blood

To the editor:

Case series of octogenarians with sickle cell disease

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Survival of patients with sickle cell disease (SCD) has increased progressively since the 1980s.[1-5] Patients with SCD in their sixth or seventh decade have been described previously.[6] This report describes 4 patients with SCD who survived beyond the age of 80 years. Three of these were US citizens enrolled in the Sickle Cell Center of Thomas Jefferson University. The center and all its projects were approved by the institutional review board (IRB). The report of the fourth Brazilian patient was approved by the IRB of the Instituto Estadual de Hematologia Arthur de Siqueira Cavalcanti. Table 1 lists the demographic and clinical characteristics of these patients, and Table 2 shows their most recent (within 3-5 years) key laboratory data at a time when they were in a stable steady state.

Old age in the general population usually refers to life expectancy of people beyond what is presumed to be the life expectancy of human beings. Specific numbers that define old age, however, vary greatly among countries, cultures, habitats, and social sciences. Thus, there are official definitions, popular definitions, subgroup definitions, and so forth. Gerontologists define subgroups in a number of ways[7,8]; however, the subgroup definitions that seem to be in common use are young-old (65-74 years), middle- or older-old (75-84 years), and oldest-old (≥85 years).[8] Using these definitions, 3 of our patients are older-old and 1 is oldest-old. These definitions may replace those that are categorized by age measured in decades, such as quinquagenarian (50-59 years).

Table 1. Demographic and clinical data of octogenarians with sickle cell disease

	Patient A	Patient B	Patient C	Patient D
Age/sex	82/F	86/F	82/F	82/F
Ancestry	African American	Italian American	African American	African Brazilian
Obstetrical history*	$G_3P_1A_2$	$G_2P_1A_1$	G_5P_5	G_2P_2
Diagnosis	SS	SS	Hb SC disease	Hb SC disease
VOCs/y	1-2	0-1	0-3	0-1
Cerebrovascular accident	No	No	No	No
Retinopathy	Yes	Yes	No	No
Cataracts	Yes	Yes, OU	No	Yes, OS
Deafness	No	No	No	Yes, left ear
ACS	No	No	No	Yes
Congestive heart failure	Yes	Yes	No	No
Hypertension	Yes	No	Yes	Yes
Avascular necrosis	Yes + right hip replacement	Yes + replacement of both hips and right knee	No	No
Leg ulcer	Yes	Yes	No	No
Splenomegaly	No	No	Yes	Yes
Cholecystectomy	Yes	No	Yes	No
Infection	Tuberculosis, pneumonia	Urinary tract infection	*Clostridium difficile* colitis	Tuberculosis
Transfusion	Frequent	Occasional	Occasional	Frequent
Iron overload	Yes	No	No	Yes
Comorbidity	Complete heart block, glaucoma OU, mild Parkinson disease	Paroxysmal AFIB, IBS, MVP, osteoporosis	Osteoma of mandible, depression	Diabetes mellitus type 2
Smoking	No	No	No	No
Alcohol	No	Occasional	No	Occasional
Body mass index	21.6	20.4	24.8	23.1
Compliance	Excellent	Excellent	Excellent	Excellent
Family support	Excellent	Excellent	Excellent	Excellent
Status	Alive	Deceased	Deceased	Deceased
Cause of death	N/A	Cardiac complications	Unknown	ACS + septicemia

A, abortus; ACS, acute chest syndrome; AFIB, Atrial fibrillation; F, female; G, gravidity; Hb SC, sickle cell–hemoglobin C; IBS, irritable bowel syndrome; MVP, mitral valve prolapse; N/A, not applicable; OS, oculus sinister; OU, oculus uterque; P, parity; SS, sickle cell anemia; VOCs, vaso-occlusive crises.

*Reported using the gravida/para/abortus system.

Table 2. Laboratory data in the patients reported

Test	Patient A	Patient B	Patient C	Patient D
Hb, g/dL	8.1	8.6	9.4	7.8
Hematocrit, %	24.4	26.4	27.3	23.2
MCV, fL	90	93	81	82
Reticulocytes, %	11.2	9.1	5.8	2.4
WBC, 10^9/L	8.6	7.8	6.8	6.5
Platelets, 10^9/L	243	238	229	125
Hb F, %	12	8.8	1.8	2
Ferritin, ng/mL	2660	464	101	1250
Creatinine, mg/dL	1.1	1.2	0.8	1.6
ALT, IU/L	10	12	10	25
AST, IU/L	27	25	14	26
LDH, IU/L	ND	322	243	154
Total bilirubin, mg/dL	1.7	1.5	0.6	1.0
ALK, IU/L	53	93	96	103
UA, mg/dL	ND	5.7	3.0	6.8
α-Genes	3	3	4	ND
β^s-Haplotype	BEN/BEN	BEN/BEN	BEN/CTYPE 1	ND

ALK, alkaline phosphatase; ALT, alanine aminotransaminase; AST, aspartate aminotransferase; BEN, Benin; Hb, hemoglobin; LDH, lactate dehydrogenase; MCV, mean corpuscular volume; ND, not done; UA, uric acid; WBC, white blood cell count.

Analysis of the data in Tables 1 and 2 shows expected and unexpected features of SCD and identifies certain parameters that may contribute to longevity. Although our report of 4 patients over the age of 80 years is anecdotal in nature, certain demographic and clinical features are unusual. In comparison, a previous prospective study in patients enrolled in the Sickle Cell Center at Jefferson showed that the mean age of death of 17 women with SS who died during 5 years of observation was 39.1 ± 14.87 years.[9] The cohort of patients with Hb SC disease at Jefferson included 172 men and women. Twenty-one (12%) of those patients were women who died at a mean age of 49.6 ± 13.22 years. In one Brazilian institution, the mean age of women with Hb SC disease at death was 28.15 ± 9.11 years (Instituto Estadual de Hematologia Arthur de Siqueira Cavalcanti, unpublished data).

The obvious feature is that all described patients are women. Sex is known to influence longevity both in the general population and in patients with SCD. Previous studies showed that the mortality rate in children with SCD is similar for boys and girls.[10-13] The divergence in the mortality rate between the sexes in favor of females becomes apparent in adults.[4,10] The reason why adult women with SCD live longer than men is not known. One possibility is relatively lower blood viscosity due to lower Hb and hematocrit levels in women.

Some of the features our patients had are known to be associated with good prognosis. These include the infrequent VOCs that required hospitalization; no history of strokes; no previous history of ACS, except in the Brazilian patient; low white blood cell count; low hemoglobin level; and normal biochemical parameters.

Another common feature in our patients is that none of them was on hydroxyurea (HU) because none met the inclusion criterion of at least 3 VOCs that required hospitalization in the immediate previous year and because HU is not approved for Hb SC disease. Nevertheless, the Hb F levels (12% in patient A and 8.8% in patient B) are relatively high. The beneficial cutoff level of Hb F has not been well determined and verified. The primary end point of the Multicenter Study of Hydroxyurea in Sickle Cell Anemia (MSH) was not the level of Hb F but the frequency of VOCs.[14] Two years after starting HU in the MSH study, the mean Hb F level in the HU group was 8.6% ± 6.8 compared with 4.7% ± 3.3 ($P = .0001$) in the placebo group.[15] It is generally believed, however, that the higher the level of Hb F, the milder the SCD. Platt et al[2] analyzed the risk factors for death in patients with SS in the Cooperative Study of Sickle Cell Disease and found that SS patients with Hb F levels >8.6% had better survival than those with Hb F levels <8.6%. It should be noted that the Hb F levels in patients A and B (Table 2) are the average of previous recent determinations. Higher Hb F levels are often seen in younger years (eg, the Hb F level of patient B was 12.2% when she was 64 years old), and Hb F levels and leukocyte counts are known to decrease with age.[1] Accordingly, the relatively high endogenous levels of Hb F in patients A and B may have contributed to their longevity.

The utilization of blood transfusion differed among the 4 patients. Patient A received blood transfusion to keep her Hb level >7 g/dL due to her cardiac complications. She developed iron overload treated with deferasirox that was later discontinued due to an increase in serum creatinine level. Patient B refused blood transfusion unless it was absolutely necessary. Patient C had a Hb level of >9 g/dL and rarely required blood transfusion. The diagnosis of Hb SC disease in patient D was made at the age of 76 years when she presented with severe symptomatic anemia with a Hb level of 6 g/dL. Workup of the anemia revealed Hb SC disease, and she was started on simple transfusion. Within a few months, she developed ACS and was placed on chronic blood transfusion. Later, she developed the second episode of ACS, which was fatal.

Another common feature among the 4 patients is the family support and adherence to medication intake, appointments, and referrals. This adherence was based on the observations of the many providers they had, including the authors.

In addition to the common features, each patient had specific favorable lifestyle factors in addition to those mentioned in Table 1. Patient A is married, and her husband is highly supportive. Although Patient B was a widow for several years before her death, her son was very supportive. Patient C was a widow with five children; her oldest daughter was very supportive. Patient D was married and had two daughters who lived with her and took excellent care of her.

Despite the longevity of these patients, they did suffer from complications of their disease and from serious comorbidities, shown in Table 1. Comorbidities encompass both sickle and nonsickle complications that may emerge in older age. Over 20 comorbidities affecting patients with SCD have been described.[16] Cognizance of the complexity of SCD and its polymorbidities and the implementation of preventative, educational, counseling, and prompt intervention measures may ameliorate the associated complexities of the disease and improve the quality of life of its victims.

In summary, the patients described had similar desirable features of SCD, despite their different ancestries, cultures, and countries. Their lifestyle of no smoking, no or occasional alcohol, normal body mass index, compliance, and excellent family support were, most likely, important contributors to their longevity. All these factors taken together indicate that these 4 women may provide a blueprint of how to live a long life, despite having a serious medical condition like SCD.

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