Pericardial Effusion Mistaken for Cardiac Enlargement in Severe Anemia

Report of Two Cases

By Louis A. Soloff, M.D., and C. T. Bello, M.D.

Anemia is sometimes the sole cause of enlargement of the so-called cardiac silhouette. Successful treatment of the anemia may then restore the silhouette to normal. The enlargement has been attributed to cardiac dilatation. Because of the recognized difficulty in distinguishing pericardial effusion from cardiac dilatation, direct puncture was attempted in two instances of anemia with the silhouette enlarged presumably due to dilatation. In each instance, the enlargement was demonstrated to be due almost exclusively to pericardial effusion.

The heart in anemia has been recently the subject of several comprehensive reviews. There is therefore no need at this time to discuss this subject in detail. It is well known that the heart is frequently involved and that symptoms and physical signs present in anemia may mimic those of organic heart disease. Individuals with anemia may complain of dyspnea and palpitation on effort, weakness and dizziness. Dyspnea is usually not present at rest. Precordial pain identical with angina pectoris may occur. Slight and later a marked degree of saeral and dependent edema may be present. The heart rate is rapid. Murmurs are frequent; the commonest is a systolic murmur at the apex. Later, systolic basal murmurs and systolic murmurs widely distributed over the precordium occur. Even a diastolic murmur, usually over the aortic region, may be audible in severe anemia. Electrocardiographic abnormalities such as low amplitude, S-T segment depressions and low, flat and even inverted T waves are noted. Finally, the heart is enlarged by clinical examination. Roentgenologic examination confirms the enlargement that is sometimes massive.

Cardiac hypertrophy has been demonstrated at necropsy in both clinical and experimentally produced anemia with no apparent other cause. The hypertrophy is usually not marked. The enlarged hearts in anemia demonstrable by roentgen study which become smaller under treatment are regarded as being due in greater measure to cardiac dilatation, because it is doubtful that hypertrophy alone can produce massive enlargement of the cardiac silhouette. Ball was the first to demonstrate by roentgenographic technic marked enlargement of the cardiac silhouette that disappeared after adequate therapy. These findings have been amply confirmed by others.

The difficulty in differentiating by roentgenographic technic cardiac dilatation from pericardial effusion is well known. The purpose of this report is to record two instances of anemia with massive pericardial effusion in which an erroneous clinical and radiologic diagnosis of massive cardiac enlargement due to anemia had been previously made. One individual was a girl with erythroblastic anemia. The other was a woman with pernicious anemia. These cases demonstrate that pericardial effusion may occasionally be the sole or major factor in the enlargement of the so-called cardiac silhouette in anemia.

Case Reports

Case 1: L. L. was first admitted to Temple University Hospital January 17, 1940, and after 13 succeeding admissions, died February 2, 1944, at 19 years of age. She had been anemic since birth. She had been given repeated small transfusions all of her life. Her admission for the first time to Temple University Hospital was for several transfusions because of severe anemia, fatigue, repeated episaxis, anorexia, dyspnea and palpitation on effort.

Physical examination revealed a pale, undernourished Greek girl with bronze colored skin, pre-

From the Department of Medicine, Temple University Medical School.
sumably that of hemochromatosis. The blood pressure was 120/60. The pulse rate averaged over 100 per minute. The heart appeared enlarged to the anterior axillary line and remained so on subsequent examinations. A systolic murmur audible all over the precordium and a diastolic murmur heard only over the aortic region were noted on all admissions. She was treated by multiple blood transfusions. The subsequent admissions were all for blood transfusions except for the last on January 26, 1944, when she was admitted for heart failure. This time she was orthopneic and had distended neck veins. She died five days later.

The hemoglobin and red blood cell count during her various admissions varied from 4 Gm. hemoglobin and 1,700,000 red blood cells to 10 Gm. hemoglobin and 4,370,000 red blood cells. It is interesting to note that only once did the liver appear to be normal in size. The liver was apparently normal in size when the hemoglobin and red blood cell count were at their highest on June 25, 1941.

One of us (L. A. S.) first studied her heart in detail on June 11, 1943. She was in the hospital for a blood transfusions and was as free of cardiac symptoms as she had ever been. All the previous clinical findings were verified. An orthodiagram and roentgenogram (fig. 1) revealed a huge cardiac silhouette compatible with the clinical findings. The electrocardiogram revealed sinus tachycardia. There was no evidence of increased venous pressure in the neck veins. Lung fields were clear. A diagnosis of huge cardiac enlargement as seen in severe anemia was made.

In the last admission to the hospital the girl appeared moribund. The cardiac findings were similar to those observed during previous admissions, but the presence of severe orthopnea with distended neck veins made one of us (L. A. S.) consider cardiac tamponade. The verbal report on the roentgenogram of the chest was that of massive cardiac enlargement. After discussion with the radiologist it was decided that nothing in the silhouette was incompatible with the diagnosis of pericardial effusion. A pericardial tap was done and about 50 cc. of blood-tinged fluid were obtained, but further drainage was stopped because it was thought that the blood-tinged fluid indicated that the cavity of the heart had been entered. She died the following day.

It was, therefore, no surprise to us that necropsy revealed a massive pericardial effusion, but we were amazed to learn that the heart was essentially normal in size.

The necropsy was performed by Dr. E. E. Aegerter, professor of pathology at Temple University Medical School, and the diagnosis was erythroblastic anemia with marked hemosiderosis of all organs. The following description of the heart is abstracted from Dr. Aegerter's report:

**Heart:** The pericardial sac was tremendously distended. It measured 19 cm. from its prominent right border to the apex and contained 44 oz. of bloody fluid. The fluid was thinner than normal blood. When centrifuged, the cellular content made up only approximately 15 per cent of the volume, indicating that the fluid was an effusion with blood contamination. Both layers of the pericardium were covered by a fibrinous exudate. The heart was about normal size. It weighed 300 grams. The epicardium was considerably thickened. The myocardium was pale, giving the gross appearance of a fatty degeneration. The coronary arteries were normal. There were no abnormalities nor evidences of inflammation on the valves.

Microscopic examination of the heart revealed fatty degeneration of the myocardium, hemosiderosis and chronic fibrosing pericarditis (fig. 2). Cultures of the pericardial fluid were sterile.

**Case 2:** S. C., a female, age 74, was admitted into Temple University Hospital October 15, 1948 and discharged November 27, 1948. When 59, she was told she had pernicious anemia. She was given liver extract that induced a remission. For two years her daughter had given her injections of liver extract, dilute rather than concentrated. In spite of this, she remained entirely free of symptoms until the day of admission, when she fell down three steps and injured her left shoulder.

Physical examination revealed an extremely pale but well-nourished woman in no obvious distress. The heart appeared normal in size and was normal on auscultation. There was slight tenderness in the left shoulder. A roentgenogram revealed an incomplete crack in the left humerus which required no specific treatment except rest.

The blood count was characteristic of pernicious anemia in relapse. There were 4.2 Gm. of hemo-

![Fig. 1. L. L. Roentgenogram of the chest showing huge so-called cardiac silhouette.](image-url)
globin and 890,000 red blood cells per cu. millimeter. The mean corpuscular hemoglobin was 47, the mean corpuscular volume was 146. The reticulocytes were 3.4 per cent, the hematocrit 13 and the blood smear showed macrocytosis. The bone marrow was megaloblastic. The gastric juice was free of acid and the gastrointestinal tract was normal by x-ray examination. The patient was given refined liver extract. At the time of discharge, an examination of her blood showed 12 Gm. hemoglobin, 3,850,000 red blood cells and a mean corpuscular volume of 98. Her family was instructed to use refined liver extract in sufficient dosage. It is important to note that at no time did she have any symptoms referable to the cardiovascular system.
When she was last seen in the out patient department the blood count was entirely normal.

The Heart: A roentgenogram of the chest revealed incidentally partial collapse of the ninth thoracic vertebra due to osteoporosis. The lung fields were clear. The heart was reported as being moderately enlarged in all its diameters (fig. 3). The electrocardiogram showed sinus tachycardia and left axis deviation. The voltage was within normal limits but appeared comparatively low for this type of body build and heart.

Based upon our experience with the first case and upon our experience with the heart in myxedema, we felt incapable of excluding pericardial effusion as a cause for the enlargement of the so-called cardiac silhouette. We therefore decided to do a diagnostic pericardial tap. We were rewarded by our ability to remove very easily 150 cc. of pale amber fluid which we replaced with 300 cc. of air. (fig. 4.)

The pericardial fluid contained 9 white blood cells per cubic millimeter. There was no growth on culture. The chemical composition of the fluid and the corresponding amounts of the blood examined on the same day were as follows:

<table>
<thead>
<tr>
<th>Pericardial Fluid</th>
<th>Blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein</td>
<td>4.0 Gm.</td>
</tr>
<tr>
<td>Albumen</td>
<td>2.9 Gm.</td>
</tr>
<tr>
<td>Globulin</td>
<td>1.1 Gm.</td>
</tr>
<tr>
<td>A/G</td>
<td>2.7</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>40 mg.</td>
</tr>
<tr>
<td>Na</td>
<td>147 mg.</td>
</tr>
<tr>
<td>K</td>
<td>4.5 mg.</td>
</tr>
<tr>
<td>Chlorides</td>
<td>391 mg.</td>
</tr>
<tr>
<td>Mucin</td>
<td>negative</td>
</tr>
</tbody>
</table>

Under no other therapy except that for the anemia, the effusion slowly disappeared and the cardiac silhouette diminished in size (fig. 5.)

**Comment**

These two cases illustrate the fact that pericardial effusion may be one cause for enlargement of the so-called cardiac silhouette in anemia as seen in the roentgen ray film. Furthermore, pericardial effusion may exist for years without producing symptoms or signs of tamponade. In our first patient, judged by the heart size at necropsy, pericardial effusion was present from her first admission into Temple University Hospital. This period represents four years. There is no way of determining how long previous to her first visit to our hospital the so-called cardiac silhouette had been enlarged. In our second patient the pericardial effusion was at no time associated with cardiac symptoms. This patient would have been regarded as a typical example of cardiac dilatation responding to therapy for anemia had not a pericardial tap been done.

It is obvious, therefore, that neither the clinical findings nor, indeed, the roentgen findings, as determined by ordinary technic, can help us at all times in distinguishing cardiac dilatation from pericardial effusion. The electrocardiographic findings obviously are not crucial. It appears likely that visualization of the cardiac chambers by Diodrast may furnish the answer to this problem in differential diagnosis. The literature on the experimental production of anemia and on the anatomic findings in anemia was reviewed in an attempt to determine how often pericardial effusion occurred as the sole or major factor in enlargement of the so-called cardiac silhouette.

Experimental production of anemia produced by bleeding has resulted in hypertrophy of the heart. The heart may double in weight if a very severe anemia is produced. The experiments upon which these conclusions are based were relatively acute ones. The possible readjustments that may occur during a slowly produced anemia have not been described. We were unable to find any reference to experimental work on enlargement of the heart with return to normal size after correction of the anemia.
Anatomic studies on untreated severe pernicious anemia will probably no longer be made except under very rare circumstances because of the excellent therapy available now for the disease. There are several anatomic reports in the pre-liver era. Cabot and Richardson reported an increase in weight of the heart in 18 of 19 instances of pernicious anemia. Only five hearts weighed more than 400 Gm. They stated that three had other possible causes for enlargement. The protocol shows five others with associated disease such as coronary artery disease or "acute" or "subacute" glomerulitis. Three hearts weighed only 285 Gm., 267 Gm., and 262 Gm., respectively. Reid later examined the hearts of 11 individuals who had pernicious anemia and found that enlargement of a degree recognizable clinically was not found. Six weighed between 200 and 300 Gm. and 5 between 300 and 400 Gm. Unfortunately the presence or absence of pericardial effusion is not mentioned. In individuals who died of congestive failure apparently secondary to pernicious anemia, serous effusions, including pericardial effusion, were present.

As far as erythroblastic anemia is concerned, we are indebted to the excellent and thorough anatomic study of Whipple and Bradford. They were primarily interested in the pigment abnormalities in this disease and did not comment specifically on pericardial effusion, but unlike so many other reports their anatomic descriptions are thorough and give specific information on the topic we are discussing. These authors stated that the heart in erythroblastic anemia may be enlarged and that serous effusions are common. They reported 3 cases, in all of which lemon-yellow hydropicardium was present.

A clinical diagnosis of cardiac enlargement was made in each instance but at necropsy only one heart was enlarged. The hearts weighed 71 Gm., 160 Gm., and 270 Gm. The pericardial cavities contained respectively 80 cc. of fluid, "a considerable excess of fluid," and 450 cc. of fluid. There is therefore more than a possibility that, in the presence of roentgenologic evidence of enlargement of the so-called cardiac silhouette in erythroblastic anemia, pericardial effusion may be a contributory factor in the enlargement of the roentgen ray shadow.

It is interesting to note that Whipple commented on the similarity of the bone marrow changes of erythroblastic anemia to those of pernicious anemia and to the similarity of the pigment changes of erythroblastic anemia to that of hemochromatosis. It is perhaps noteworthy that heart failure is a complication of hemochromatosis. This failure has been attributed both to disturbance in contraction of the myocardium because of the excessive pigment deposition and also to endocrine disturbances secondary to similar pigment deposits in the endocrine glands. But pericardial effusion has been reported as an incidental finding in hemochromatosis with and without heart failure. Chesner reported an instance of hemochromatosis with apparent clinical enlargement of the heart. Clinically the heart extended from the anterior axillary line to a point more than two fingers breadth to the right of the sternum, yet the heart at necropsy was grossly normal and weighed 250 Gm. This discrepancy is not explained in the necropsy protocol. It would appear that interest was so centered on the problem of hemochromatosis that the pericardial effusion was not described.

The cause of the occasional presence of pericardial effusion in these blood dyscrasias is not clear. It may be that excessive pigment deposits in the pericardial membranes act as irritants to produce effusion. In support of this concept is the report of a case by Dubus who describes the anatomic findings in a man of 66 years who died in heart failure. Anatomic examination revealed a massive pericardial effusion of 1500 cc. The fluid was sanguinolent. Microscopic examination revealed fibro-adipose thickening of the visceral epicardium with excessive blood pigment deposition. No other cause for the pericardial effusion was discovered. Dubus called this lesion hemopigmentary pericarditis with effusion.

It is also possible that in anemia there may be a redistribution of fluid within the functional compartments of body water as Sokalchuk, Bello and Soloff found in myxedema. In the latter disease, the interstitial fluid, including
the pericardial fluid, is increased and the blood volume is decreased. Under thyroid therapy, the blood volume increases and the interstitial fluid, including the pericardial fluid, decreases. In anemia, the blood volume is reduced and there is a well-known tendency to formation of edema. There does appear to be a general relationship, other things being equal, between blood volume and cardiac size. This is most clearly seen in diseased states with rapidly changing blood volumes. In addisonian crisis, for instance, the cardiac silhouette is extremely small and the blood volume is sharply reduced. With the exhibition of desoxycorticosterone acetate, there is a rapid increase in blood volume and cardiac size. But if excessive amounts of this drug are used, fluid accumulations appear in the serous cavities and in the subcutaneous tissue. The further increase in size of the so-called cardiac silhouette can very well be due to fluid accumulations within the pericardial sac. There is persuasive indirect evidence for this assumption but we did not feel it safe to tap the pericardium of a patient who exhibited the phenomena of overdosage with this drug. A similar train of events may possibly occur in anemia. The heart in anemia dilates, but at some critical point, which may vary in different types of anemia and from patient to patient, fluid accumulations occur. The pericardial effusion may simply be more easily detectable than accumulations of fluid elsewhere, or, once present, its reabsorption may be difficult.

Finally, these two cases may be rare exceptions to the usual course of events in anemia.

CONCLUSIONS

1. A case of erythroblastic anemia of Cooley and one of pernicious anemia are reported in which massive pericardial effusions were present and were mistaken clinically and roentgenologically for cardiac enlargement.

2. The possible causes of these effusions are discussed.

REFERENCES

Pericardial Effusion Mistaken for Cardiac Enlargement in Severe Anemia: Report of Two Cases
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