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CONGENITAL HEMOLYTIC JAUNDICE—REPORT OF AN INTERESTING CASE

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Congenital Hemolytic Jaundice—Report of an Interesting Case[1]

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CASES of congenital hemolytic jaundice are of sufficient interest as well as rarity to warrant the description of an additional case.

Mrs. A. T. S. aged thirty-four years entered the Church Home and Infirmary on September 1, 1920, with the complaint of jaundice and pain in the left upper abdomen. Her family history is of some interest. Her father was born in Germany, but moved to South Carolina in his youth, and died at seventy-one years of age with an obscure stomach disorder. He was jaundiced all his life, and was subject to attacks of colic following which the jaundice would deepen. One paternal uncle died aged seventy-seven years, but the patient does not know that he ever had jaundice though two of his five children were affected with jaundice very definitely quite as she has been throughout their entire lives, and in consequence were frequently forced to discontinue work.

The patient has three brothers and one sister living; none of these were affected with jaundice, yet one brother who died of typhoid had had jaundice much like that observed in our patient. The maternal history is negative.

There are two children of the patient living, who are seven and four years old, respectively, and are both healthy. There is therefore a definite history of persistent jaundice in the patient's father and two first cousins; perhaps in her grandfather and brother. It is interesting to note that all of the members of her family affected with jaundice were males.

The patient was born and has lived all of her life in South Carolina. In addition to her occupation as housewife she has been quite active with farm work especially with cotton picking. She has always led an extremely regular life, taking much rest, and sleeping well, but frequently indulged in excessive eating. She drinks coffee freely, but is not addicted to the use of drugs or alcohol.

The patient had "dropsy" of the legs when five years of age, measles when thirteen, scarlet fever when fourteen; there is no history of malaria, rheumatism, tuberculosis or any other affection.

The patient has been jaundiced all of her life, but at times this discoloration deepens. Since her sixteenth year she has been affected with sharp acute pain, beginning under the right costal arch, and extending over the abdomen, and at this time she noted a deepening of the jaundice. Between these attacks she was usually comfortable, and had a good appetite, frequently overindulging in food. She has always been somewhat constipated, but her stools have never been clay colored, nor have they ever contained blood or mucus. With the attacks there was frequently nausea and vomiting, the vomitus being bile tinged. The attacks of vomiting were accompanied with chilly sensations, fever and sick headaches. A diagnosis of choleli-

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thiasis was made, and in December, 1911, gall stones were removed, and the gall bladder drained. The attacks, however, soon recurred, and became so violent that in March, 1917, cholecystectomy was performed when numerous gall stones were obtained; at the same time an appendectomy was done. Since then the patient has no longer been affected with the attacks of pain originating in the gall bladder region, but the acute attacks of nausea, vomiting, sick headaches, and chilly sensations have continued and with each attack there has been a rise of temperature with increase in the jaundice. A pain of minor importance under the left costal arch noted at the time of her last operation in 1917, has become greatly intensified with each attack, when the patient herself observed an enlargement and tenderness in this area. Even between the attacks there has been a constant aching in this region. There is in addition constant fullness and discomfort in the epigastrium and abdomen, which seems to bear little or no relation to the ingestion of food. Food does, however, at times produce some discomfort and indigestion.

The patient has herself been unaware of the enlargement of the spleen until informed of this condition recently. There is little else of importance in the history of the patient. Since October, 1919, she has had attacks of weakness and faintness, but without loss of consciousness. These sensations are aggravated by exertion, though they have made their appearance when the patient is at rest in bed. These attacks have been much less frequent during the past six months. The patient's power for sustained effort has been greatly decreased so that she is able to perform but little work. There is slight dyspnea on exertion.

The menstrual periods began between the seventeenth and eighteenth years, have never been profuse, and are fairly regular, and are not in any way related to the onset of the acute abdominal attacks. There have been no urinary disturbances, though the urine is frequently highly colored. The maximum weight of the patient has been 144 pounds two years ago, her average weight is 110 pounds, her present weight is 96 pounds.

Physical examination

The patient is a female thirty-four years of age, poorly nourished and weighing 96 pounds. Her skin is smooth, and presents no eruptions or scars, but is markedly jaundiced. The icteric appearance is also revealed in the conjunctivae. The depth of the jaundice fluctuates slightly from day to day; being deeper following the attacks of pain on the left side. It is greater over the chest and abdomen, being nearly absent from the cheeks and hands. No glandular enlargements are present, the epitroclear, inguinal and axillary glands being barely palpable. The muscles are flabby and hypotonic and there is but little subcutaneous fat present. The eyes and ears are negative, the teeth normal, and the mucous membranes pale. The thyroid is palpable and slightly enlarged, no bruits can be elicited. The lungs and heart are normal.

The abdomen. The walls of the abdomen are thin and relaxed, the contour is flat. There are present two scars of former operations: a right rectus incision and a McBerney's; the liver is enlarged 2 cm. below the costal margin. The spleen is elongated and easily palpable, extending in the mid-axillary line to 2 cm. above the crest of the ilium; the splenic notch is palpable. The spleen is of moderate consistency, tender on pressure, pulsations are not pronounced. The abdomen is markedly enteroptotic. The genito-urinary tract is negative and the reflexes are normal.

Laboratory findings

The urine. The daily output of urine varies from 1500 to 1850 cc. It has a specific gravity of 1020; is usually amber in color, though at times it presents a dark yellow appearance; it contains neither bile nor albumin (except a trace of albumin on one occasion); sugar is absent and the test for urobilin is positive. The microscopic examination is negative.

Phenolsulphonephthalein test

Output for first hour, 450 cc., 30 per cent; output for second hour, 400 cc., 11 per cent; total, 850 cc., 41 per cent.

Blood

Wassermann reaction negative.
Red blood corpuscles, 3,200,000.
White corpuscles, 6000.
Hemoglobin, 75 to 85 per cent.

Differential count

	FIRST EXAMINATION	SECOND EXAMINATION
Small mononuclears....	30	28.5
Large mononuclears....	12	7.5
Polynuclear neutrophiles.....	51	62.0
Eosinophiles.....	1	0.8

An examination of the blood smears indicates slight secondary anemia; no poikilocytosis and but slight anisocytosis; moderate polychromatophilia; no myelocytes; no neucleated red blood corpuscles.

Resistance of the erythrocytes to hypotonic salt solution. Maximum 0.48 first examination, minimum 0.30; maximum 0.45 second examination, minimum 0.25.

The subcutaneous tuberculin test is negative.

Gastric secretion

Ewald test breakfast, 60 cc. of well digested clear secretion was obtained, total acidity 40, free HCl 32.

Rehfuss fractional analysis

HOURS	FREE HCl	TOTAL ACIDITY
¼	20	32
½	26	34
¾	42	58
1	36	48
1¼	34	48
1½	28	40
1¾	16	24
2	12	22
2¼	6	20
2½	20	32
2¾	20	34
3	64	80

Duodenal contents

The duodenal content is yellow turbid and contains much mucus. On stimulation with magnesium sulphate, there is a free flow of very dark and cloudy bile, containing an almost pure culture of streptococci.

A fractional analysis of the duodenal contents according to the Einhorn method is as follows:

	ALKALINITY	TRYPSIN	AMYLOPSIN	STEAPSIN
		mm.	*mm.*	*mm.*
Fasting stomach.....	20	4	2	15
One-half hour after stimulation with bouillon..	18	1	5	10
One hour after stimulation with bouillon.....	20	6	2	10
One and one-fourth hours after stimulation with bouillon.....	18	3	2	12
Two hours after stimulation with bouillon.....	18	2	0	9

Stools

The stools are normal in appearance, brownish in color, contain no blood, and but a slight trace of mucus. The examination for parasites and ova is negative. A few undigested meat fibres are observed and urobilin is present.

DISCUSSION

It was in 1885 that Murchison published a report of an interesting condition which he termed chronic acholuric jaundice, which was associated with anemia and splenomegaly, but did not present the usual manifestations of biliary intoxication. Subsequently LeGendre, Hayem, and Wilson reported similar observations, but it was not until 1900 that Minkowski clearly described the syndrome now recognized as congenital hemolytic jaundice occurring in certain individuals, members of the same family. Since then, numerous valuable contributions have appeared, regarding this affection.

Among the most interesting cases published are those of Thayer and Morris. These authors present an unusually valuable review of this entire subject together with a complete bibliography up to 1911.

Hemolytic jaundice may appear in one of three well established groups: the familial, congenital and acquired forms. According to Whipple and Harper this affection termed hemolytic jaundice is now established upon a definite scientific basis. It is possible that the rapid change from hemoglobin to bile pigment is brought about through the endothelium of the blood vessels, where great destruction of the erythrocytes takes place producing a rapid discharge of free hemoglobin into the blood. These investigators therefore conclude that hemoglobin can be rapidly altered into bile pigment in the blood without the action of the liver.

On the other hand, Naunyn has called attention to the fact that not sufficient attention has been directed to the possible existence of obstruction in hemolytic jaundice. He is convinced that the liver plays a rôle in all cases and regards the jaundice as an infectious disease in which a cholangitis is an important factor. He feels that if more careful studies of the liver would be made, at least partial obstruction would be detected.

Recently Gerhart has also come to a similar conclusion and believes that careful repeated examinations will disclose symptoms of biliary obstruction.

The etiology of this disease has, as yet, however, not been satisfactorily established. Hayem holds the view that syphilis is a prominent causative factor while Chauffard considers it due to congential syphilis or to tuberculosis, to which there has been added some disturbance of the spleen.

It was Chauffard who first pointed out that there is present in this affection an increased fragility of the erythrocytes; in consequence of the increased susceptibility of the red cells to hemolytic agents, the anemia develops, the marked destructon of the red cells leading to an increase in the production of bile pigment, and consequently to icterus.

Others, as Banti, failing to observe hemolysins in the blood, assume that the destruction of the erythrocytes has its origin in the spleen and in consequence of the added work there is necessarily produced an enlargement of this organ. Widal, on the other hand, is strongly of the opinion that the destructon of the red cells occurs in the blood itself, and that the splenomegaly is due to the increased activity placed upon the spleen by the accumulation of the corpuscular debris.

In addition to the congenital form of hemolytic jaundice, there is an acquired form which appears in adult life with symptoms much like those present in the congenital type. This condition may arise without apparent cause or may appear after some acute disease or following an accident or may be associated with an acute infection.

The symptomology of congenital hemolytic jaundice is quite characteristic, the most prominent manifestations being chronic non-obstructive jaundice, splenomegaly and anemia, together with certain blood changes, diminished resistance of the red cells, and urobilinuria. Heredity

is a most important factor in most instances.

The jaundice is chronic in character, and usually dates its appearance from birth or infancy, though it occasionally occurs later in life; it is not associated with bile in the urine or with clay-colored stools; it usually deepens at certain periods when exacerbation of the disease takes place. At times there may be a marked or entire disappearance of this symptom for a variable period of time. The enlargement of the spleen so characteristic of this affection is usually increased during the periods of exacerbation; at this time colicky pains usually manifest themselves in the splenic area and as the attack vanishes the spleen again diminishes in size. There is in addition a marked decrease in the osmotic resistance of the red cells to hemolizing agents; that is, increased fragility of these cells.

The method for determining the resistance is as follows: The red blood cells are separated from the plasma, washed and then placed in a series of test tubes in which are contained varying strengths of hypotonic salt solution varying from 0.7 per cent down to 0.36 per cent. In normal blood hemolysis begins at 0.44 per cent, and is complete at 0.36 per cent; in this affection however, it begins at some higher point, taking place at 0.6 or even 0.7 per cent. The blood changes usually present a moderate anemia, there is a reduction in the number of red cells with a decrease in the hemoglobin, the white cells usually presenting no variation from the normal; the red cells present a diminution in diameter, anisocytosis is present with polychromotophilia, rarely are nucleated red cells observed. Jolly bodies and basophilic granules are ordinarily noted. In addition, attention has been called to the occurrence of a peculiar net work of granules in the red cells when the blood is treated with a basic dye by means of post-vital staining. These are known as substantia-granulo-reticulo-filamentosa. These are abundantly present in hemolytic jaundice and are therefore of great diagnostic value.

The urine contains urobilin but bile is usually absent.

The stools are well colored, and contain bile and urobilin.

Post mortem findings. The autopsy findings as observed in a number of individuals by various writers are quite constant. There is usually present a marked siderosis of the spleen, liver and, in less degree, of the kidneys, and in no instance was there an indication of biliary obstruction.

In the treatment of this affection Banti reports in 1903 a complete cure by splenectomy. Similar results have been noted by Micheli, Frosi, Umber, and Roth. In many instances as has been confirmed by Richards and Johnson, beneficial effects have followed the continous administration of iron. In the congenital forms there is no serious interference with the patient's health; he may enjoy a fairly comfortable existance and live to old age. The question of operation should only be considered when the symptoms become aggravated in the form of pain which may be due to biliary colic and which is accompanied by fever together with an increase in the jaundice. As a rule, however, aside from the jaundice, these patients are usually free of the

subjective symptoms ordinarily observed in jaundice, there being none of the signs of biliary intoxication present, ordinarily observed in this affection.

In conclusion, it is quite evident that the case presented by us represents a well defined instance of congenital hemolytic jaundice. In addition to the family and personal history the presence of chronic jaundice deepening at certain periods with exacerbations of the disease, and associated with anemia and splenomegaly, but without any manifestations of biliary intoxication points directly to this affection. There was present in addition a marked fragility of the erythrocytes. The urine contained urobilin, but was free of bile, while the stools were of normal color, and contained both urobilin and bile. Of some interest too are the findings of the contents of the stomach duodenum and of the bile. The gastric secretion presented normal values as to total acidity and free HCl on fractional examination up to three hours when a marked hyper-acidity manifested itself (total acidity 80 free HCl 63). The biliary secretion removed with the duodenal tube was dark and cloudy and revealed a marked infection. Fractional analysis of the duodenal contents presented normal alkalinity curves with normal trypsin and unusually good steapsin values, but with quite poor amylopsin findings, which according to our experience is quite at variance with those observed in cases of obstructive jaundice, in which low values of all of the ferments are ordinarily noted.

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