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CASE REPORT

Hb J-Guantanamo: a Rare Hemoglobin Variant Identified in Morocco Following Unexpected HbA1c Results

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ABSTRACT

Background: **While hemoglobin variants are common worldwide, many remain undetected due to their silent clinical expression. Some, however, may compromise the reliability of diagnostic markers such as HbA1c. We report a rare β-globin variant, hemoglobin J-Guantanamo, identified in Morocco.**
Methods: **A hemoglobin variant was incidentally discovered in a 59-year-old patient during hemoglobin A1c measurement. Multiple phenotypic methods were employed for characterization, including capillary electrophoresis, high-performance liquid chromatography, and hemoglobin gel electrophoresis.**
Results: **Based on the concordance of phenotypic findings, the variant was identified as Hb J-Guantanamo. Although the patient remained asymptomatic with no hematologic abnormalities, the variant interfered with HbA1c measurement, highlighting its potential impact on diabetes monitoring.**
Conclusions: **This case underscores the diagnostic challenges associated with rare hemoglobin variants, emphasizes the necessity of multiple analytical methods for accurate identification, and contributes to the limited data on hemoglobinopathies in Morocco.**
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KEYWORDS

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INTRODUCTION

Hemoglobin (Hb) abnormalities may result either from a reduced synthesis of one of the globin chains or from structural alterations. Point mutations represent the most common cause of Hb variants, the majority of which are clinically benign [1]. However, in certain cases, they may lead to severe disorders such as sickle cell disease or thalassemia [2]. In Morocco, while well-known variants such as Hb S and Hb C have been extensively studied, the overall genetic diversity of hemoglobins remains underexplored [3]. Among the underreported hemoglobin variants, many are clinically silent but may nonetheless interfere with laboratory analyses, particularly the quantification of glycated hemoglobin (Hb-

Table 1. Biological parameters of the Patient.

Parameter	Result	Normal value
Red blood cell count (10^6/µL)	5.25	3.9 - 5.5
Hemoglobin (g/dL)	15.3	13 - 17
Hematocrit (%)	46.7	41 - 53
Mean Corpuscular Volume (fL)	84.6	82 - 98
Mean Corpuscular Hemoglobin (pg)	27.7	27 - 33
C-reactive protein (mg/L)	< 1	< 5.0
Ferritin (ng/mL)	17	23.9 - 336.2
Total Bilirubin (mg/L)	5	3 - 10
Lactate dehydrogenase (UI/L)	179	125 - 243
Fasting plasma glucose (g/L)	1.49	0.7 - 1.05

A1c) [4]. In this context, hemoglobin J-Guantanamo serves as a notable example. It is a rare variant that remains poorly documented in Morocco. It was first identified in Guantanamo, Cuba, from which its name is derived, and has been sporadically reported in other countries, including China, Benin, Chile, and Japan [5].
Hemoglobin variants are often detected incidentally, particularly during HbA1c measurement [6]. The recommended approach for their identification involves combining high-performance liquid chromatography (HPLC), capillary electrophoresis (CE), and, when possible, isoelectric focusing (IEF). In more complex cases, molecular biology techniques may be required [7]. In our case, based on phenotypic analysis, the presence of a heterozygous Hb J-Guantanamo variant was demonstrated.

CASE PRESENTATION

We report the case of a 59-year-old Moroccan patient, known to be HIV-positive since 2016 and maintained on regular antiretroviral therapy with consistent clinical follow-up. The patient had no significant medical or surgical history and no known family history of hematological disorders.
As part of a routine metabolic screening, the patient underwent laboratory testing, including HbA1c measurement, a complete blood count (CBC), and a standard biochemical panel. The results showed no significant abnormalities, except for an elevated fasting blood glucose level of 1.49 g/L (Table 1). However, the HbA1c assay yielded an unexpected finding, which prompted additional investigations.
HbA1c measurement by capillary electrophoresis, using the CAPILLARYS 3 OCTA system (Sebia®), revealed a distinct peak located between the HbA1c and HbA0 fractions, accompanied by a baseline shift (Figure 1A). Similarly, hemoglobin analysis by high-performance liquid chromatography (HPLC), performed with the ADAMS A1c HA-8180T system (Arkray®), showed a significant abnormal peak accounting for 26% of total hemoglobin, eluting just before the HbA0 peak, with a retention time of 0.85 minutes (Figure 1B).
This abnormal peak interfered with HbA1c quantification, rendering the assay uninterpretable. As a result, accurate assessment and monitoring of glycemic control using HbA1c proved impossible, highlighting the clinical relevance of this variant.
Alkaline pH capillary electrophoresis, performed using the CAPILLARYS 3 OCTA system (Sebia®), confirmed the presence of an abnormal hemoglobin fraction migrating just before the HbA0 zone, specifically in zone 11, and was also associated with a baseline shift (Figure 1C).
Acid pH gel electrophoresis of hemoglobin, carried out with the Hydrasys 2 Scan system (Sebia®), revealed a variant band located below the HbA band (Figure 1D). Based on the concordance of findings obtained through the various phenotypic methods, the variant was identified as consistent with hemoglobin J-Guantanamo.
During follow-up, the patient remained hematologically asymptomatic, with no evidence of anemia or hemolysis. Although clinically silent, the hemoglobinopathy significantly interfered with HbA1c measurement, highlighting the importance of considering such variants in the context of diabetes diagnosis and management.

DISCUSSION

Hb J-Guantanamo is a rare variant of the beta-globin chain of hemoglobin. It was first identified in 1977 in a pregnant woman of African descent living in Cuba [8]. Subsequently, cases were reported in China in 1985, Benin in 1988, Chile in 1990, and Japan in 1993. To date, only one case of the J-Guantanamo variant has been reported in Morocco [9,5].

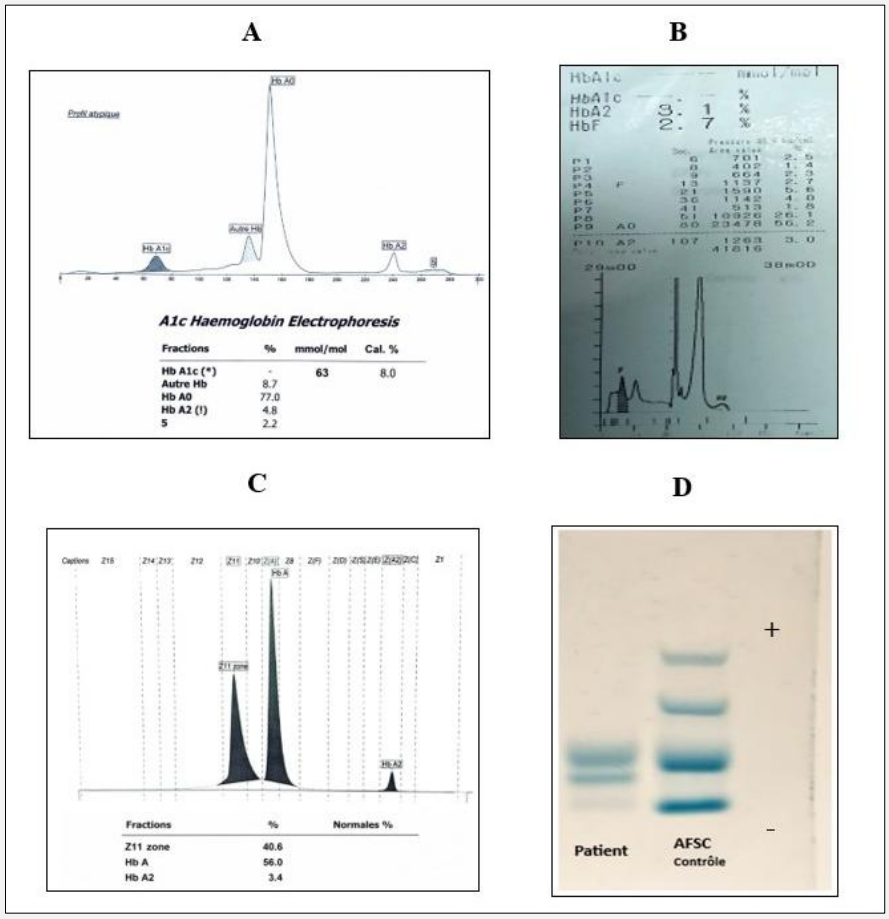

Figure 1.

A: HbA1c electrophoresis trace generated by the Sebia CAPILLARYS OCTA 3 system. HbA1c mode.
B: HPLC chromatogram. Arkray ADAMS A1c HA-8180T automated analyzer.
C: Alkaline pH hemoglobin electrophoresis trace. Sebia CAPILLARYS OCTA 3 system.
D: Acid hemoglobin electrophoresis trace. Sebia HYDRASYS system.

This variant results from the substitution of an alanine (Ala) residue with an aspartic acid (Asp) residue at position 128. This position is particularly important, as it is involved in the contact between the α1 and β1 subunits of the hemoglobin tetramer [10].

The J-Guantanamo variant is characterized by mild hemoglobin instability, which in heterozygous cases reported in Cuba and Benin manifested as moderate hemolytic anemia, slight reticulocytosis, and morphological abnormalities, notably the presence of target cells in peripheral blood [8,9]. Nevertheless, the other heterozygous forms described in the literature are generally asymptomatic and show no hematological abnormalities. To date, no documented homozygous case has been reported in the medical literature.

Without clinical signs suggestive of hemoglobinopathy, hemoglobin variants are often discovered incidentally. In our case, the variant was initially detected through HbA1c measurement using capillary electrophoresis, a technique recognized for its high resolution in hemoglobin analysis. This method enables precise quantification of HbA1c as well as the detection of Hb F, Hb A2, and various hemoglobin variants [11]. In the present case, Hb J-Guantanamo was identified, producing a variant peak that eluted between the HbA1c and HbA0 peaks, thereby interfering with the automated calculation of HbA1c [5].

Capillary electrophoresis at alkaline pH is a widely used method for detecting hemoglobin variants, offering clear and easily interpretable profiles. Automated identification of the HbA fraction is followed by zone adjustment based on the electrophoretic migration pattern

[12]. In this regard, a study by Ouzzif et al. demonstrated that Hb J-Guantanamo migrates rapidly and is located in zone 11, ahead of HbA. The study also showed that, under acidic pH electrophoresis, the variant appears as a narrow band migrating between the HbA and HbF fractions [5].

Literature data on high-performance liquid chromatography (HPLC) retention times for Hb J-Guantanamo remain highly variable. The previously reported Moroccan case showed a retention time (Rt) of 0.31 minutes, compared to 0.85 minutes in our case. The chromatogram presented by Ouzzif et al. showed Hb J-Guantanamo eluting just before HbA0, which is consistent with our findings [5].

A thorough understanding of the clinical context, combined with hematological and biochemical examinations, and particularly with phenotypic analysis of hemoglobin, can greatly aid in achieving an accurate diagnosis. However, in cases involving rare variants, genotypic analysis may sometimes be necessary for more detailed characterization.

CONCLUSION

This study highlights the importance of combining various laboratory techniques-such as high-performance liquid chromatography (HPLC), capillary electrophoresis (CE), and electrophoresis at both alkaline and acidic pH-for the accurate identification of rare hemoglobinopathies.

Given the diagnostic challenges these variants may pose, their recognition and the awareness of clinicians regarding their potential impact are essential in the context of metabolic and hematological evaluations.

This is the second reported case of this variant in Morocco, thereby providing valuable insight into the genetic diversity of hemoglobinopathies in the region. Moreover, this observation raises questions regarding the precise geographic distribution of hemoglobin J-Guantanamo and the possible existence of a genetic or historical link between this variant and the Moroccan population.

Declaration of Generative AI in Scientific Writing:
None.

Declaration of Interest:
None.

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