A Mirror of Hospital Practice

A CASE OF QUININE HÆMOGLOBINURIA

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THE production of hæmoglobinuria by quinine is often reported in the tropics and this is one of the reasons why quinine is administered with great caution to debilitated and anæmic patients. It is difficult, with our present knowledge regarding this condition, to state with any degree of certainty whether this hæmoglobinuria is due (*i*) directly to the action of quinine, (*ii*) to the infection for which quinine is being administered, or (*iii*) to some inherent pathological condition of the red blood corpuscles, quinine serving merely as an indirect stimulus. Numbers of cases of blackwater fever are encountered in certain parts of Bengal and Assam every year. Many of the patients give histories of repeated attacks of malaria and medication with quinine for prolonged periods.

The following case will be of interest :—

S., a Hindu female from Jessore, aged 11 years, was admitted into the Hospital for Tropical Diseases under the senior author on the 15th of January 1935 with a history of repeated attacks of malaria and occasional attacks of passing black water. The patient was anæmic and the spleen and the liver were enlarged. At the time of admission she had no fever.

History.—The patient had been suffering from repeated attacks of malarial fever for the last six months and frequently used quinine to control them. During an attack a month and a half ago when her temperature was 104°F., the patient started passing black-coloured urine four hours after taking a tablet of quinine. Quinine was at once stopped and the condition subsided. Three weeks later, she again had another attack of malaria and though no quinine was given this time, she again passed black-coloured urine. This lasted for one week when the condition again settled down. The patient came to hospital for investigation and treatment. On admission the patient had no temperature and passed apparently normal urine.

Laboratory examination.—Four consecutive examinations of stools showed no protozoa nor any non-lactose fermenting bacteria, and were also negative for helminths.

Urine.—No hæmoglobin was found but it gave a definite reaction for urobilin and indican and showed the presence of a few crystals of urates and oxalates of calcium.

Blood.—No malarial parasites could be detected in the peripheral blood; no microfilariæ were seen and the serum tests for kala-azar (aldehyde and antimony) were negative. The blood also gave a negative Wassermann's reaction. The physical and biochemical characters of the blood were examined in detail and the results are given in the following table:—

Details of blood examination

Details	Case under investigation.	Normal
A. Physical characters (cap. tube method):—		
I. Coagulation time ..	2 min. 40 sec.	3 min. 30 sec.
II. Fragility		
Initial hæmolysis ..	0.55%	0.45%
Complete ..	0.35%	0.35%
III. Diameter of cells ..	7.32 μ	6.9μ to 7.5μ
IV. Electric charge (migration rate 10)—		
(*a*) Saline suspension	5.75	11.2
(*b*) Glucose suspension	20.85	29.3
V. Surface tension of serum.	58.3	60.1
VI. Viscosity of serum ..	1.6	1.6
VII. pH	7.36	7.48
VIII. Buffer action ..	6.27	6.88
B. Biochemical:—		
I. Uric acid ..	0.0033%	0.002% to 0.004%
II. Cholesterol ..	0.283%	0.14% to 0.17%
III. Calcium ..	0.0082%	0.0053% to 0.0068%
IV. Proteins—		
(*a*) Total proteins ..	6.99%	7.44%
(*b*) Albumin ..	3.27%	4.61%
(*c*) Pseudoglobulin ..	3.20%	2.65%
(*d*) Euglobulin ..	0.52%	0.18%
C. Blood count:—		
Total red cells ..	4,410,000	
„ white cells ..	7,800	
„ hæmoglobin ..	65%	
„ polymorphonuclears	34%	
„ lymphocytes ..	54%	
„ large hyaline ..	nil.	
„ eosinophils ..	12%	

Occurrence of hæmoglobinuria.—In order to see whether quinine had any effect in bringing about the condition, six grains in two equal doses were administered by the mouth on the 16th January. The patient started passing black urine which on examination showed quite a large amount of hæmoglobin and gave a fairly strong reaction for urobilin and indican. The patient had no fever, she did not feel ill and the condition subsided of itself after 3 days. On the 30th of January, the patient was given atebrin by the mouth in three doses of 0.1 gm. each, in order to see if this precipitated an attack and on the 1st of February, 0.0099 gm. of plasmochin was given in addition to 0.3 gm. of atebrin. The urine remained quite normal in colour and on examination showed neither hæmoglobin nor urobilin. A subsequent administration of six grains of quinine sulphate on the 5th February did not produce any attack. On the 10th February three doses of quinine, three grains each, were again given. Hæmoglobinuria again started four hours after the first dose, but its duration was short and after the third dose of quinine the colour of the urine became normal.

Discussion.—The special features in connection with this case are: (*a*) increased fragility of the corpuscles, (*b*) reduction in the electric charge of the corpuscles, and (*c*) diminution in serum albumin, but increase in euglobulin, pseudoglobulin, cholesterol and calcium contents. Although some of these factors may be

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indirectly responsible for the disintegration of the corpuscles, it will be observed that atebrin and plasmochin did not precipitate the attack, whereas quinine succeeded in bringing it about on two occasions out of three. It would appear, therefore, that the hæmoglobinuria is not dependent on quinine alone, but some other factors also play a part in the production of this condition. What these factors are remains to be worked out. Many of the cases of black-water fever met with in Bengal and Assam are of this nature and it is possible that the substitution of atebrin for quinine in the treatment of malaria will bring about a reduction in the occurrences of such cases.

A CASE OF PAROXYSMAL TACHYCARDIA AND ITS SEQUEL

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The attack.—S. L., Hindu male, aged 23, was admitted to hospital on 7th March, 1934, with the complaint of continuous palpitation of four days' duration. He gave no history of any previous disease other than occasional fever; he denied venereal infection. He had been subjected to recent severe mental strain, as in the Bihar earthquake in January his house came down and all his family except himself were killed.

Severe and continuous palpitation started while he was in the train four days previously; the discomfort was increasing, but there was no pain, no œdema anywhere, and no subjective dyspnœa; the patient was very cyanosed.

The pulse was 180 per minute, perfectly regular, and of normal volume and tension. The cardiac impulse was diffuse, and the apex beat 1 inch outside the nipple line; there was a systolic thrill and the impulse was forcible; a soft systolic murmur was audible in the mitral and tricuspid areas, and the pulmonary second sound was accentuated. Beyond his colour, which was almost blue, and some basal pulmonary congestion, there were no other positive findings.

The Wassermann test was negative.

After a day's observation, during which he was on glucose and insulin, 5 units, the pulse remaining steady between 170 and 180, he was given intravenously one injection of strophanthin 1/125th grain, and the next day three of 1/100th grain with no effect. He was then put on 5 gr. doses of quinidine thrice daily, and after the sixth dose the pulse rate fell suddenly to 90, and remained at that rate thereafter. His colour became normal, and he left hospital relieved on 23rd March. The paroxysm had lasted for about ten days.

The sequel.—On 24th September, 1934, the patient was re-admitted for pain in the left back, fever, and dyspnœa, all of some 12 days' duration. He was found to have a left pleural effusion of clear fluid, some of which was removed and replaced by air on two occasions. Very shortly he developed a pericardial rub and then an effusion; this also was aspirated, and tubercle bacilli were demonstrated in it. There were no intra-pulmonary signs. The patient ran a continued fever of low degree, and became progressively worse until his death on the 7th December, 1934.

Post-mortem findings

Lungs: Right.—Slightly emphysematous. Right side of the pericardium was adherent to the lung on the right side. The adhesions were recent. The pleural cavity contained four ounces of fluid.

Left.—Covered with thickened pleura and collapsed at its base, where a sac had formed by the collection of some fluid in between the two layers of the thickened pleura. A chain of enlarged tuberculous glands was found in the left side of the neck. This chain had continued on to the anterior mediastinum, connecting up with the enlarged tracheo-bronchial chain of glands, which were found adherent to the pericardium and also to the left auricle whose walls were practically fixed to the posterior mediastinum, probably due to a previous adhesive mediastinitis, tuberculous in origin.

Heart.—The heart with its pericardial covering was very much enlarged—the greatest dimensions (after opening the pericardial sac and withdrawing the fluid) were 8 inches by 7 inches. The sac contained 8 ounces of dirty fluid, in which flakes of fibrin were seen floating. The inner side of the parietal pericardium was studded with tubercles, while it was adherent to the right lung with recent adhesions, but on the left side it had completely fused with the pleura. No adhesions of old standing were found in between the two layers of the pericardium. The visceral pericardium was covered with flakes of fibrin and was very rough. It could be compared to a 'bread and butter heart' where butter was applied more profusely and irregularly. The heart as a whole was displaced to the right and at the same time slightly rotated to the left, so that the enlarged right ventricle had formed the apex, while the left ventricle was much smaller and formed the posterior surface of the heart. The left auricle was so adherent to the posterior mediastinum, that it could not be approached from outside. The mitral valve did not show any stenosis; the tricuspid admitted the tips of more than three fingers. The right auricle was enlarged. The blood vessels arising from the heart were covered with fibrin, but no actual strangulation by fibrous tissue was noticed around them.

Liver, spleen and kidneys.—Showed marked chronic venous congestion.

Morbid histology

Pericardium.—Showed uniform fibrosis with islets of small round cells here and there. Caseous foci were present at different places with some attempt at giant-cell formation.

Heart muscle.—Showed no fatty changes. Brown atrophy present in its early form.

Lymph gland.—Tuberculous.

Comments.—It is interesting that nine months before his death no signs of the infection from which he died were found in this patient. At that time it seemed probable that an emotional factor was the prime cause of the paroxysmal attack. This having ceased, there was no evidence of disease of the heart, a normal electrocardiogram being obtained. It is difficult to believe that, if a tuberculous focus had been the exciting cause, the normal rhythm would have been restored so easily.