Int J Legal Med (2004) 118 : 95–97
DOI 10.1007/s00414-003-0412-5

CASE REPORT

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Sudden death due to a haemoglobin variant

Received: 28 May 2003 / Accepted: 14 October 2003 / Published online: 21 November 2003

Abstract A previous healthy 35-year-old man was found dead in his truck. Shortly before death he merely complained of influenza-like symptoms. The histological examination revealed evidence of a massive accumulation of sickle cells in smaller blood vessels. After molecular genetic analysis, the preliminary diagnosis of "sickle cell disease" was finally changed to the diagnosis of a sickle cell trait. It is presumed that an epileptic attack which also has to be considered as a concurring cause of death, precipitated sickling of the erythrocytes and led to a fatal sickle cell crisis.

Keywords Sickle cell trait · Sudden death · Forensic pathology

Introduction

Genetic diseases, in particular heterozygous forms, are often clinically inapparent and may be verified exclusively by molecular genetic investigations [1, 2, 14]. In contrast to the homozygous form of sickle cell disease (SS haemoglobinopathy), in the heterozygous form or sickle cell trait, only one of the beta globin genes is affected (AS haemoglobinopathy) [9]. As people with sickle cell trait have no sickle cells under normal conditions and therefore show no increased hospitalisation or mortality rates compared to people without the trait, it is not widely recognised as a cause of life-threatening illness or death [15]. However, sudden deaths due to sickle cell crises of individuals with sickle cell trait have been described repeatedly [3, 4, 6, 7, 8, 10, 11, 12, 13, 15]. Physical activity with exertional rhabdomyolysis as well as pathological processes such as heat stress, hypoxic stress, viral illness and poor physical condition that may cause hypoxia, acidosis, dehydration, hyperosmolality, hypothermia or elevated erythrocyte 2,3-diphosphoglycerate (DPG) levels, all of which may transform the silent sickle cell trait into a syndrome resembling sickle cell disease and therefore may contribute to development of a sickle cell crisis [10, 13, 15].

Sickling of erythrocytes leads to vascular obstruction, vasoconstriction, disseminated intravascular coagulation and local tissue damage [7], resulting in pain, renal failure, splenic infarction, muscle damage or sometimes in sudden death due to cerebral and cardiac ischemia [5, 8, 15].

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Case report

A 35-year-old Turkish truck driver was found dead in his truck after he had left his colleague half an hour before. In the morning he had merely complained of influenza-like symptoms and had taken antipyretic, antimicrobial and antiviral medicines such as Aspirin (acetylsalicylic acid), Sobelin (clindamycine), Dolomo (acetylsalicylic acid, caffeine and paracetamol), Grippin (amantadin=antiviral substance) and Panalgine (paracetamol). Serious dyscrasias were not known in his medical history.

Macroscopic findings

Autopsy showed an acute haemostasis of the parenchymatous organs, cerebral and lung edema, minute erosions of the stomach mucosa as well as localised bleeding in the glossa compatible with a lesion caused by biting. Furthermore there were signs of chronic haemostasis of liver and spleen and a slight endocardial fibrosis of the right heart.

Toxicological findings

Except for small quantities of paracetamol, codeine, diclofenac and metabolites of carbamazepine, toxicological findings were negative.

Histological findings

Histological investigations showed haemostasis of all organs. In the smaller blood vessels and capillary vessels of internal organs, a massive accumulation of sickle cells, which completely filled the lumina, was obvious (Fig. 1a,b).

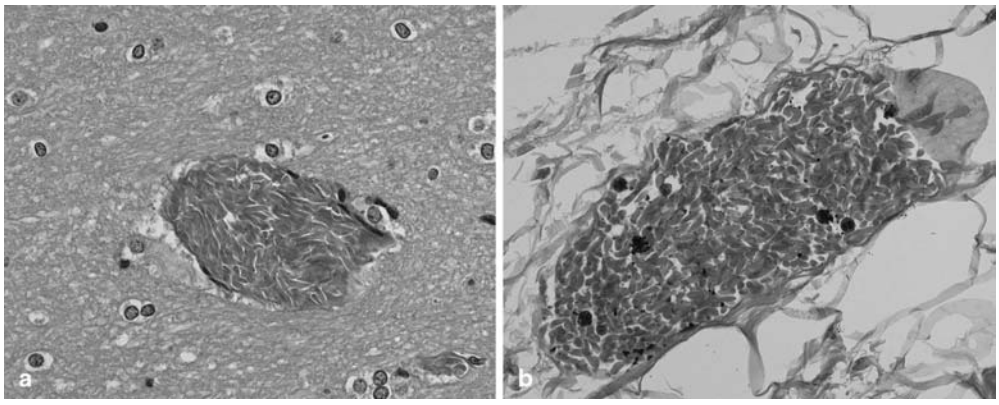

Fig. 1 Accumulation of sickle cells in blood vessels of the cerebrum **a** as well as in the left heart ventricle **b** (HE, magnification ×380)

Table 1 Molecular genetic analysis of the beta globin gene, codon 6 (performed by the Institute of Human Genetics, University of Münster, Germany)

	Allele 1	Allele 2
	β A	β S
Codon 6	Wild type	A >T
Finding	Heterozygous for HbS	

β A normal allele.
β S sickle cell allele.

Further findings were cerebral and lung oedema, minimal inflammatory infiltrations in the liver and heart, a slight fatty tissue ingrowth in the muscle of the right heart ventricle, a moderate hypertrophy of the left heart muscle and small erosions of the stomach lining.

Molecular genetic analysis

The molecular genetic analysis was carried out at the Institute of Human Genetics, University of Münster, Germany and showed a heterozygosity for HbS, which led to the diagnosis of a sickle cell trait (Table 1).

Discussion

Sickle cell disease is a haemoglobinopathy caused by a base substitution in codon 6 (GAG→GTG) of the beta globin gene, resulting in the replacement of glutamine by valine. In deoxidation, intracellular haemoglobin is transformed from a soluble into a gelatinous state with oriented structures and the red blood cells take on the rigid sickle cell form that leads to a disturbed capillary passage. Compared to the homozygous sickle cell disease, the oxygen tension that leads to a sickling of erythrocytes is very low in sickle cell trait, the heterozygous form of sickle cell disease.

Although the clinical course of sickle cell trait is mostly inapparent, the coincidence with conditions such as heat stress, dehydration, viral illness or poor physical condition as well as physical activity, may lead to major complications, like the symptoms of the homozygous form of sickle cell disease.

As a result of lower oxygen tension, the red blood cells transform to a sickle cell form, which leads to a haemostasis in the capillary vessels. The increasing deoxygenation of the red blood cells results in a conversion of more and more erythrocytes into the sickle cell form, a vicious circle resulting in vascular occlusion as the final state.

The fact that individuals with sickle cell trait show an unremarkable medical history for decades seems to be typical for this disease. Most of the published cases deal with well-conditioned, apparently healthy people who suddenly died under conditions of stress; typically, the sickle cell trait was diagnosed postmortem [8, 10, 15].

In the presented case, the stimulus for the sickle cell crisis might have been multifold. Besides a poor physical condition, which the man had complained of some hours before his death, the carbamazepine found in the blood sample and the little morsus in the glossa make it conceivable that an epileptic attack led to a hypoxic state and therefore was the trigger for the transformation of erythrocytes to the sickle cell state.

Knowing the results of all analyses, this case of a sudden unexpected death can be explained by an acute sickle cell crisis with obstruction and occlusion of smaller blood vessels and capillary vessels by sickled erythrocytes, leading to ischemia of the internal organs. The cerebral hypoxia led to a cerebral oedema, and the cardiac ischemia might have caused arrhythmias, resulting in lung oedema and in congestion of the internal organs that were found at autopsy. Despite the fact that a prolonged seizure attack could be considered not only the trigger for sickling of erythrocytes but also as a concurring cause of death, it has to be kept in mind that the sickle cell trait must be viewed as a potentially fatal disorder [15].

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