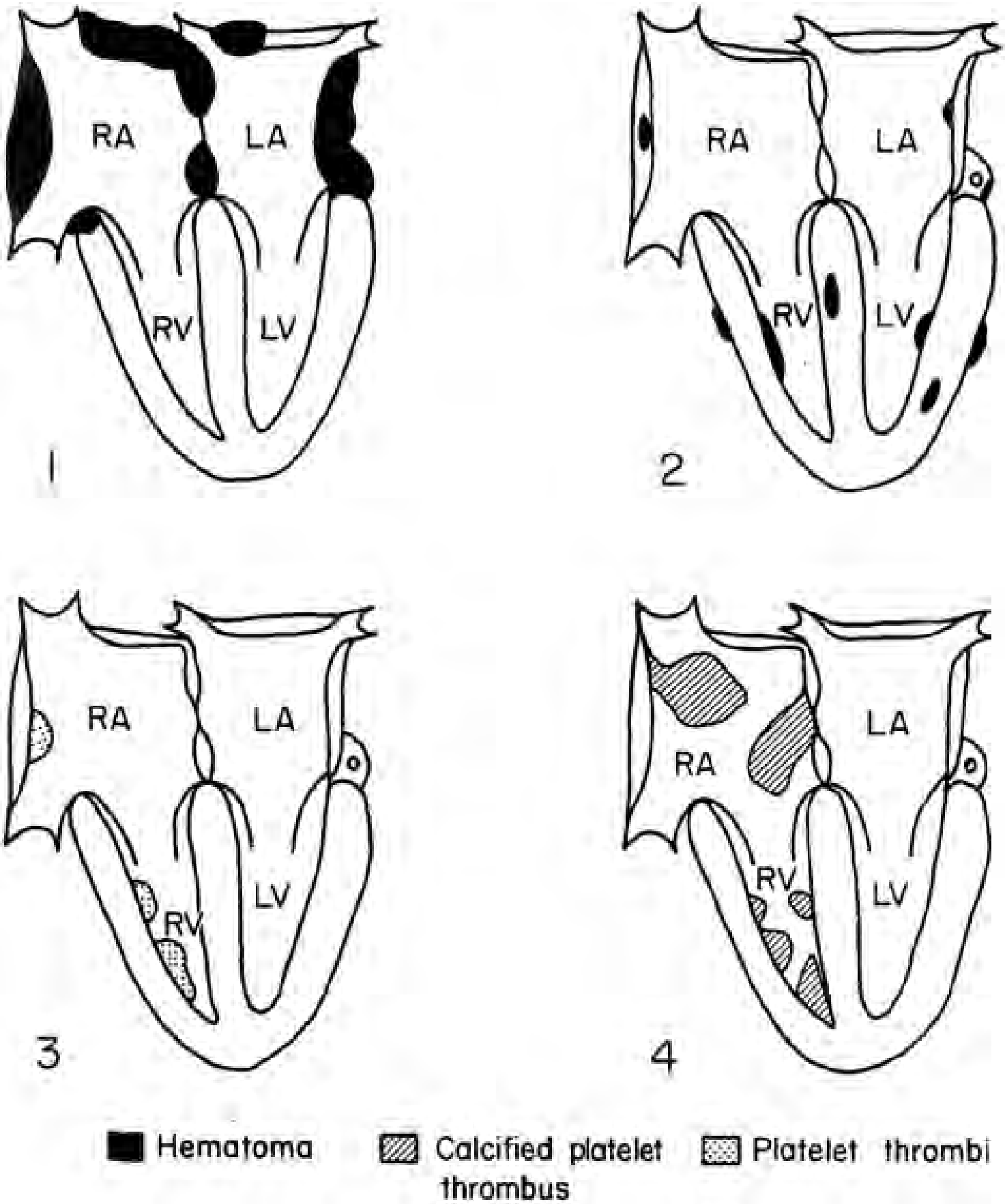
RA
LA
RV
LV
1
RA
LA
RV
LV
2
RA
LA
RV
LV
3
RA
LA
RV
LV
4
Hematoma
Calcified platelet thrombus
Platelet thrombi

Figure 2

Figure 3

Figure 4

Figure 5

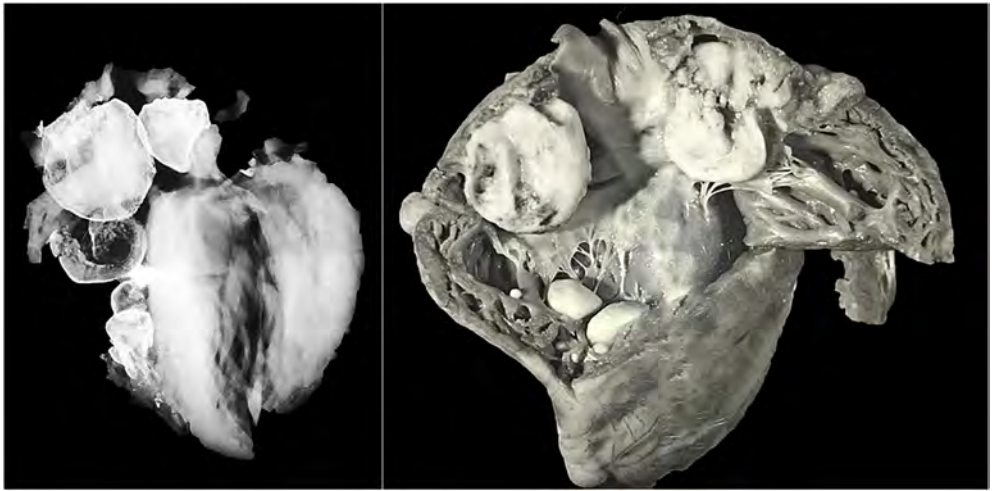

Figure 6

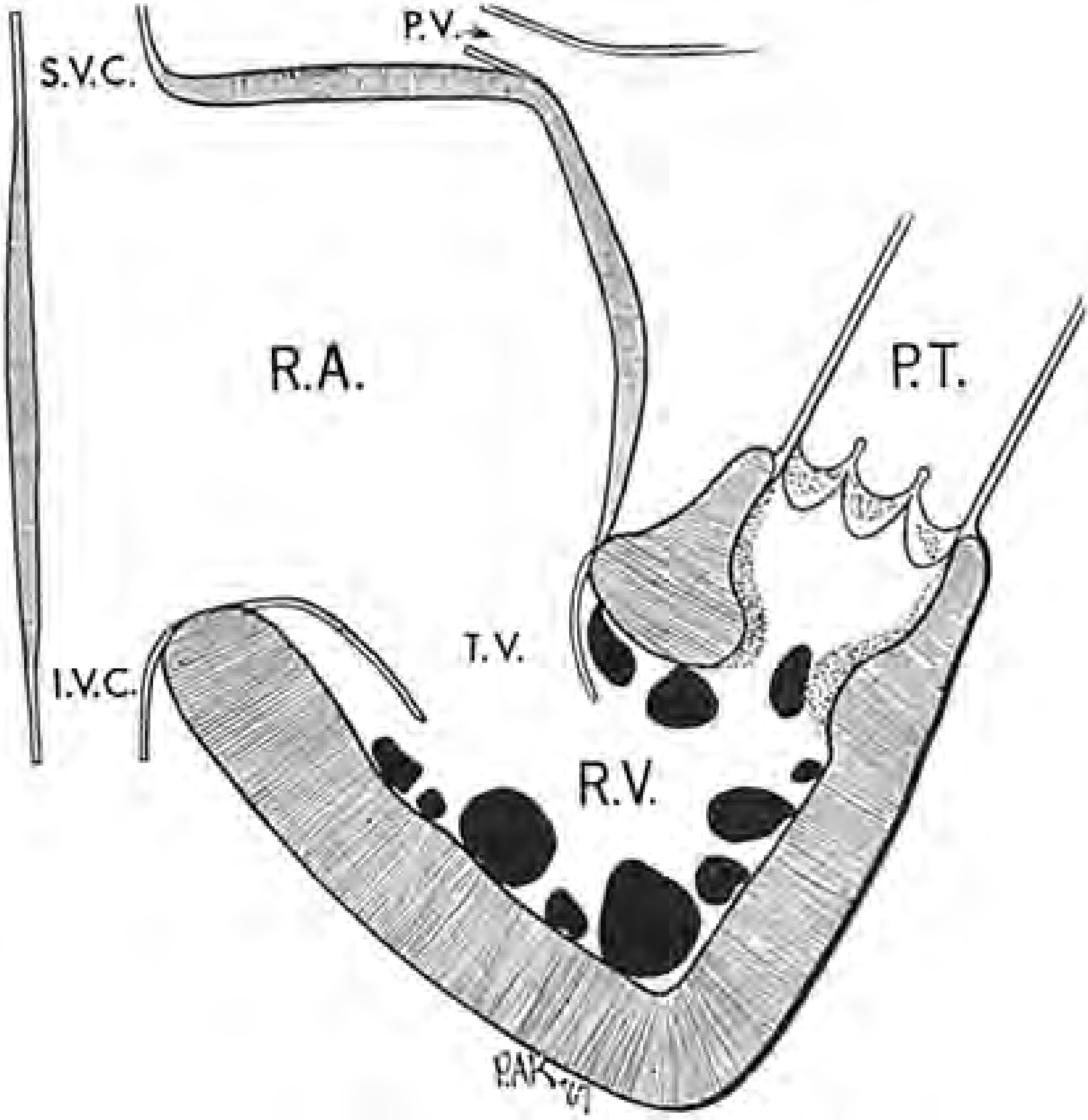

Figure 7

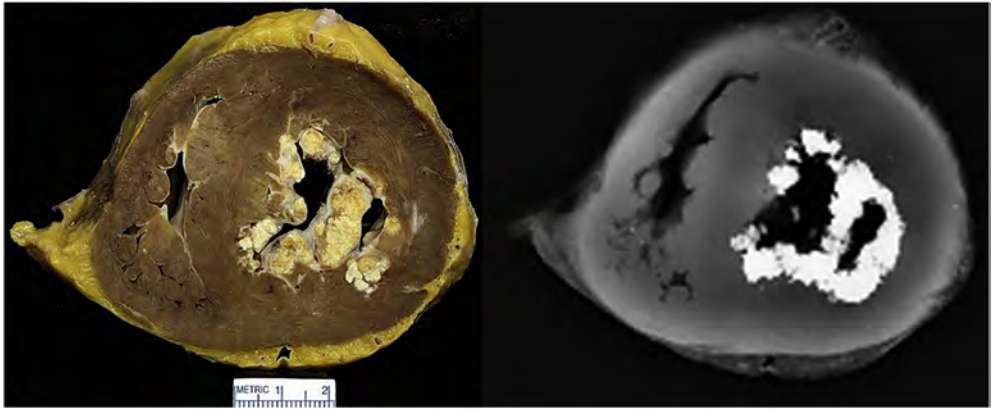

Figure 8