The syndrome of hyperosmolar non-ketotic diabetic acidosis following craniotomy: A case report

by
Nadason Arumugasamy
MBBS (Mal), MD (S'pore), FICS
and
Edir B. Siqueira
MS, MD

(From the Division of Neurological Surgery of the Chicago Wesley Memorial Hospital, and Department of Surgery of Northwestern University Medical School).

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SINCE 1957, when the syndrome of non-ketotic hyperosmolar coma was first described in a diabetic [9] well over 100 cases have been reported. The 32 cases of Danowski and Nabarro [3] and the 63 cases reviewed by Schwartz and Apfelbaum [10] are two of the larger series. The majority of cases have been in patients with severe infections, extreme burns [2,5,8] or problems involving the pancreas, usually a pancreatitis [6] or carcinoma. However, there has been insufficient emphasis of this syndrome in surgical literature.

Ashworth et al described two patients who developed this syndrome – one with burns covering 20% of the body surface and the other, a patient with Pemphigus Vulgaris. None of the patients underwent a major surgical procedure. However, they did draw attention to the relationship of this syndrome to certain surgical problems.

Once the syndrome is well developed, the prognosis is poor. Mortality rates of 44% [4] and 41% [10] have been reported. Recently, following a frontal craniotomy and near total excision of a suprasellar meningioma, one of our patients developed this syndrome. She became comatose on the 24th postoperative day. She was fortunate in revovering from the metabolic derangement.

This case is being reported to draw the attention of surgeons to this syndrome. Moreover, it is the first reported case of its kind to follow an intracranial

surgical procedure.

Early recognition of the hyperosmolar non or mildly ketotic patient is imperative if either the resultant hypovolemic state or the state of coma is to be avoided. Examination of the blood sugar and careful check of the electrolyte status are indicated post-operatively in susceptible patients. An outline of the treatment rendered is also given. The metabolic mechanisms responsible for the syndrome are briefly discussed, with particular reference to the case presently being reported.

Case Report

The patient is a 56-year-old right-handed white woman. She was admitted to the Chicago Wesley Memorial Hospital on February 11, 1969. Essentially, she complained of progressive loss of vision in her left eye over an eight-year period. Three years previously, she had become blind in that eye. She was seen by an ophthalmologist at that time. He advised hospitalisation for "some tests". Being fearful of possible surgery, she did not return to see her doctor.

A year prior to admission, she noticed that the vision in her right eye was being affected. She began bumping into objects to the right of her. In January 1969, she was unable to read her newspapers. She sought medical treatment the same month.

There was no history of headaches, diplopia, cold intolerance, recent weight gain polyuria or polydipsia. She had reached her menopause ten years previously. The past history was insignificant. She had been in good health previously, prior to the onset of her visual complaint.

On examination, she was a rather short (height 4' 11") somewhat obese female, weighing 150 pounds. Mentally she was dull. She was oriented to time and place. In the neurological examination, the main findings were in the visual system. She was blind in her left eye, there being no light response both directly and consensually. Both pupils were dilated to four millimeters. Visual acuity on the right was a paltry 2/100. Her visual fields are illustrated (Fig. 1). Funduscopy revealed bilateral optic atrophy. The left fundus was more severely affected. There were no long tract signs and no pathologic reflexes.

Review of her remaining systems was unremarkable. Her blood pressure was 140/70 millimeters of mercury.

Laboratory investigations: Hematocrit was 42 (hemoglobin 13.7 gms.%). Total white blood cell count was 5,600 – 46% polymorphonuclear leukocytes and 42% lymphocytes. Blood serology (VDRL) was negative. Urine specific gravity was 1.005 and the rest of the examination was unremarkable. Serum electrolytes were as follows: Sodium 144 mEq./L, Potassium 4.1 mEq/L, Chlorides 102 mEq/L, $c0_2$ combining power 27 vol.%. The 24-hour urine, 17-keto and ketogenic steroids and T4 uptake were normal. Blood urea nitrogen (BUN) was 20 mgm%. Fasting blood sugar was 125 mgm%.

Radiologic studies: Skull X-rays were normal and unremarkable. Radioactive brain scan with Technetium 99^m revealed an increased area of isotope uptake in the suprasellar area, both in the anteroposterior and lateral projections. Bilateral cerebral angiography was performed. This study confirmed the presence of a suprasellar tumor. There was a stretching and elevation of the first portions of both anterior cerebral arteries and a displacement laterally of the left carotid artery in its intracranial portion. A suprasellar vascular "blush" could be discerned in the late venous phase.

On 2-17-69, a left frontal craniotomy was performed, following the infusion of 500 ml 20% Mannitol and a lumbar puncture for continuous spinal drainage. Preliminary elevation of the left frontal lobe revealed a circumscribed tumor on its under aspect. A left frontal lobectomy was then carried out delineating the tumor well. All the tumor was then removed but for a small fragment attached to the left carotid artery. Both optic nerves were found to be considerably flattened, discolored and displaced lateral to their normal locale. The main feeding vessels to the tumor entered its medial aspect and were clipped and divided. It is entirely possible that some of these vessels contributed to the blood supply of the diencephalon. When the tumor was removed, it was also evident that its bed was partly formed by the hypothalmus.

Postoperative course: She was started on steroids (Dexamethazone 6 mgm every 6 hours). Within 24 hours, she developed diabetes insipidus. On the day following surgery, she passed 900 ml. of urine with a specific gravity of 1.0003 in a little over an hour-and-one-half. She required Pitressin. On the seventh postoperative day, the steroids that had been tapered previously were discontinued. At this time, Cortisone replacement was begun (25 mgm. Cortisone a.m. and 12.5 mgm. p.m.).

Neurologically, she was able to talk and eat by this time. In her affect, she was "frontal lobish". She moved all her extremities at request. In the second post-operative week, her appetite was excellent. She ate voraciously everything given to her. However, on the 21st postoperative day, her appetite palled and

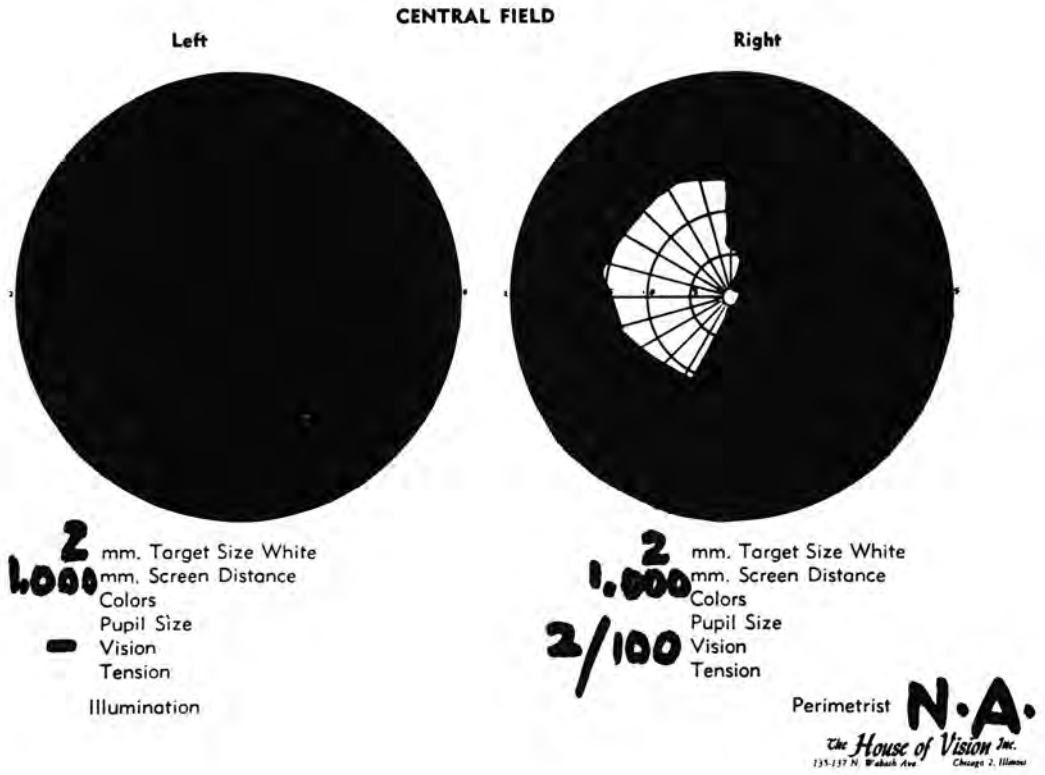
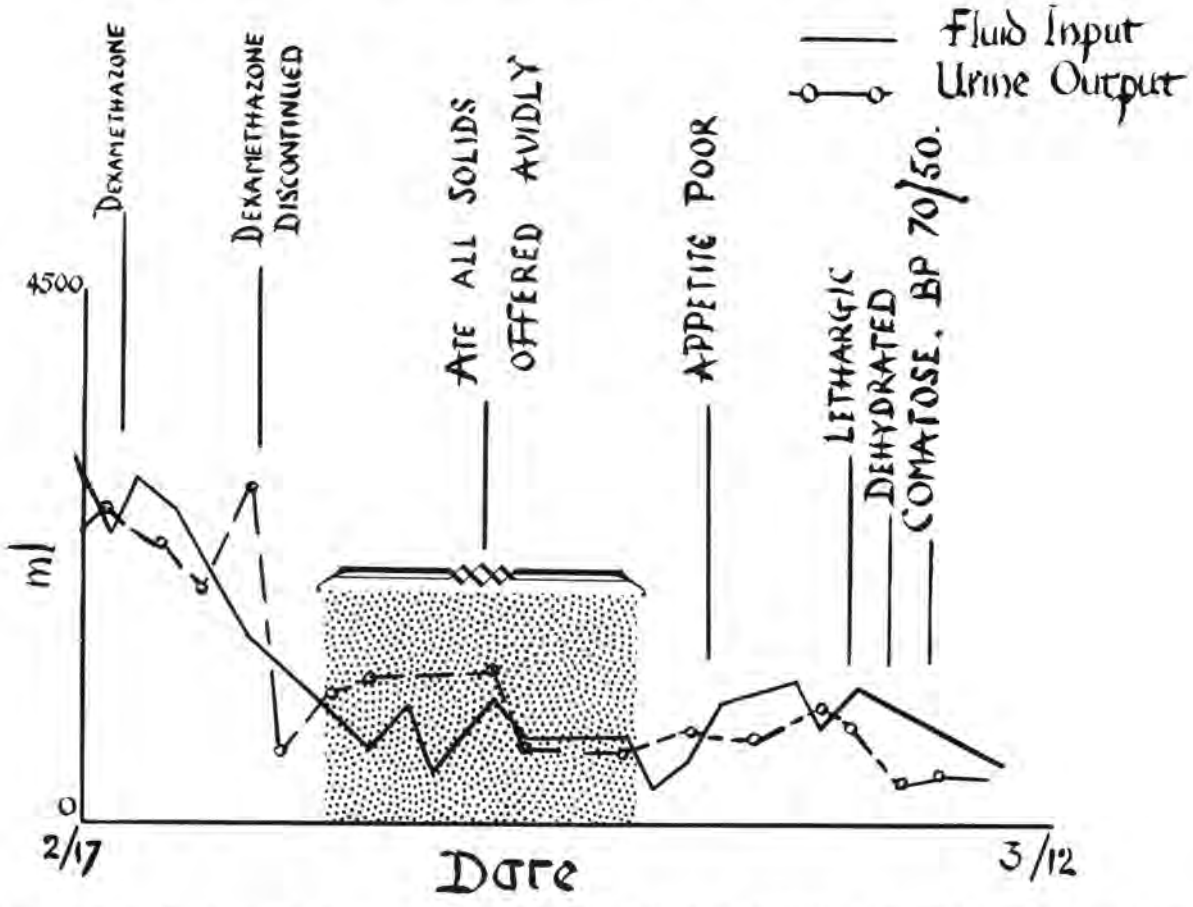


Fig. 1: **A copy of the visual fields and visual acuity in our patient as determined on 2.12.69.**

Table I indicates the serum electrolytes, blood sugar and blood urea values on the dates indicated.

Date:	Blood Sugar	Blood Urea	Serum Electrolytes			
			Na	K.	C1.	CO2
2-12-69	125	20	144	4.1	102	27
2-19-69	175	28	140	4.2	101	24
2-22-69			157	3.9	98	24
3-11-69	1,230	98	163	4.2	128	19
3-12-69 A.M.	900	78	137	5.2	111	13
P.M.	840	76	123	6.1	90	9
3-13-69 A.M.	280		128	4.3	101	14
P.M.			125	5.2	99	14
3-14-69	375	40	125	3.4	98	23
3-15-69	370		132	3.2	99	15
3-16-69	230		142	4.5	108	16
3-18-69	230	48				
3-19-69			152	9.2	118	20
3-20-69			144	4.4	112	20
3-21-69	225	30	139	4.4	113	19
3-27-69	225	25	146	4.1	110	20

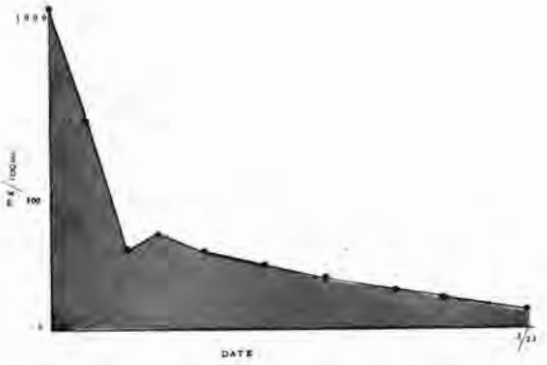


Graph I showing fluid input and urinary output from 2/17/69 to 3/12/69. The temporal occurrence of some pertinent events that led to her comatose state are also indicated.

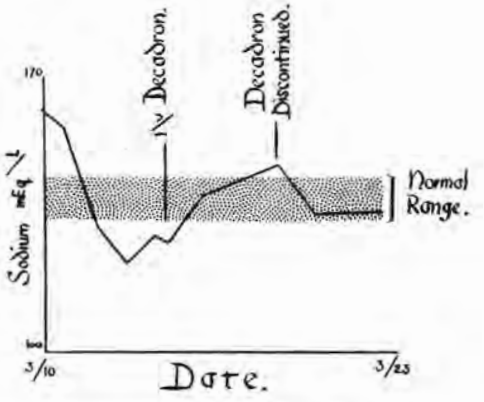
she refused all solids. She drank only fluids and this quite inadequately. Two days later, she became somewhat somnolent (Graph 1). Examination of her serum electrolytes revealed a hypernatremia with a Sodium of 163 mEq/L (Table I). The following morning, when these results became available, she was not responding to verbal stimuli. She was in a coma responding only to deep pain. Examination of her urine revealed 4+ sugar with a faint trace of acetone. Determination of blood sugar gave the phenomenal figure of 1,230 mgm%. Serum osmolality was 432 mOsm. (normal = 280 mOsm). This, with the hyperna tremia in the face of a comatose patient, prompted the diagnosis and immediate corrective treatment. At this time, she was dehydrated, with a blood pressure of 70/50.

Graphs II and III depict the blood sugar and serum sodium patterns respectively during her treatment. A blood sugar level of over 1,000 mgm%, and a BUN of 98 mgm% indicated that renal damage was present[6]. She was treated with regular insulin and hypotonic (0.45N) saline, followed three days later with water via a nasogastric tube. She was carefully followed with serial blood sugar and serum electrolyte estimations, two to three times a day. These were done until her dehydration was corrected and the blood sugar had reached levels which were nearly normal.

Some four days after the onset of her coma, she developed generalised edema due possibly to water overload in the face of poor renal function. She ceased to "put out" urine. Edecrine (50 mgm.) was given intravenously. At this time, she developed a respiratory stridor. Laryngoscopy revealed edema of the larynx, and this rapidly cleared following Dexa-



Graph II indicates the serum blood sugar levels and their trend with treatment after the onset of her coma.



Graph III represents the serum sodium levels during treatment. The time I/V Decadron was given corresponds to the time of her laryngeal edema.

methazone (dose – 4 mgm intravenously every eight hours). It will be evident from Graph III that this induced a hypernatremia which cleared when the steroid was discontinued four days later.

Presently, the patient continues to require Lente insulin 20 units daily. There is no glycosuria. Her blood sugar is in the range of 180 mgm% – 200 mgm%. She awaits placement in a nursing home.

Discussion

In the majority of cases reported to date, this syndrome was associated with diabetes mellitus of adult onset. In 65% of the 63 patients in one series, the development of this syndrome was the first manifestation of the diabetic state. In our patient, the fasting blood sugar level of 125 mgm% at the time of admission, perhaps, should not have been overlooked. It was interpreted as being high normal. In addition to this initial high level of blood sugar, several other factors contributed to the development of the hyperosmolar state. Amongst these were the use of steroids post-operatively, the ketone sparing effect of increased consumption of carbohydrate in the second post-operative week, the diuresis, and the poor fluid intake due to an absent or inadequate response to thirst.

Serum osmolality rises as a direct linear correlate of the blood sugar (180 mgm. glucose = $\frac{180}{18}$ = 10 m osmoles). As blood sugar levels reach proportions of 850 – 1,000 mgm% or more, the kidneys are unable to handle the osmotic load. The usual range of blood sugar levels in the reported cases is between 690 – 1,200 mgm% with a mean blood sugar of 910 mgm%.[10] At these levels, there is little reabsorption of water by the kidneys, and water is lost at the expense of sodium and urea, adding further to the hyperosmolar state. That sodium and urea increase osmolality [11] is well illustrated by the formula:

Plasma osmolality = 2 (sodium + potassium concentrations + $\frac{\text{glucose (mgm\%)}}{18}$ + $\frac{\text{BUN (mgm\%)}}{1.4}$)

On March 11, 1969, the serum osmolality in our patient was 432, sodium was 163 mEq/L, potassium 4.1 mEq/L, serum glucose level of 1,230 mgm% and a BUN of 98 mgm%. Based on the above formula, serum osmolality estimation confirms the role of the electrolytes and urea and sugar in increasing the hyperosmolar state.

Treatment should be directed toward the hyperglycemia and the hypovolemia. If the hyperglycemia is treated by the judicious use of regular insulin, then adequate and correct type of fluid replacement will reduce the blood glucose values to acceptable levels. Potassium replacement should not be overlooked during this period. The choice of fluid should be such as not to induce hemolysis of red blood cells. A 0.45 N saline solution is ideal for this purpose. Alternately, water may be given via a nasogastric tube. Water is to be preferred as it does not increase the hyperosmolality while making good the electrolyte imbalance.

A central venous pressure catheter is advised in

patients with hypotension and hypovolemic states until clinical improvement occurs. Our failure to do so earlier resulted in water overload, no doubt due to the renal damage present. If the blood sugar level is over 1,000 mgm%, renal impairment is almost definite to be present . As the hypotension is a reflection of the state of dehydration, it needs no specific therapy outside of the correction of the dehydration.

That steroids aggravate the condition is evident in our case when it was given for four days to combat laryngeal edema. This induced a significant hypernatremia in our patient which corrected itself once the steroid was discontinued (Graph III).

If lactic acidosis is evident, correction with bicarbonate may be necessary.

The frontal lobectomy on her dominant side accounted for her apathy and some of the disorientation. It would be easy to account for some of her lethargy and hyperhagic state by attributing it as being secondary to the lobectomy. Failure to recognise the syndrome early almost led to her demise. Its possible occurrence in the obese, latent diabetic is emphasised. Diagnosis will be established by the extremely high blood sugar levels without ketosis, and hypernatremia in a patient with progressively decreasing sensorium. Once recognised, there should be no delay in therapy if the quality of the survival is to be enhanced.

Summary

1. A case of hyperosmolar non-ketotic diabetic acidosis is described in a patient following craniotomy and removal of a suprasellar tumor.
2. An awareness of its possible occurrence is important to surgeons if it is to be prevented and adquately treated in the post-operative patient.
3. Its treatment is briefly discussed. Early recognition and treatment can hope to reduce the high mortality and morbidity attendant with this condition.
4. That the hypothalamus may play a role in it is suggested and needs further investigation.

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