

Special Article

Osborn Waves in the Electrocardiogram, Hypothermia Not Due to Exposure, and Death Due to Diabetic Ketoacidosis

ABDUL M. SHEIKH, M.D., AND J. WILLIS HURST, M.D., MACP

Department of Medicine and the Division of Cardiology, Emory University School of Medicine, Atlanta, Georgia, USA

Summary: Hypothermia usually occurs because a patient has been exposed to a cold environment; however, a number of nonenvironmental conditions may produce hypothermia. This report relates the clinical course of a patient whose hypothermia was due to severe diabetic ketoacidosis. In addition, we review the causes of hypothermia and Osborn waves beyond exposure to cold temperature. Hypothermia due to diabetic ketoacidosis is an uncommon complication of a common disease that carries with it clinically significant consequences. Accordingly, we believe that all clinicians should be aware of this potential complication of diabetic ketoacidosis and should be able to recognize the importance of the electrocardiogram in such patients.

Key words: Osborn waves, hypothermia, ketoacidosis

Address for reprints:

J. Willis Hurst, M.D.
Division of Cardiology, Emory University
1462 Clifton Road, NE, Suite 301
Atlanta, GA 30322, USA
e-mail: jhurst@emory.edu

Received: September 19, 2003

Accepted: September 25, 2003

TABLE I Laboratory data

Laboratory	Patient's result	Reference
Sodium	126 mEq/l	135–145 mEq/l
Potassium	6.1 mEq/l	3.5–5.0 mEq/l
Chloride	90 mEq/l	100–110 mEq/l
Bicarbonate	7 mEq/l	20–32 mEq/l
Blood urea nitrogen	84 mg/dl	7–25 mg/dl
Creatinine	4.9 mg/dl	0.6–1.4 mg/dl
Glucose	1354 mg/dl	65–110 mg/dl
Total protein	5.1 g/dl	6.4–8.5 g/dl
Albumin	2.7 g/dl	3.5–4.8 g/dl
Calcium	9.5 mg/dl	8.5–10.5 mg/dl
Magnesium	2.6 mEq/l	1.5–2.4 mEq/l
White blood cell count	18.1 (1000/ml)	3.6–11.1
Granulocytes %	76	
Lymphocytes %	23	
Monocytes %	1	
Eosinophils %	0	
Hemoglobin %	11.8 g/dl	12.9–16.1 g/dl
Hematocrit %	36.5	37.7–46.5
Platelet count	302 (1000/ml)	150–400
Partial thromboplastin time	36.1 s	24.0–38.0
Protime	21.0 s	12.3–14.9
International Normalized Ratio (INR)	1.84	
Creatine kinase (CK)	15,298 U/l	49–397
CK-MB	342 ng/ml	<5 ng/ml
Troponin I	0.22 ng/ml	<0.05 ng/ml
Myoglobin	47,173 ng/ml	<70 ng/ml
Lactate	2.6 mEq/l	0.5–2.2 mEq/l
Beta-hydroxybutyrate	95.1 mg/ml	0.0–3.0 mg/dl
TSH	0.23 IU/ml	0.34–5.60 IU/ml
T4	3.8 µg/dl	4.6–12.0 µg/dl
Free T4	1.1 ng/ml	0.5–1.6 ng/dl
T3	34 ng/ml	59–174 ng/dl
Cortisol	58 µg/dl	5–25 µg/dl (in A.M.)

Abbreviations: IU = International Units, TSH = thyroid-stimulating hormone.

lar veins. The pulse was regular but slow at a rate of 56 beats/min. There were no murmurs or gallop sounds. The remainder of the physical examination was normal.

The patient was somnolent and only responded to tactile stimuli. His cranial nerves were believed to be intact. His pupils were equal and responsive to light bilaterally. He was moving all extremities, but without purpose.

Laboratory Data

Laboratory data are shown in Table I. Three sets of blood cultures (September 3, 2002) grew no organisms after 5 days. A urine culture (September 3, 2002) did not grow any organisms. An electrocardiogram (ECG) recorded at 10:50 A.M. on September 3, 2002, was abnormal (see Fig. 1, and legend). Computed tomography of the head revealed no abnormality.

Hospital Course

Those in attendance were concerned that they might overlook a myocardial infarction and performed coronary arteriography; the coronary arteriogram was normal. Systolic ejection fraction was 60%. The patient was then transported to the intensive care unit for further care and was rewarmed using an external rewarming blanket and warm intravenous fluids. When the patient became warmer, the ECG changed considerably. The Osborn waves disappeared and the tracing revealed transient atrioventricular block that prompted the placement of a transvenous cardiac pacemaker. The subsequent tracing also showed low amplitude of the QRS complexes and ST-T changes suggestive of digitalis, although the patient had not been receiving digitalis.

In addition to being warmed, the patient was treated for diabetic ketoacidosis with intravenous insulin as well as with bicarbonate infusion. Electrolytes were monitored closely and

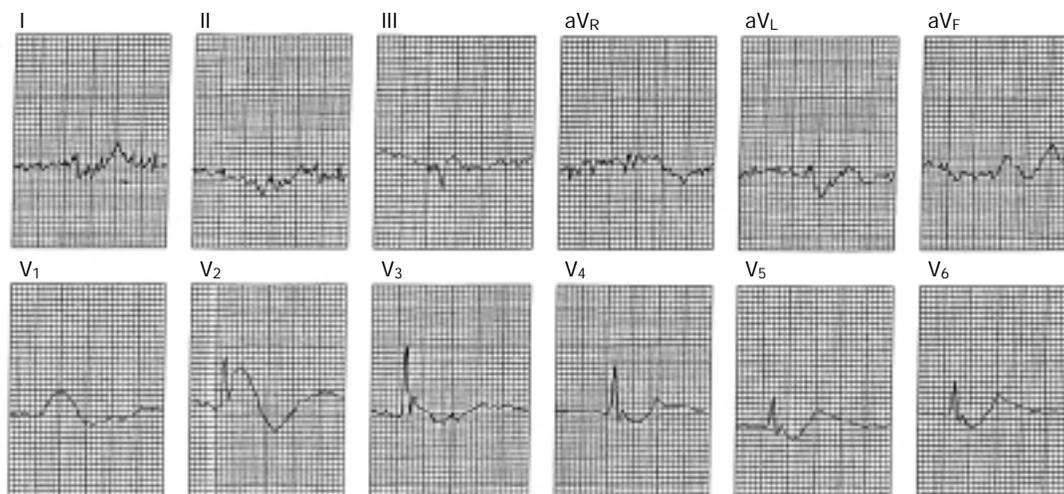


FIG. 1 This electrocardiogram, showing giant size Osborn waves, was recorded at 10:52 A.M. on September 3, 2002. Note the shiver artifact in the extremity leads. The heart rate is 80 depolarizations/min. The P-R interval is 0.18 s (see leads V₂ and V₃).

The markedly elevated deflections seen in leads V₁–V₃, along with the inverted T waves in the same leads, are believed to be giant-sized Osborn waves. Therefore, the duration of the QRS complexes is markedly prolonged because Osborn waves are due to postexcitation of the ventricles and are, therefore, part of the QRS complex.

The large size and duration of the abnormal waves usually signify, in hypothermic patients, that the condition has been present for a prolonged period of time and that the core body temperature is extremely low.

Could these abnormal waves be Brugada waves? This is not likely because there is no evidence of right ventricular system blocks and the shape of the waves is not similar to the triangular S-T segments, saddle-back S-T segments, or coved S-T segments that have been designated as Brugada waves. The patient reported here was hypothermic and the unusual waves disappeared as the patient was warmed.

The fact that the Osborn waves disappeared with warming while the neurologic condition deteriorated suggests that the abnormal waves were due to hypothermia rather than due to hypothalamic dysfunction.

treated as necessary.

The patient continued to deteriorate and multiorgan failure ensued. He died at 12:50 P.M. on September 4, 2002. The patient's family denied the request for an autopsy.

An Assessment of the Abnormalities Observed in this Patient

This critically ill and deteriorating patient presented with numerous clinical and laboratory abnormalities. Exposure to cold weather was obviously not the cause of hypothermia or the abnormalities in the ECG, because the outside temperature in Atlanta, Georgia, on the date of admission was 26.1°C and he was discovered unconscious in a warm hotel room.

Unfortunately, no family members or colleagues were with the patient prior to his being found by the hotel staff. Therefore, it is impossible to know the symptoms the patient might have had or whether he had been taking his insulin in the hours and days prior to the last event.

The patient's confusion and purposeless movements were due to his profound hypothermia and the severe metabolic derangements secondary to diabetic ketoacidosis.

The electrolyte derangements found in the patient's laboratory studies are consistent with severe diabetic ketoacidosis, as is the tremendously elevated beta-hydroxybutyrate.

The fact that the patient appeared well-nourished but had a low albumin without evidence of proteinuria on urinalysis is suggestive of an acute medical illness.

His hemogram was significant for the elevated white blood cell count, with a left shift, which could be due to an infection or be caused by elevated endogenous steroids due to severe physiologic stress.

Finally, the significant elevations in creatine kinase and myoglobin with slight elevations in the MB fraction and troponin could be due to either hypoperfusion of skeletal muscle or direct pressure injury caused by falling and remaining on the floor for an unknown period of time.

Discussion

Many patients have diabetes mellitus and many of these will have hypoglycemia caused by insulin overdose or coma due to ketoacidosis related to inadequate amounts of insulin. Some patients who have hypoglycemia or diabetic coma will also exhibit hypothermia and Osborn waves in their ECGs. Accordingly, because hypothermia and Osborn waves are not always recognized, this discussion will include a brief dissertation about them.

Hypothermia and Osborn Waves Due to Exposure to Cold Weather

The most common cause of hypothermia and Osborn waves occurs in individuals who, for various reasons, are exposed to cold weather.^{1,2} The patient may be an elderly woman who has no means of heating her home during cold weather. The patient who is under the influence of alcohol may sleep outdoors during cold weather. In fact, alcohol may contribute to the problem because alcohol abuse alone may be the cause of hypoglycemia, which definitely increases the chance that exposure to cold weather may precipitate hypothermia. Diabetic patients with mild ketoacidosis may also be more susceptible to the production of hypothermia by exposure to cold weather than patients without diabetes. Finally, individuals who travel in cold weather may, because of an accident, be exposed to cold weather.

In addition to hypothermia, many of these patients will show abnormal J deflections known as Osborn waves in the ECG.

Nonenvironmental Causes of Hypothermia (Table II)

Hypothermia and Osborn Waves Due to Sepsis

Drake and Flowers reported a patient with hypothermia (34.4°C) believed to be caused by sepsis from an unidentified source.³ Blood cultures grew a species of enterococcus. The initial ECG revealed no Osborn waves. The hypothermia subsided by Day 7, but the patient became hypothermic again on Day 21 of his hospital stay. Osborn waves were noted in the ECG at that time, and the patient subsequently died. Drake and Flowers offer an explanation that is based on the views of Thompson *et al.*^{3,4} Drake and Flowers state,

The basic hypothalamic neurochemical processes in hypothermia from sepsis are the opposite of those in exposure or induced hypothermia. In sepsis with hypothermia, the hypothalamus set point for thermoregulation is moved downward, and there is a cooling effect by peripheral vasodilatation and decreased metabolic rate. In exposure, however, the set point is unchanged, but the hypothalamic drive tends to cause vasoconstriction and shivering with an increase in metabolic state.³

The patient reported here was diabetic, and the white blood count was greatly elevated, but there were no external signs of a source of infection and three sets of blood cultures and a culture of the urine did not grow any organism. Therefore, we do not believe that sepsis was responsible for the hypothermia and giant-size Osborn waves.

Hypothermia Due to Neuroleptic Drugs

Hägg *et al.* wrote an instructive letter to the editors of the *Journal of Clinical Psychopharmacology*⁵ in which they pre-

TABLE II Nonenvironmental causes of hypothermia

Endocrine
Hypothyroidism
Hypopituitarism
Hypoglycemia
Diabetic ketoacidosis
Neurologic
Cerebrovascular accidents
Infections
Antipsychotic medications
Alcohol

sented a report of a psychiatric patient who developed repeated episodes of hypothermia because of the use of haloperidol, levomepromazine, olanzapine, and thioridazine, but not with the use of alimemazine and dixyrazine. They state that, in humans, body temperature regulation is located in the hypothalamus and that the dopaminergic, noradrenaline, and serotonin systems are considered to be involved in its regulation.⁵

The patient reported by Hägg *et al.* was somnolent and hypotensive. Her ECG revealed atrioventricular block and a prolonged QT interval. No mention was made of the presence of Osborn waves. This, of course, does not guarantee that Osborn waves were not actually present. The references cited in their communication are so important that they are listed again here.⁶⁻¹¹

According to his family, the patient presented here was not known to be taking any antipsychotic or neuroleptic drugs, and no pill bottles were found on his person or in his hotel room.

Hypothermia Due to Catastrophic Cerebral Events

An expert neuroradiologist was questioned about the patient reported here. The neuroradiologist pointed out that a computed tomography scan cannot detect a lesion of any type when it is localized to the hypothalamus. The best that can be done is to surmise that hypothalamic damage could be present when a large area of cerebral damage occurs in a region of the brain that is near the hypothalamus. The patient reported here had no such lesion.

Four neurologists were asked the following question: "Do you believe an isolated lesion in the hypothalamus could cause hypothermia?" The answer was "Yes." When asked whether they had ever seen such a patient, the answer was "No."

We know of one unreported patient who developed hypothermia, Osborn waves, and died following a massive cerebral hemorrhage that was thought to involve the hypothalamus.¹²

As discussed later, acute cerebral catastrophes may also produce Osborn waves when the patient is normothermic.

Hypothermia Due to Hypoglycemia

Hypoglycemia, defined as a plasma glucose concentration of ≤ 50 mg/dl, was studied by Field, who reported that hypo-

thermia, hyperthermia, or localized neurologic findings may be observed in patients with hypoglycemia. He did not report on the presence or absence of Osborn waves in his patients.¹³

Malouf and Brust reported that hypoglycemia was observed in patients with diabetes mellitus, in patients who abused alcohol, and in patients who were septic.¹⁴ These three conditions accounted for 90% of 125 visits for patients with symptomatic hypoglycemia to the Harlem Hospital Emergency Room.¹⁴ Other causes included advanced cancer, fasting, gastroenteritis, insulin abuse, and myxedema. Three patients had hemiparesis. Eleven patients had hypothermia, but there was no mention of Osborn waves.

Fruehwald-Schultes *et al.* made the interesting observation that hypothermia during hypoglycemia was not influenced by antecedent hypoglycemia, nor by circulating blood levels of insulin.¹⁵ The presence of Osborn waves was not mentioned in their report.

Hypothermia Due to Diabetic Ketoacidosis

We believe that hypothermia due to diabetic ketoacidosis is underappreciated, underrecognized, and underreported. The reason for hypothermia in diabetic ketoacidosis is speculative, but it has been postulated to be due the inability of adequate amounts of glucose to enter cells due to the lack of an adequate amount of insulin, which leads to a subsequent lack of substrate for heat production.¹⁶

In the largest report on such patients,¹⁷ Gale and Tattersall reported that diabetic ketoacidosis accounted for 11.8% of all causes of hypothermia that they observed over a 7-year period, making it the most common nonenvironmental cause of hypothermia during that time period. Like the patient presented in this report, many of their patients were seen during a time of year when the outside temperature was not cold, and no alternative explanations for their hypothermia were found.

The medical care of patients who present with diabetic ketoacidosis and hypothermia is challenging. The mortality of such patients has been reported to be between 30 and 60%.^{17, 18} Resistance to insulin has been observed in hypothermia and could complicate therapy. Furthermore, there is a high incidence of infection in patients with diabetic ketoacidosis, estimated in some studies to be from 25 to as high as 80%.^{17, 18}

Causes of Osborn Waves in Normothermic Patients

Although Osborn waves in normothermic patients have not been studied adequately, two such examples will be cited.

Hypercalcemia

Hypercalcemia can produce Osborn waves in the ECG in normothermic patients.^{19, 20} The serum calcium was normal in the patient presented here.

Subarachnoid Hemorrhage and Other Catastrophic

Cerebral Events

De Sweit reported a patient with a subarachnoid hemorrhage who was not hypothermic, but who developed Osborn waves in the ECG.²¹ He wrote, "Hypothalamic involvement in subarachnoid hemorrhage of spontaneous origin can well be visualized in the presence of extensive bleeding at the base of the brain, which is known to cause hyperglycemia, excessive sweating, and pyrexia." He accepted the idea that an elevation of catecholamines produced by hypothalamic stimulation might cause the ECG abnormality. This must be extremely rare because subarachnoid hemorrhage may cause generalized epicardial ischemia, which is precipitated by direct myocyte damage and coronary constriction due to a catecholamine storm initiated by the hypothalamus.

There was no evidence that subarachnoid hemorrhage had occurred in the patient reported here.

Other Causes of Osborn Waves in Normothermic Patients

Patel *et al.* reported their observations on eight patients who were normothermic and who exhibited Osborn waves in the ECG.²² Three of these patients had inferior myocardial infarction, two had noncardiac chest pain, two had systemic arterial hypertension and left ventricular hypertrophy, one had chest pain due to cocaine abuse, and in one it was caused by haloperidol toxicity.

The clinical and laboratory data on the patient reported here revealed no clues for any of the conditions reported by Patel *et al.*²²

Unanswered Questions about Hypothermia and Osborn Waves

Many of the reports of patients with hypothermia due to various nonenvironmental causes do not state whether or not they had Osborn waves. Therefore, it is not possible to state how often Osborn waves occur in patients with nonenvironmental hypothermia.

The cause of Osborn waves in normothermic patients is a conundrum. The comments in the literature suggest that Osborn waves that are observed in patients with sepsis, who take certain drugs, or who have certain cerebral catastrophes are due to their action on the hypothalamus.

The cause of hypothermia in hypoglycemia and ketoacidosis in patients with uncontrolled diabetes mellitus is apparently due to the poor production of heat. This occurs because the proper amounts of insulin and glucose needed to permit glucose to enter the cells of the body, where it becomes the substrate for energy and heat production, are not present.

The Osborn waves, caused by postexcitation of the ventricular myocardium in patients who have hypothermia due to exposure to cold weather, are believed to be due to severe cooling of the lateral portion of the left ventricle. One wonders whether hypothermia due to exposure to cold weather could cool the brain, including the hypothalamus?

While Yan and Antzelevitch have offered an excellent ex-

planation for the myocardial cellular basis for Osborn waves, their interest was not focused on the initiating cause of the condition.²³

Obviously, much more research is needed to clarify the mechanisms involved in the creation of hypothermia and Osborn waves.

Conclusions

The patient reported here developed hypothermia and Osborn waves due to severe diabetic ketoacidosis. Although such cases have been reported previously, we believe these complications of diabetic ketoacidosis are underappreciated, underrecognized, and underreported. Therefore, we suggest that those who care for patients with diabetic ketoacidosis become familiar with Osborn waves and measure the core body temperature of such patients with a low-reading thermometer.

Acknowledgment

The authors wish to thank Dr. Randall Patterson for his permission to report this unusual patient.

References

1. Clements SD, Hurst JW: Diagnostic value of electrocardiographic abnormalities observed in subjects accidentally exposed to cold. *Am J Cardiol* 1972;29:729-734
2. Okada M, Nishimura F, Yoshino H: The J wave in accidental hypothermia. *J Electrocardiol* 1983;16:23-28
3. Drake C, Flowers N: ECG changes in hypothermia from sepsis and unrelated to exposure. *Chest* 1980;77:685-686
4. Thompson R, Rich J, Chmelik F: Evolutionary changes in the electrocardiogram of severe progressive hypothermia. *J Electrocardiol* 1977;10:67-70
5. Hägg S, Mjörndal T, Lindqvist L: Repeated episodes of hypothermia in a subject treated with haloperidol, levomepromazine, olanzapine, and thioridazine. *J Clin Psychopharmacol* 2001;21:113-115
6. Weinberg AD: Hypothermia. *Ann Emerg Med* 1993;22:104-110
7. Harada H, Igarashi M, Sugae S, Okamoto K, Tsuji M, Nakajima T: A schizophrenic patient who developed extreme hypothermia after an increase in the dose of haloperidol: A case report. *Jpn J Psychiatry Neurol* 1994;48:595-598
8. Phan TG, Yu RY, Hersch MI: Hypothermia induced by risperidone and olanzapine in a patient with Prader-Willi syndrome. *Med J Aust* 1998;169:230-231
9. Weihe WH: The effect of temperature on the action of drugs. *Ann Rev Pharmacol* 1973;13:409-425
10. Dilsaver SC: Effects of neuroleptics on body temperature. *J Clin Psychiatry* 1988;49:78-79
11. Young DM: Risk factors for hypothermia in psychiatric patients. *Ann Clin Psychiatry* 1996;8:93-97
12. Personal Communication from Dr. Spencer Palmer, April 2003
13. Field JB: Hypoglycemia. Definition, clinical presentations, classification, and laboratory tests. *Endocrinol Metabol Clin North Am* 1989;18:27-43
14. Malouf R, Brust JC: Hypoglycemia: Causes, neurological manifestations, and outcome. *Ann Neurol* 1985;17:421-430
15. Fruehwald-Schultes B, Kern W, Dantz D, Born J, Fehm HL, Peters A: Preserved hypothermic response to hypoglycemia after antecedent hypoglycemia. *Metabolism: Clinical and Experimental* 2000;49:794-798
16. Matz R: Hypothermia in diabetic acidosis. *Hormones* 1972;3:36-41
17. Gale E, Tattersall R: Hypothermia: A complication of diabetic ketoacidosis. *Br Med J* 1978;2:1387-1389
18. Guerin JM, Meyer P, Segrestaa J: Hypothermia in diabetic ketoacidosis. *Diabetes Care* 1987;10:801-802
19. Otero J, Lenihan D: The "normothermic" Osborn wave induced by severe hypercalcemia. *Texas Heart Inst J* 2000;27:316-317
20. Sridharan M, Horan L: Electrocardiographic J wave of hypercalcemia. *Am J Cardiol* 1984;54:672-673
21. De Sweit J: Changes simulating hypothermia in the electrocardiogram in subarachnoid hemorrhage. *J Electrocardiol* 1972;5:193-195
22. Patel A, Getsos J, Moussa G: The Osborn wave of hypothermia in normothermic patients. *Clin Cardiol* 1994;17:273-276
23. Yan G, Antzelevitch C: Cellular basis for the electrocardiographic J wave. *Circulation* 1996;92:372-379