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HYPERGLYCEMIC HYPEROSMOLAR NONKETOTIC SYNDROME: A SERIES OF CASES

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Abstract: Hyperglycemic hyperosmolar nonketotic syndrome (HHNKS) is a rare acute complication of type 2 diabetes, which is often the first symptom of the disease. HHNKS is characterized by a high mortality rate (5-20%; according to other sources – 17-50%). Therefore, this topic is of particular relevance when studying the causes of sudden, unexplained death. The aim of this paper is to analyze deaths associated with the hyperglycemic hyperosmolar nonketotic syndrome (HHNKS) and to overview the relevant literature.

Keywords: Hyperglycemic hyperosmolar nonketotic syndrome, sudden death, hyperglycemia, autopsy.

INTRODUCTION

Hyperglycemic hyperosmolar nonketotic syndrome (HHNKS) is a life-threatening clinical condition that occurs as a complication of diabetes. It is most commonly associated with type 2 diabetes but rarely occurs in type 1 diabetes [1]. HHNKS is characterized by severe hyperglycemia, hyperosmolality, and dehydration in the absence of significant ketoacidosis [3]. The disorder was first described in 1880 by Won Frerichs and Dreschfeld. It has been observed that some patients with diabetes and profound hyperglycemia and glucosuria do not have the classic Kussmaul breathing and do not have detectable ketones in the urine, which is common in diabetic ketoacidosis [1].

HHNKS is rare, occurring in only 1% of all diabetes hospitalizations [1, 13], but has a high mortality rate (5-20%, other sources suggest – 17-50%) [2, 9]. This is 10 times higher (1.2-9 times higher according to other sources [14]) than in diabetic ketoacidosis [1]. The high mortality from this syndrome is due to the development of vascular changes such as myocardial infarction, stroke, or thrombosis of peripheral arteries and veins. Neurological complications such as cerebral edema and osmotic demyelination syndrome are also associated with this syndrome [12]. HHNKS is a life-threatening syndrome and there is still a lack of scientific research on this issue.

METHODS

SFMS Vilnius Division retrospective analysis of impersonal data, patients who died suddenly and were diagnosed with hyperglycemia at autopsy. In all selected cases, an autopsy was performed, and a toxicological test of the body's internal environment for alcohol and glucose levels was performed. Cases with advanced decay were excluded.

RESULTS

A series of 9 cases were analyzed, all patients were under 50 years of age. All of these patients had no history of hyperglycemia in their medical records, with only severe hyperglycemia diagnosed post-mortem. Patient characteristics and post-mortem examination data are presented in Table 1.

Patient 1

The body of a 44-year-old female, delivered from her home, was examined. The context of the task states that she had not been to the doctors and had no history of any illnesses. Later, the circumstances were clarified: the sources from the patient's close circle informed that for about a year before her death, she had complained of weight fluctuations, was in a depressed and upset mood, felt weak and "lack of strength". She noticed that her eyes "bulged out". The cause of death

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was unknown. The initial suspected cause of death by the forensic doctors was tanatogenesis.

On post-mortem examination, the external findings were only marked eyelid edema. Internal examination revealed thyroid lobes 9x6x4 cm, with multiple small nodules in sections, and a heart weight of 505 g (normal 148-296 g [4]). The liver was fatty, its weight was 2450 g (normal 603-1767 g [5]), the right lung weighed 585 g (normal 142-835 g [5]), the left lung weighed 430 g (normal 108-736 g [5]). The brain weighed 1090 g (normal 1033-1404 g [5]), gyri and sulci were straight. Additional tests showed a minimum ethyl alcohol concentration of 0,80‰ (promille) in blood. However, the plasma glucose concentration was found to be more than 33.3 mmol/l (normal 4.0-6.0 mmol/l [7]).

Given that the diagnosis of catamnesis was unclear and not well known, the primary diagnosis, based on the International Classification of Diseases (ICD), was E74.9 Carbohydrate metabolism disorder, unspecified.

Patient 2

A young male with type 1 diabetes aged 22 years was examined. Post-mortem internal examination revealed a right lung mass of 120 g (normal 185-967 g [6]), a left lung mass of 460 g (normal 186-885 g [6]), and a brain mass of 1390 g (normal 1070-1767 g [6]). Fatty liver was detected. Additional tests revealed acetonuria, plasma glucose levels were found to be above 33.3 mmol/l (normal 4.0 - 6.0 mmol/l [7]).

Patient 3

21-year-old female. Post-mortem internal examination revealed a right lung mass of 634 g (normal 142-835 g [5]), a left lung mass of 645 g (normal 108-736 g [5]), and a brain mass of 1750 g (normal 1033-1404 g [5]). Fatty liver was detected. Additional tests showed a plasma glucose concentration of 32.9 mmol/l (normal 4.0-6.0 mmol/l [7]). The primary diagnosis is unspecified carbohydrate metabolism disorder, E74.9.

Patient 4

29-year-old female. Fatty liver was detected. Plasma glucose concentration was found to be above 33.3 mmol/l (normal 4.0-6.0 mmol/l [7]). The primary diagnosis is unspecified carbohydrate metabolism disorder, E74.9.

Patient 5

A 35-year-old female died of asphyxiation due to compression of the neck. Internal examination revealed a right lung mass of 405 g (normal 142-835 g [5]), a left lung mass of 351 g (normal 108-736 g [5]), and a brain mass of 1305 g (normal 1033-1404 g [5]). Plasma glucose concentration was found to be above 33.3 mmol/l (normal 4.0-6.0 mmol/l [7]).

Patient 6

A 20-year-old car driver who suffered a fatal

Table 1.

No.	Gender	Age	Primary diagnosis	Comorbid pathology	[GL]	Alcohol in blood	Alcohol in urine	Acetone in urine	Toxicological test
1	F	44	E74.9	HCM, AA grade II 3, Fatty liver, AS grade II 25 stenosis	**33.3**	0.80	-	-	-
2	M	22	Type 1 diabetes	Fatty liver, TBC, IHD	**33.3**	0	0	0.83	not found
3	F	21	E74.9	Fatty liver	**32.9**	0	-	-	not found
4	F	29	E74.9	Fatty liver	**33.3**	0	0	-	not found
5	F	35	Asphyxiation with compression of the neck	AA grade II 2, Coronary artery grade II 25 stenosis, epilepsy, hyperglycemia	**33.3**	0	-	-	-
6	M	20	Chest contusion (car driver)	Hyperglycemia, toxicological test	**33.3**	0	-	-	tetrahydrocannabinol carboxylic acid
7	F	45	E74.9	AA grade II 2; coronary artery grade I 50 stenosis; fatty liver	**33.3**	0	0	0	not found
8	M	0 (infant)	Asphyxia due to compression of the neck	-	**33.3**	0	0	0	not found
9	M	4.5 month-old	E74.9	Fatty liver	**28.0**	0	0	0	not found

Hypertrophic cardiomyopathy (HCM), Ischemic heart disease (IHD), Aortic atherosclerosis (AA), Cerebral atherosclerosis (AS), Tuberculosis (TBC).

chest contusion. Post-mortem internal examination: right lung mass of 998 g (normal 185-967 g [6]), left lung mass of 824 g (normal 186-885 g [6]), a brain mass of 1357 g (normal 1070-1767 g [6]). Toxicological test positive for tetrahydrocannabinol carboxylic acid in blood. The plasma glucose concentration was found to be above 33.3 mmol/l (normal 4.0-6.0 mmol/l [7]).

Patient 7

45-year-old female. Plasma glucose was found to be above 33.3 mmol/l (normal 4.0-6.0 mmol/l [7]). The primary diagnosis was unspecified carbohydrate metabolism disorder, E74.9.

Patient 8

A male infant died of asphyxia due to compression of the neck. Plasma glucose was found to be more than 33.3 mmol/l (normal 4.0-6.0 mmol/l [7, 8]).

Patient 9

A 4.5-month-old boy with post-mortem examination showed fatty liver and plasma glucose levels above 28.0 (normal 4.0-6.0 mmol/l) [7, 8]. The primary diagnosis was unspecified carbohydrate metabolism disorder, E74.9.

DISCUSSION

According to the sources of literature, the incidence of HHNKS and mortality rates vary widely. The incidence rate in the literature is rather abstract: less than 1% of all hospitalizations for diabetes [1, 13]; no precise data was available. With regard to mortality in HHNKS, different authors give different ranges, with mortality rates ranging from 5 to 50% [2, 9]. Ranges as high as or higher than 20% are often reported in the literature [1, 2, 9, 13], but there is no consensus of opinion to date.

This variability in statistics may be due to the fact that cases of this rare syndrome are recorded in hospitalized patients and cases of sudden deaths are not analyzed. In addition, in diabetes cases, the coexistence of DKA and HHNKS may occur [15], which complicates the diagnostics of this syndrome and may affect the reliability of epidemiological data.

The data from the study shows that the main disease HHNKS is found in female individuals aged 21-45 years. It was also the leading cause of death in a 4.5-month-old male infant. According to the sources of literature, the majority of HHNKS cases occur in the fifth and sixth decades of patients' life [1], but the number of hospitalizations for HHNKS in children and young adults has increased significantly due to the growing problem of obesity, uncontrolled type 2 diabetes and high carbohydrate intake [10, 11].

This is in line with data from most recent sources - HHNKS is no longer the cause of death in patients over 50 years of age. Furthermore, the data from this study showed that HHNKS was more commonly diagnosed in women, which is also reported in the literature [9].

We believe that with the increasing incidence of type 2 diabetes over the past decades and in the future [16], the phenomena caused by HHNKS need to be thoroughly investigated. In post-mortem investigations in cases of sudden, unexplained death, great attention should be paid to a relatively simple test - the determination of serum glucose levels.

In conclusion, this study shows that serum glucose test in sudden death cases is meaningful for the diagnosis of HHNKS. Therefore, a serum glucose test is appropriate in cases of sudden death. This will help to determine the exact prevalence of HHNKS and mortality due to this syndrome, especially in cases of sudden deaths in the 30-50-year age group or even younger. This data would also contribute to improving the diagnostics and treatment of HHNKS and contribute to an overall deeper understanding of diabetes.

Conflict of interest

The authors declare that they have no conflict of interest.

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