CASE REPORTS

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Development of Porphyria During Chloroquine Therapy for Chronic Discoid Lupus Erythematosus

IRWIN H. LINDEN, M.D., CHARLES GEORGE STEFFEN, M.D., VICTOR D. NEWCOMER, M.D., and MYRON CHAPMAN, M.D., Los Angeles

PORPHYRIA and the metabolism of porphyrins have been objects of interest for many years despite the rarity of the disease. This interest has resulted in investigative endeavor which has constantly added to the knowledge of the subject and dispelled much of the confusion in the concepts and terminology of earlier investigators. There is not, however, unanimity of opinion as to a system of classification and the etiologic delineation of the disease remains obscure. Most authorities[1, 8, 15] do agree that in order for porphyria to develop a patient must have an overt or latent inborn error of metabolism.

There are three main types of porphyrins that are significant in the understanding of porphyria: uroporphyrin, coproporphyrin and protoporphyrin. A related compound, porphobilinogen, is also excreted in some cases. These porphyrins have in common a basic cyclic structure, the porphyrin nucleus, and differ only in the attached side chains.[11] The porphyrin nucleus is also a fundamental component of many other important chemical structures including hemoglobin, the cellular respiratory enzymes and the chlorophyll molecule.[8] The physiologic role of uroporphyrin and coproporphyrin is not definitely known, but there is evidence that they are the precursors of protoporphyrin which is combined with iron and protein to form hemoglobin.[14]

Porphyria has been classified by Waldenstrom[13] into three main varieties: congenital, acute intermittent and cutanea tarda. The congenital type is rare and has its onset in early childhood. The cutaneous lesions occur on exposed surfaces and are characterized by bullae and eventual scarring. The skin lesions are thought to be due to the photosensitivity possessed by these patients. Other findings include red teeth, red bones and hypertrichosis. The rather constant presence of anemia and splenomegaly and the large amounts of uroporphyrin in the immature erythrocytes led Lowry and co-workers[7] to classify this variety as porphyria erythropoietica.

Acute intermittent porphyria begins later in life, usually in the second to fourth decades. Onset is sudden and the symptoms consist of abdominal colic, obstipation, transient increase in blood pressure and neurologic and psychic disturbances. Spontaneous remissions in acute porphyria are the rule, but recurrences are common and the disease is frequently fatal.

The usual onset of porphyria cutanea tarda, or chronic porphyria, is characterized by a bullous eruption on the exposed skin of adults. This is thought to occur in response to light, heat or minor trauma.[3] Photosensitivity is not as prominent in the cutanea tarda variety as it is in congenital porphyria and trauma is usually a necessary precipitating factor.[17] The patients usually have a dusky complexion, hypertrichosis and hyperpigmentation. There is frequently evidence of hepatic dysfunction. The cutanea tarda form of porphyria is distinguishable from the acute form by the presence of skin lesions and the absence of abdominal or neurologic manifestations.

There is an increased excretion of a uro-type porphyrin in all the varieties of porphyria. The excretion of large amounts of uroporphyrin is considered to be so important that the diagnosis of porphyria cannot be established without this finding. Porphyrinuria, on the other hand, alludes to the excretion of increased quantities of porphyrins of any type, usually coproporphyrin. The excretion of coproporphyrin occurs in many unrelated diseases and its significance is unknown. These two terms, porphyria and porphyrinuria, must be clearly differentiated.

The excretion of porphyrins has been studied in many skin diseases. Lupus erythematosus has been one of the most frequently investigated. Brunsting in 1939[2] reported seven cases of lupus erythematosus of all varieties. Increased coproporphyrin excretion occurred in only one of the cases, that of a patient with discoid lupus erythematosus. There were no

From the Medical Service, Veterans Administration Center General Medical and Surgical Hospital, Los Angeles 25, and the Division of Dermatology, Department of Medicine, University of California School of Medicine, Los Angeles 24.

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instances of uroporphyrinuria. Zeligman[16] in 1946 reported elevated urinary coproporphyrin excretion in eight of 34 patients with the discoid variety and in all of four patients with acute disseminated lupus erythematosus. Porphyrinuria in these latter four cases was attributed to low-grade hyperpyrexia. Zeligman found no excretion of uroporphyrin in any of the above patients or in 88 other patients with miscellaneous diseases of the skin.

So far as could be determined there is no report of the occurrence of porphyria in a case of lupus erythematosus with the classic urinary findings including the presence of large quantities of uroporphyrin. Schoch,[10] in a recent review article on the cutaneous manifestations of porphyria, said that lupus erythematosus has been reported in association with porphyria. However, the authorities[4, 6] cited by Schoch said only that porphyrins were excreted in lupus erythematosus. They did not mention the type of porphyrins and therefore no conclusions can be drawn as to the possible presence of porphyria.

The purpose of the present communication is to present a case report of a patient with chronic discoid lupus erythematosus of six years' duration who had an episode typical of acute intermittent porphyria while receiving chloroquine therapy.

REPORT OF A CASE

A 48-year-old Negro man was admitted to the hospital July 16, 1953, with complaint of chills, fever, vomiting, abdominal pain and "blood in the urine" of one day's duration. Upon physical examination the patient appeared to be acutely ill. The temperature was 100.2° F. The blood pressure was 130/80 mm. of mercury. Scattered over the face, chest, arms and scalp were discrete, atrophic, pigmented and depigmented plaques varying in size from 8 to 25 mm. in diameter. Some of them were erythematous and scaling; others appeared to be old scars. Pronounced tenderness in the right upper quadrant of the abdomen, without muscular rigidity, was noted. No organs or masses were palpable and the bowel sounds were normal.

The hemoglobin content was 13.8 gm. per 100 cc. of blood. Leukocytes numbered 20,100 per cu. mm. —91 per cent polymorphonuclear cells. The urine was burgundy red in color and contained a moderate amount of albumin. It fluoresced brightly under a Wood's light. Spectroscopic examination of the urine, acidified with an equal part of 25 per cent hydrochloric acid, revealed an absorption maximum at 552 millimicrons. This indicated the presence of a uroporphyrin.[11]

Past history. The patient was hospitalized for "pellagra" at the age of 14. He did not recall clearly any of the symptoms of that time.

He had a positive reaction to a serological test for syphilis in 1943 upon entry into the Army and he was treated with weekly injections of arsenic and bismuth for three months. The results of serologic tests after that varied from negative to slightly positive. Cerebrospinal fluid examinations were performed in 1944 and again in 1950. They were normal on both occasions. The result of a treponemal immobilization test (TPI) performed in February 1954 was positive. The patient received 4.2 million units of penicillin in 1949 for an intercurrent infection.

TABLE 1.—*Urinary porphyrin excretion of patient and relatives*

Date	Coproporphyrins (micrograms) Per 100 cc.	Coproporphyrins (micrograms) Per 24 hrs.	Uroporphyrins (micrograms) Per 100 cc.	Uroporphyrins (micrograms) Per 24 hrs.
Normal:		10-120		5-20
July 16, 1953	1.43		13.8	
July 18, 1953	1.12		16.0	
July 20, 1953	0.82		10.5	
July 24, 1953	2.30	37.8	6.0	91.0
July 25, 1953	0.42	8.8	8.9	187.0
July 30, 1953	0.68	12.8	3.0	57.0
Aug. 5, 1953	1.23		6.3	
Aug. 11, 1953	0.56	12.9	1.6	37.5
Nov. 24, 1953		0		0
Son	0.32		0	
Sister	0.06		0	
Brother	0.45		0	

The patient was first observed in the Dermatology Clinic of the Veterans Administration Hospital in May 1947, at which time he complained of several areas of alopecia on the scalp and one in the left eyebrow of three months' duration. The clinical impression was chronic discoid lupus erythematosus and this was confirmed by several biopsies. During the following six years the patient received most forms of therapy advocated for chronic discoid lupus erythematosus, including bismuth, gold, cortisone, testosterone, alpha tocopherol, liver extract and local therapy with carbon dioxide, phenol and hydrocortisone ointment. Despite these measures there was slow progression of the dermatosis, with new lesions appearing on the trunk, arms, hands, face and scalp. Bullae were not observed at any time.

The patient had many subjective complaints from time to time, most of them referable to arthralgia and tenderness in the skin lesions. No evidence suggestive of disseminated lupus erythematosus ever was noted in pertinent laboratory studies. Approximately one month before admission, roentgenograms revealed a possible duodenal ulcer, for which the patient was given Donnatal. Five days before admission, chloroquine, 0.5 gm. daily, was given for the discoid lupus erythematosus.

Course in the hospital. All previous medications were discontinued upon admittance to hospital. The acute symptoms disappeared two days after admission and did not recur. The leukocyte content decreased to 9,000 per cu. mm. of blood the day following admission and results of all further laboratory examinations were within normal limits except for the presence of porphyrins in the urine. Data on urinary excretion of porphyrins by the patient (and, for controls, by members of his family) are summarized in Table 1. The patient was discharged from the hospital January 13, 1954, and thereafter worked regularly as a truck driver.

DISCUSSION

The diagnosis and classification of the disease in the case herein reported was puzzling until all the clinical features were evaluated. An adult with chronic scarring dermatosis who begins to excrete uroporphyrin would normally be considered to have porphyria of the cutanea tarda type, and this diagnosis was seriously entertained. However, it is believed that in the present case there were two diseases — chronic discoid lupus erythematosus and acute porphyria. The cutaneous lesions were typical clinically and histologically of chronic discoid lupus erythematosus. They occurred on other than exposed areas and were not produced by trauma or light, unlike the findings in porphyria cutanea tarda. There were no bullae noted during the six years this patient had been under observation. Similarly, there was no abnormal melanosis or hypertrichosis as is seen in patients with porphyria cutanea tarda.

The clinical features and laboratory data were also not those of porphyria cutanea tarda. There was sudden onset of systemic manifestations and early spontaneous remission. Uroporphyrin excretion occurred only during the acute episode and then was absent for a period of more than eight months during which the patient was under observation. Chronic hepatic damage, a regular finding in porphyria cutanea tarda, was not demonstrable.

Analysis for the various porpyhrins did not help to differentiate the specific type of porphyria. Porphyria cutanea tarda and acute intermittent porphyria are generally characterized by the excretion of uroporphyrin and a zinc porphyrin complex.[11] Classically, porphobilinogen is also regularly found in acute intermittent porphyria, but it has been reported in porphyria cutanea tarda.[3] In the present case uroporphyrin and the zinc porphyrin complex were excreted, but not porphobilinogen. Brunsting[3] stated that it is not possible to separate the clinical classes of porphyria on the basis of the laboratory studies of the urine and feces alone.

The occurrence of porphyria during the administration of a drug has been reported previously.[9, 15] In such instances it was concluded that the drug precipitated clinical manifestations of a latent inborn error in metabolism. There is increasing experimental evidence, however, that porphyria can be produced by a drug, *per se*. The excretion of uroporphyrin and syndromes closely resembling the two major types of porphyria have been produced in animals by the administration of Sedormid, phenylhydrazine and lead and ultraviolet light.[9, 12] Granting that in the majority of cases involving drugs, reported to date, the condition was owing to inborn errors of metabolism, it must be considered in the light of this recent evidence that porphyria can be produced in persons who have no such constitutional predisposition. The recognition of persons of this kind is therefore of more than academic interest because such reactions may be amenable to therapy, as are other drug reactions, and are of more favorable prognosis. In the patient reported upon herein there was no history or clinical evidence of any preexisting porphyria. It must, therefore, be considered that a drug was the etiologic agent in this patient.

The drugs he was taking at the onset of the attack of porphyria were Donnatal and chloroquine. The former is a combination of phenobarbital and the alkaloids of belladonna. Although porphyria following the ingestion of barbiturates has been reported,[3] it is not felt that the phenobarbital precipitated the attack in this patient because he had had phenobarbital on several occasions during the preceding years, had been taking the drug for one month before the onset of the attack, and took the drug after the attack with no untoward reaction. The most likely causative agent, therefore, would be the chloroquine that the patient received for just five days before the onset of the attack. Chloroquine is generally innocuous. The usual toxic symptoms are pruritus and mild gastrointestinal disturbances,[5] and there have been no previously reported instances of porphyria following administration of the drug. However, the timeliness of onset of porphyria makes it possible that chloroquine was of etiologic significance. Chloroquine was not readministered because of the possibility of severe consequences.

There appears to be no significant relationship between porphyria and lupus erythematosus. As was mentioned previously, there have been no recorded cases in which the two diseases occurred in one patient. The fact that the two diseases occurred simultaneously in this patient is merely coincidental and no common etiologic mechanism is evident.

SUMMARY

A case of acute porphyria in a patient with chronic discoid lupus erythematosus is reported. This is believed to be the first instance in which the two diseases occurred in the same patient. The possibility of drugs as causative agents in porphyria is pointed out and the role of a drug, chloroquine, in this case is discussed.

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Spontaneous Hematoma in the Rectus Abdominis Muscle

ROBERT H. KASS, *M.D.*, and
GLENN A. YOUNG, *M.D.*, Fresno

HEMATOMA of the rectus abdominis muscle is a definite clinical entity with more or less constant basic symptoms and physical features. It was accurately described by the ancient Greek physicians and since then has been mentioned periodically. The so-called "spontaneous" hematoma is not a rare occurrence but is sufficiently uncommon that most practitioners will not see a case during an entire career.

The condition is of interest, clinically, because it may closely simulate acute intra-abdominal disease. It is due to a rupture of the fibers of the rectus abdominis muscle or a tear in one of the epigastric vessels with hemorrhage into the sheath of the rectus muscle. It is usually unilateral and below the level of the umbilicus. Since the epigastric vessels are on the dorsal surface of the rectus muscle, bleeding occurs between the muscle and the posterior sheath above the fold of Douglas and between the muscle and the peritoneum below the fold. Brodel,[2] discussing the anatomic reason for this, noted that the lower one-third of the muscle is the most powerful portion and that greater changes in length occur there. Also, extramuscular branches of vessels are longer in the lower one-third to compensate for the excessive change in length.

Although the cause is often unknown, the condition tends to occur in the following three groups:

1. Persons with normal muscles. Here hemorrhage is due to muscular effort such as sudden violent movement, cough or sneeze.

2. Persons with disease or inanition of the muscles—particularly those with pendulous abdomens as in pregnant multiparous women.

3. Persons with advanced diseases of the blood vessels.

Wohlgemuth[7] collected reports of 127 cases prior to 1923. Of these, 107 were of traumatic origin; they occurred mostly in young males who were soldiers or athletes.

Teske[6] reviewed reports of 100 cases in the literature and himself reported a case. He noted the incidence was three times as great in men as in women. The etiologic factors in the cases he reviewed were as follows: Idiopathic, 53; associated with pregnancy, 22; traumatic, 19; associated with disease, 6. Ages of patients ranged from 17 to 83 years with the average 46.8 years. Pain was a symptom in 97 cases, mass in 78, tenderness in 71, rigidity in 49, nausea in 23 and vomiting in 15. In nearly all cases in which results of examination of the blood was reported there was an increase in leukocyte content. Platelet count, bleeding time and coagulation time were (in all cases in which reported) within normal limits.

Treatment consists of making an incision directly over the mass, evacuating the clot and ligating the bleeding vessels. If the hematoma has not extended through the peritoneum into the abdominal cavity and there is no indication for the exploration of abdominal viscera, the peritoneal cavity need not be opened. If the wound is clean and dry, closure may be done without drainage; but if there is much oozing of blood from the torn ends of muscle tissue, as is frequently the case, it is best to drain the wound. Prognosis is generally favorable.

In a survey by the authors of the literature on the subject only one case was found in which a blood dyscrasia was known to exist. It is for this reason alone that the following case is reported.

REPORT OF A CASE

The patient, a 26-year-old white man, was seen the evening of December 10, 1953, with complaint of abdominal pain of eleven hours' duration. He stated that as he was sitting in a truck eating lunch a mild constant pain developed and he noticed a tender mass in the right suprapubic area. He had no nausea or vomiting. A normal bowel movement occurred after the onset of the pain but the character of the pain was not changed. The pain and swelling increased gradually during the following six hours and then remained constant. The pain was made worse by lying down and was eased by sitting. There was no history of recent strain such as lifting, coughing or sneezing. There was no history of bleeding in the patient or his family.

Upon physical examination it was noted that there was a well healed incision just below the angle of the left scapula. Located to the right of the mid-line and extending from the pubis to just below the umbilicus was a fusiform, tender mass about 4 cm. in width at its inferior pole and widening to about 8 cm. at the upper pole. There was no other area of