CORONARY THROMBOSIS AND MYOCARDIAL INFARCTION, WITH GLYCOSURIA

BY

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Glycosuria associated with coronary thrombosis is now becoming recognized as a definite syndrome. The following case is of interest because it illustrates this syndrome, and because the course of the patient's illness presented some unusual features.

CLINICAL HISTORY

A retired railway porter, aged 68, came under my care in the Glasgow Royal Infirmary. He had a severe degree of cardiac failure; there was oedema of the limbs, back, and face, also cyanosis and orthopnoea. There was no anginoid pain, pericardial friction, or leucocytosis. The cardiac area was enlarged, the left border of dullness being one inch outside the nipple line and the right border at the right sternal margin. The heart sounds were of poor quality and the beats irregular in force, but there were no murmurs. The radial pulse was regular, the rate being 96. The radial and brachial arteries were thickened and tortuous, and the blood pressure was 140/104 mm. Hg. The urine contained a cloud of albumin, and there was incomplete reduction of Fehling's solution. On clinical examination no arrhythmia could be made out, but an electrocardiogram showed the abnormalities typical of branch-bundle block. QRS had a W-shaped deformity in all the leads, with distinct prolongation in Lead 1. There was also a tendency to inversion of T in Lead 1. The patient's condition did not improve. There were no attacks of precordial pain, but the signs of gross cardiac failure increased, and he died fifteen days after admission to the ward.

POST-MORTEM EXAMINATION

A post-mortem examination was made by Dr. Alice J. Marshall. The heart was soft and there was marked dilatation of the right auricle and right ventricle. There was an infarction of the muscle of the left ventricle involving the whole of the apical region and extending outwards for at least two inches on the anterior wall. In the left lateral wall of the left ventricle there was also a small recent infarction which lay midway between apex and base, in the line of the left lateral descending branch of the posterior coronary artery. Old thrombus was adherent to the inner surface of the left ventricle over the infarcted area. There were no gross changes in the valves, but the aorta showed advanced syphilitic aortitis. The orifices of the coronary arteries were of normal calibre, but the vessels were atheromatous. The right coronary artery was patent throughout its course, though its walls were much thickened. There was marked narrowing of the main descending branch of the left coronary artery, three-quarters of an inch from its orifice, while the lateral descending branch was completely obstructed by old thrombus about one inch from its orifice. The left lateral transverse branch was sclerotic. Other points worthy of note were the presence of advanced chronic interstitial nephritis, and fibrosis of the pancreas. There was hypostatic congestion of the lungs, chronic cholecystitis, and gastro-intestinal catarrh.

PREVIOUS HEALTH

The previous history of the patient contains some points of importance. He had been an apparently healthy man until about three years before his death, and had never suffered from any serious illness. When he was about 65 years of age he began to complain of cramp-like pains in the legs, which he regarded as rheumatic in nature. He then had a minor injury to one of his toes, and, as healing was slow, he was admitted to a surgical ward in the Royal Infirmary. It was then found that he had glycosuria, but this symptom cleared up without any intensive treatment.

About seven months later he began to have swelling of his feet, and dyspnoea on exertion. After being treated at home for six weeks, he was admitted to Professor Hunter's ward in the Royal Infirmary suffering with orthopnoea, cyanosis, and generalized oedema. The urine contained albumin and casts as well as 0.5 per cent. of sugar. The Wassermann reaction of the blood was positive. Examination of the heart at this time showed a degree of decompensation, but not much increase in the area of cardiac dullness. The sounds, particularly those at the apex, were of poor quality; the second sound at the base was accentuated. No murmurs were heard, and the rhythm was regular. The pulse rate was about 96, and the blood pressure was 140/90 mm. Hg.

Shortly after admission to the ward the patient's condition began to improve. The signs and symptoms of cardiac insufficiency became less severe, and the blood pressure rose to 170/120. He had been given large doses of digitalis, and after he had been under treatment for about a month a 2:1 heart-block developed, the pulse rate falling to 54. This block seems to have cleared up, for the pulse was running between 80 and 96 for several weeks before the patient was sent home. The glycosuria, which was associated with a hyperglycaemia (blood sugar = 190 mg. per 100 c.cm.), was rather resistant to treatment, but the urine eventually became sugar-free on a diet of 1,329 calories covered by 40 units of insulin. When the patient was discharged from the ward after eight weeks he appeared to be in fair health, and when he came up to report himself a month later he was still free from symptoms of cardiac failure and there was no glycosuria. His insulin had been cut down, and his diet was only slightly modified.

About five months after leaving hospital the patient developed dyspnoea, cough, and oedema. These symptoms continued to increase in severity up till the time of his second admission to the ward a month later.

COMMENT

The possibility of a relationship between coronary disease and diabetes was suggested in 1922 by Levine,¹ who found that in a series of cases of angina pectoris 7 per cent. of the patients had previously shown well-defined diabetes. The same writer in 1929,² in analysing a series of 145 cases of coronary thrombosis, found either glycosuria or a history of diabetes in 34 (23.7 per cent.). In some of these patients there was only a transient glycosuria during the early days of the attack; in others there were large quantities of sugar in the urine, and it was considered that a well-established diabetes was present. Between these extremes there were cases in which no appreciable amount of sugar appeared in the urine, even in the days immediately following a coronary occlusion, in spite of the fact that diabetes had been found previously and had been controlled by dietary measures. Levine considers that the relation of glycosuria to coronary thrombosis is a causal one, and states that "among the disease entities that are etiologically related to coronary thrombosis, diabetes is second in importance only to a previously existing hypertension."³ It seems more probable that the two conditions result from atheromatous changes in the coronary and pancreatic vessels respectively. It is difficult to imagine how glycosuria *per se* could determine the onset of coronary thrombosis.

In the case here recorded there are several points of special interest. The first is the widespread distribution and the severity of the atheroma, which affected not only the coronary circulation, but also that of the kidneys and the pancreas. The myocardium, the kidneys, and the pancreas all showed fibrosis and degenerative changes at necropsy, while clinically there occurred hypertension followed by cardiac failure, albuminuria, and glycosuria. Another point is the slow development of the extensive myocardial infarctions. These produced increasing cardiac failure, but never gave rise to the cardinal signs and symptoms which make up the clinical picture of coronary

thrombosis. It is remarkable, too, that a glycosuria so severe as to require 40 units of insulin per diem for its control should have cleared up in spite of progressive deterioration in the state of the cardio-vascular system. This is all the more surprising when it is remembered that during the patient's first residence in hospital the blood sugar had been well above the limits of normal, and that at post-mortem examination the pancreas was found to be shrunken and fibrosed. It seems possible that these variations in the carbohydrate metabolism may have been related to the chronic inflammation which was present in the biliary tract and to the pathological state of the kidneys.

SUMMARY

1. A case is described in which syphilitic aortitis, coronary thrombosis, and extensive myocardial infarctions were associated with glycosuria and hyperglycaemia.
2. Widespread atheroma with degenerative and fibrotic changes in the kidneys and pancreas and chronic inflammation in the biliary tract were found at necropsy in addition to the cardiac lesions.
3. The relationship between glycosuria and coronary thrombosis is discussed. It is considered more probable that these two conditions result from a common cause (vascular degeneration) than that glycosuria is an etiological factor in the production of coronary thrombosis.

I wish to thank Professor W. K. Hunter for permission to use the clinical records of this case, Dr. J. H. Wright who made the electrocardiogram, and Dr. Alice J. Marshall who performed the necropsy.

REFERENCES

- ¹ Levine, S. A.: *Journ. Amer. Med. Assoc.*, 1922, lxxix, 928.
- ² Idem: *Coronary Thrombosis: its Various Clinical Features*, 1929.
- ³ Idem: *Ibid.*, p. 9.

PLEURAL EFFUSION*

BY

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Pleural effusion occurs under several conditions, and its treatment is largely dependent on the cause and character of the fluid. For practical purposes effusions may be considered as either clear or thick, and I suggest the following classification.

A. CLEAR EFFUSION

Causation	Appearance	Coagulable Protein	Specific Gravity	Cytology
1. Transudates:		Per cent.		
Renal	Very pale	2	1008	Endothelial cells
Cardiac	Pale yellow	3	1015	
Neoplasm	Pale yellow or haemorrhagic	3	1016	
2. Exudates:				
Tuberculous	Straw colour	Over 4	1020	Small lymph.
Pyogenic	Turbid yellow	Over 5	1024	Polymorph.

B. THICK EFFUSION

1. Non-purulent opaque fluids vary from the cloudiness due to a slight excess of cells to the dense opacity of true chylous effusions. The density may be increased by the presence of blood. A true haemothorax is usually the result of trauma, but bleeding with an effusion is not uncommon, especially in malignant disease; it occurs in about 50 per cent. of cases of carcinoma of lung. Haemorrhage does occur in tuberculosis and other effusions, and should not therefore be taken as diagnostic of neoplasm. The fluid may be rendered opaque by the presence of cholesterol in an effusion of long standing,

or by cells which have undergone fatty degeneration. True chylous effusions are not common, but may occur as a result of occlusion of the left subclavian vein, injury to the thoracic duct or pressure on it by tumours, or by filariasis.

2. Purulent effusion or empyema may be due to one of many causes, such as malignant disease, ruptured abscess of lung, septic emboli, actinomycosis, etc., but for practical purposes it may usually be considered as (a) pneumococcal, (b) streptococcal, or (c) tuberculous.

CLEAR EFFUSION

Before considering treatment I should like to say a little more about the laboratory findings of these fluids. On microscopical examination a few red corpuscles are usually seen. Their presence may be due to bleeding as a result of the pleural puncture, but they are not of clinical significance unless they are sufficiently numerous to be observed by the naked eye. Polymorphonuclear cells may also be present in proportion to the red corpuscles, but if these white cells are in excess it suggests that the fluid is due to a pyogenic organism, and that it will probably become purulent. Eosinophil cells may be regarded as intermediary between an acute infection where polymorphonuclear cells are in excess and a chronic state in which small lymphocytes predominate. A large number of eosinophil cells is said to be evidence against tuberculosis; it also suggests that the fluid will not become purulent. Eosinophilia is present in only 35 per cent. of cases of hydatid disease. As a rule, hydatid cysts of the lung do not leak; unless they do, eosinophilia does not occur. Hydatid fluid may be confused with pleural effusion; it is characterized by the presence of hooklets, not of eosinophil leucocytes. Usually it is like water, but during suppuration it resembles water into which one or two drops of milk have been put. Small lymphocytes occur in chronic inflammatory conditions, the commonest example of which is tuberculosis; therefore an excess of small lymphocytes strongly suggests this disease. Syphilis of the pleura is extremely uncommon, but when it does occur there is an excess of lymphocytes. Endothelial cells come from the lining of the pleura, and are in excess in transudates. They are rarely present in excess in cases of tuberculosis or of pyogenic infections, so that if renal or heart disease can be excluded, a preponderance of these cells in a pleural effusion makes us think of neoplasm. They have sometimes been mistaken for carcinoma cells, especially when they have undergone some degree of degeneration. Lymphocytes have been confused with sarcoma cells, but it is doubtful if neoplastic cells are ever present in an effusion; if they occur, it is very seldom, though they have often been described in error. The absence of tubercle bacilli should not be taken as evidence that the condition is non-tuberculous, for these organisms are hardly ever found in the early stages of an effusion unless a very large quantity of the fluid is used. The bacilli can usually be found in long-standing effusions, and they are present in almost every case of tuberculous empyema.

Treatment of Clear Effusions

When pleural effusion forms in a case of renal disease it is usually bilateral. Repeated aspiration is necessary, as the fluid tends to reaccumulate quickly. In cardiac cases it is best to remove the fluid early, as even a small collection in the pleural cavity embarrasses the heart. In the case of neoplasm, aspiration is necessary only when dyspnoea or pressure symptoms make the patient uncomfortable. I have seen a case of mediastinal tumour and a large effusion which, although the patient lived for six months, did not re-form after aspiration. As a rule, the fluid rapidly reaccumulates, especially in a case of endothelioma of the pleura. Indeed, the presence of an effusion which re-forms after each aspiration is very

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