Albinism and Sicklemia in a Negro Family*

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ALBINISM IN THE CAUCASIAN presents a well-recognized clinical picture that is unlikely to be overlooked. Although albinism in the negro is at least as striking and probably more common, it differs in many respects from the picture seen in the caucasian. These differences seem worthy of re-emphasis and are well illustrated in the family to be discussed. The simultaneous occurrence of sicklemia in this family provided an opportunity to study two inherited anomalies in the same family.

The propositus and available family members were carefully examined with reference to the color of the skin, hair, and eyes, and the presence of nystagmus, photophobia, or strabismus. In addition the following blood studies were carried out: complete blood counts, sickle cell preparations, hemoglobin electrophoresis, and fetal hemoglobin determinations.

CASE REPORT OF PROPOSITUS

E. B., (VUH # 247585), a 26 year old single female with negroid features, was referred to the Vanderbilt University Hospital by a vocational rehabilitation service because of extremely poor vision and anemia. The parents were typical negroes though of moderately light skin pigmentation. Since birth the patient had been "white" and had light yellow hair, pale gray eyes, and "twitching of the eyes." In school she was unable to compete with other children, and apparently because of poor vision only completed the fourth grade. For many years she had had recurrent ankle ulcers recalcitrant to therapy. The patient's family physician discovered anemia about four years prior to her Vanderbilt admission.

The patient was a very tall, thin female with a towering skull, long thin extremities, narrow hips, and arachnoidactily (figure 1). The skin presented a most striking appearance. There was virtually total absence of pigmentation of the skin, nipples, genitalia, and oral, pharyngeal, and nasal mucosa. There were no freckles. The skin over the neck, shoulders, arms, and hands was very thick, coarse, and wrinkled ("elephant skin"). The hair of the scalp and body was very pale yellow (virtually white), and the distribution was typically female.

The irises were very pale gray. The marked lateral nystagmus and extreme photophobia present prevented adequate funduscopic visualization. Vision was impaired and the patient could read only newspaper headlines. Examination of the heart revealed no remarkable findings. The liver and spleen were not palpable. The only other finding of note was the presence of an indolent ulcer 2 cm. in diameter just proximal to the internal malleolus of the left ankle. This particular ulcer had been present for approximately two years.

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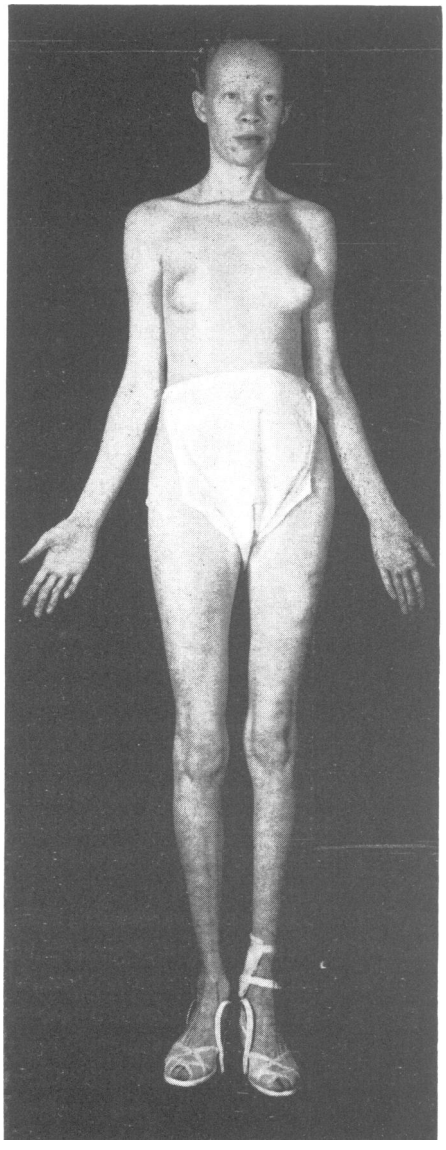

FIGURE 1. PROPOSITUS E. B. NOTE THE ABSENCE OF CUTANEOUS PIGMENTATION, THE DRESSING OVER THE ANKLE ULCER, AND THE HABITUS OF SICKLE CELL ANEMIA

The serological test for syphilis and routine urinalysis were negative. Blood counts were: volume of packed red cells 18 per cent, RBC 1.9 million per cmm., hgb. 6.5 grams per cent, reticulocytes 7.1 per cent, WBC 15,700 per cmm., and normal white cell differential count. Hemoglobin electrophoresis revealed a pattern of classical sickle cell anemia (SS). Fetal hemoglobin was 25 per cent.

FAMILY STUDY

Eleven members of the family including the mother, six siblings, one niece, and two nephews were available for the study. The father and one sister of the propositus were deceased. However, this sister's child was available for study. Consanguinity was denied. An additional niece and nephew were unavailable for examination. Statements were obtained from the mother of the propositus regarding skin, hair, and eye color as well as presence of photophobia and nystagmus in her deceased husband, father, mother, three sisters, and one brother. None of these was a definite albino although the mother's brother (uncle of propositus), and mother's parents (maternal grandparents of propositus) were "light-colored" negroes. The former was thought to have light gray eyes as well. In all, reliable information regarding albinism was obtained for four generations, and members of three generations were seen and examined for the presence of albinism and abnormal hemoglobin.

The four examples of albinism were the propositus, two siblings, and one niece. The propositus was the only individual examined who was homozygous for the sickle cell gene (classical sickle cell anemia, SS) although eight of ten remaining individuals were heterozygous (sickle cell trait, SA) for the abnormality. Two were normal (AA). All of the albinos were either homozygous or heterozygous for sicklemia. Only the

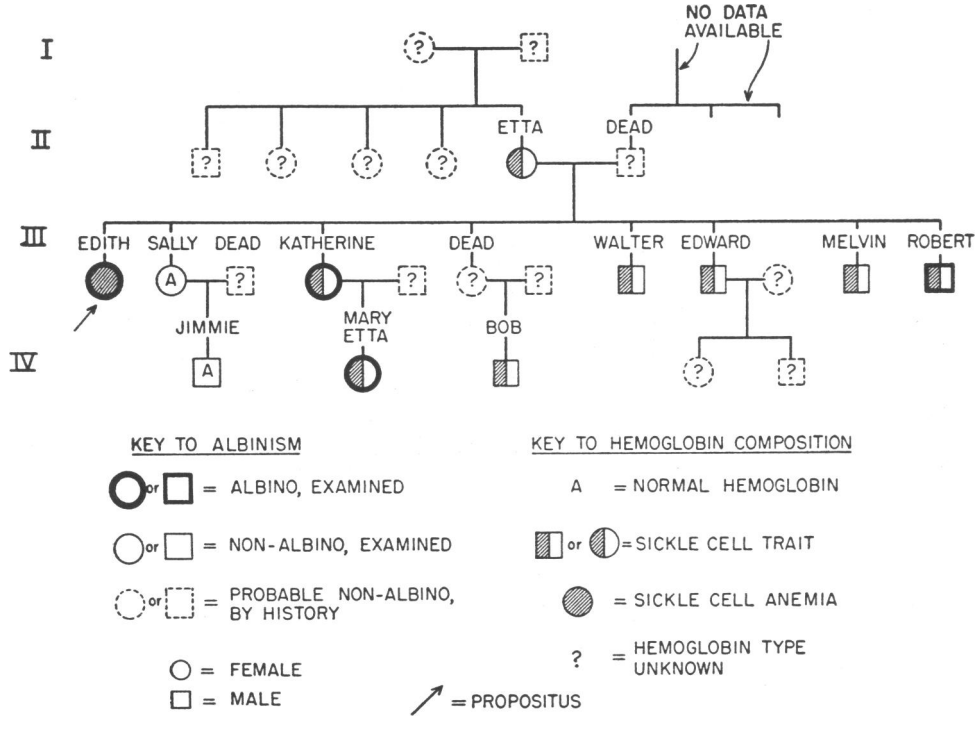

FIGURE 2. FAMILY TREE OF NEGRO FAMILY WITH ALBINISM AND SICKLEMIA. ONLY NAMED MEMBERS OF THE FAMILY WERE EXAMINED

TABLE 1. PHYSICAL CHARACTERISTICS AND LABORATORY STUDIES ON MEMBERS OF FAMILY AVAILABLE FOR EXAMINATION

Name and relationship to propositus	Color of skin	Color of eyes	Nystagmus	Volume of packed red cells—%	Sickle cell preparation	Hemoglobin electrophoretic pattern	Fetal hemoglobin
							%
1. Edith (propositus)	albino	very light gray	present	28	positive	SS	25
2. Etta (mother)	"very light"	gray	absent	43	positive	SA	<2
3. Sally (sister)	"light"	dark brown	absent	42	negative	A	<2
4. Katherine (sister)	albino	very light gray	present + strabismus	42	positive	SA	<2
5. Walter (brother)	"very light"	gray	absent	49	positive	SA	<2
6. Edward (brother)	"light"	dark brown	absent	49	positive	SA	<2
7. Melvin (brother)	"dark"	dark brown	absent	52	positive	SA	2.4
8. Robert (brother)	albino	very light gray	present + strabismus	41	positive	SA	<2
9. Jimmie (nephew) age 8	"dark"	dark brown	absent	42	negative	A	4.7
10. Mary Etta (niece)	albino	very light gray	present	39	positive	SA	<2
11. Bob (nephew)	"dark"	dark brown	absent	39	positive	SA	<2

propositus was anemic and had leg ulcers, body habitus, and other stigmata of sickle cell anemia. Figure 2 presents details of the family tree. Table 1 lists detailed observations on the family members studied.

The father of the albino female in generation IV (Mary Etta) is deceased. While no data is available as to his hemoglobin pattern, the description of his skin, eyes, hair, etc. given by his albino widow and the mother-in-law does not suggest albinism. The possibility of incestuous relationship to account for the albino in generation IV was denied. The albino mother (Katherine), her siblings, and her albino daughter (Mary Etta) are no longer available for further study regarding the occurrence of albinism in generation IV.

DISCUSSION

Albinism is considered to be an inherited disorder involving loss of cutaneous and mucosal pigmentation, ocular abnormalities, and frequent mental retardation (Musser, 1924). The inheritance pattern is thought to be a simple Mendelian recessive with the homozygous state therefore necessary for albinism to be manifest. The incidence has been reported to be 1 in 2900 in Italy, 1 in 9600 in Norway (McCrackin, 1937), and 1 in 144 in southwest Nigeria (Barnicot, 1952). Male and female appear

to be equally affected. Very extensive family data confirming these statements is included in Pearson, Nettleship, & Usher's monograph (Pearson et al, 1913).

In the negro the color of the skin may vary from virtual absence of pigmentation to a light tan color (Barnicot, 1952). Freckling is not uncommon (Musser, 1924; Barnicot, 1952). Thick, coarse wrinkled skin over exposed areas such as the face, neck, hands and arms, is almost universally present (Barnicot, 1952). In the family herein reported all four albinos had almost complete absence of skin pigmentation, and all had the "elephant skin" phenomenon. Freckling and areas of increased pigmentation are thought to be the result of overexposure to sunlight (Barnicot, 1952). This cutaneous change was not observed in our cases.

It has been claimed that there are no negro albinos with pink irises such as occur in caucasian albinos (Barnicot, 1952). In the negro the most common color has been gray, light blue, or rarely brown. All four cases observed in the present family had light gray eyes.

Nystagmus and photophobia are almost universally present (Barnicot, 1952), and were seen in our four cases. Strabismus is frequent in occurrence (Barnicot, 1952), and was present in two of our four albinos. The occurrence of partial albinism or semi-albinism has been postulated (McCrackin, 1937; Loewenthal, 1944). In this situation the skin color has been variously described as "yellow", "red", or "mulatto-like", the hair as reddish-brown or brown, and the irises as pale buff or definitely blue (McCrackin, 1937). The occurrence of nystagmus in partial albinism has been reported by some (Loewenthal, 1944) and denied by others (McCrackin, 1937). "White", "yellow", and "red" negroes appear not only in the same regions in Africa (Loewenthal, 1944) but in the same family (Turner, 1933). It has been stated that semi-albinos are likely to have a high incidence of albinos among their offspring.

The mode of inheritance of the abnormal hemoglobin in sickle cell trait and classical sickle cell anemia has been summarized by Neel (Neel, 1951). The presence of two well understood inherited anomalies in one family provides an excellent opportunity to study linkage. Each of the parents of the individuals of generation III is

TABLE 2. THE GENOTYPES OF THE LIVING OFFSPRING OF THE PARENTS OF GENERATION II AND THE NECESSITY (+) OR LACK OF NECESSITY (−) FOR CROSS-OVERS FOR THEIR DERIVATION, ASSUMING THE MATING IS (1) REPULSION X REPULSION, (2) REPULSION X COUPLING, (3) COUPLING X COUPLING (SEE TEXT FOR FURTHER EXPLANATION)

Genotype of child	Sex	Assumed mating 1	2	3
1. SS cc	F	−	+	+, +
2. ss C	F	−	−	+
3. Ss cc	F	+	−	+
4. Ss C	M	−	−	−
5. Ss C	M	−	−	−
6. Ss C	M	−	−	−
7. Ss cc	M	+	−	+

Note: c = gene for albinism
S = gene for sickle hemoglobin

doubly heterozygous. If the genes are linked they may, in each parent (generation II), be in coupling or in repulsion, giving rise to three possible types of mating. As follows:

(1) $\frac{Sc}{sC} \times \frac{Sc}{sC}$

(2) $\frac{Sc}{sC} \times \frac{SC}{sc}$ c = gene for albinism
S = gene for sickle hemoglobin

(3) $\frac{SC}{sc} \times \frac{SC}{sc}$

Table 2 shows the genotypes of each of the surviving offspring and whether or not a cross-over is required for a child's genotype to have been derived from the assumed cross. It is clear that at least one cross-over is required to explain the genotypes of the seven children comprising generation III regardless of the true genotype of the parents. Hence the data exclude absolute linkage. Looser linkage, of course, remains a possibility. Considerably more data will be required to exclude this possibility.

SUMMARY

A negro family with four albinos, one with classical sickle cell anemia and three with sickle cell trait, is reported. The physical characteristics of negro albinos are discussed and contrasted with those seen in the caucasian albino. The present study demonstrates that if the hypothesis of simple Mendelian recessive inheritance in albinism is correct, absolute linkage between the genes for albinism and for sicklemia does not occur, but looser linkage is possible.

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