# Abnormal Activity of Serum CPK and Syndrome Malin

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## INTRODUCTION

As one of the severe side-effects caused by psychotropic drugs, during the treatment of psychosis, mention is made of "syndrome malin".

While the number of such cases is not large, its prognosis is very poor, as the name indicates, and there are many fatalities with only a short clinical course. Its identity still remains unknown and early elucidation is being called for.

Recently, cases showing abnormal activity of serum CPK during the course of syndrome malin have been reported[1)-3)], and subsequently its relationship with malignant hyperpyrexia during anaesthesia has become the object of debate.

In this report, we will illustrate and discuss one case of syndrome malin we have encountered.

## CASE REPORT

38 year-old male, agricultural worker

Family and hereditary history: Not contributory. Past history: Immediately after graduation from senior high school (age 18), he developed hebephrenic type schizophrenia, and after that, was hospitalized on nine separate occassions.

Present illness: In 1973, he developed psychomotor excitation and was hospitalized for the 10 th time, and at present is still in the hospital.

Up to the middle of July, 1977, he had been doing well, and daily doses of the following psychotropic drugs had already been administered: levomepromazine, 75 mg, chlorpromazine, 75 mg, and perazine, 75 mg. These doses are all considered to be the lower limit of the usual doses.

From the middle of July, the patient started complaining of occassion-

al sleeplessness, and became ill-humored. Muttering to himself, he would walk around the corridor or shout out of the window; so from July 25, intramuscular injections of Cocktelin H®, 25 mg, were given for three consecutive days. However, the psychiatric symptoms remained bad. At one time, he ate while laying himself out flat on a wooden floor, and when questioned about it, he started hitting the nurse. On July 29, he was restless from the morning and began showing salivation and dysarthria. On the 30 th, he showed a delusional mood; perspiration was conspicuous and pulse weak. Syndrome malin was suspected, and on July 31, administration of the psychotropic drugs was discontinued and intramuscular injections of biperidin, 5 mg, were given twice a day. Chest X-ray, erythrocyte sedimentation rate and urinalysis showed no evidence of abnormality.

From August 1, massive substitution infusion was started concurrently with intramuscular iniections of biperiden in daily doses of 10 mg, along with the administration of antibiotics. The patient showed pallor, marked perspiration, weak pulse, heart rate 130/min and a body temperature rising to 39°C. When exposed to strong light, he closed his eyes, and when spoken to, he made no reaction whatever. Muscular rigidity was prominent. There was no sign of accentuated brain pressure. Due to the retention of urine, a catheter was introduced.

With the room temperature lowered and his body chilled with an ice bag, his body temperature declined by 1-2°C.

A laboratory examination, on August 2, revealed a white cell count of 9,000, blood sugar, 98 mg/dl, serum LDH, 680 u., serum GOT, 20 u., serum GPT, 27 u., alkaline phosphatase, 6.6 u., CCLF 2, NPN, 63 mg/dl, urea N, 45 mg/dl, creatinine, 2.8 mg/dl, uric acid, 11.5 mg/dl, serum CPK, 538mU/ml, with no abnormality in serum electrolytes.

On August 3, his body temperature fell to 38°C, heart rate improved to 100/min, and the retention of urine became less severe, although the clouding of consciousness, muscular rigidity and salivation were of a high degree. His blood pressure became less fluctuating and settled at around 120/72.

With the serum CPK decreasing at 300 mU/ml on August 4 and 280 mU/ml on the 5 th, the clouding of consciousness became less severe. On August 6, the body temperature declined to 37°C and the patient could eat, although only a small quantity, with the aid of a nurse. The white cell count was 7800. A spinal fluid test performed on that day day showed no abnormal findings. Findings of the electroencephalogram gave a slightly low voltage.

On August 7, the patient got over the crisis completely. Laboratory examination performed on that day revealed, a white cell count of 6400, A/G ratio, 1.12, LAP, 200 u., LDH, 655 u., serum GOT, 45 u., serum GPT, 29 u., alkaline phosphatase 9.2, NPN, 35 mg/dl, urea N, 17mg/dl, creatine, 1.6 mg/dl, uric acid, 6.3 mg/dl and serum CPK, 319 mU/ml.

The patient showed complete amnesia for the period from the end of July to August 5.

Since the patient has had delusions of persecution again since August 10, chlorpromazine, 75 mg/day, is being administered.

## DISCUSSION

This case showed marked neuro-circulatory symptoms, such as perspiration and tachycardia, as well as fever, muscular rigidity, and akinetic mutism subsequent to the parenteral administration of psychotropic drugs to psychomotor excitation.

Various sequela, left after recovery from the above-mentioned symptoms, are in agreement with the clinical course of "syndrome malin" in cases hitherto reported.

Regarding differential diagnosis, mention is made of encephalitis, "tödliche Katatonie"[4], "délire aigu"[5], heat stroke[6] and exhaution syndrome[7].

Encephalitis may be differntiated from this diesease judging from its neurological findings and clinical course.

Differentiating "tödliche Katatonie" from this disease is not necessarily difficult, since the extrapyramidal symptom is of a high degree in the former.

"Délire aigu" presents a different picture from that of this disease in that acute delirium stands in the foreground.

In "délire aigu", heat stroke and exhaution syndrome, poor nutritional condition, hypohydration and physical exhaution are combined to form a "preparatory state", and administration of psychotropic drugs under such a state is believed to have upset the equilibrium in the body for the onset of the disease. Therefore, differentiating them would require further studies.

The parenteral administration of psychotropic drugs is a possible catalyst to this upsetting of the equilibrium state that leads to syndrome malin. Particulary, when drugs with a high mg potency are administered, the possibility of danger becomes higher.

According to reports hitherto published, syndrome malin often

develops in patients at puberty, particularly in females. Also, it is said to be often found in elderly persons. Furthermore, the possibility of this disease developing becomes higher, if the physical condition of the patient is poor. According to our experience, this disease develops in the summer in 6 out of 12 cases, including case not yet published. This suggests that high temperature and high humidity lower the physical strength of the patient, and that a dehydrated state is associated with the development of this syndrome.

Two cases in our report were complicated with diabetes mellitus[9], and cases reported by Sumiyoshi et al.[3] also had diabetes concurrently. This is an interesting factor regarding the patient, although the relationship between diabetes mellitus and this syndrome is unknown.

In the laboratory findings, mention is made of hyperleukocytosis, increased erythrocyte sedimentation rate, high values of serum GOT, GPT, BUN, presence of urine protein, and abnormal activities of serum CPK and LDH. Particularly, abnormal activities of serum CPK and CDH parallel the severity of the clinical symptoms of this syndrome. Previously, it was reported that serum CPK is mainly of the MM type deriving from the skeletal muscle, and that serum LDH is $LDH_5$[3]. It is malignant hyperpyrexia during anaesthesia that resembles these findings.

In malignant hyperpyrexia, a sharp rise in the body temperatur and muscular rigidity all over the body from several minutes to several hours after administration of halothane and succinyl choline chloride appears, and death results in many cases.

However, malignant hyperpyrexia is considered an abnormal reaction to anaesthetics. It shows a rise in GOT, GPT and LDH and abnormal activity of CPK, as does syndrome malin[10]. There are many points of agreement between the two, except that the clinical course progresses very rapidly in malignant hyperpyexia. However, further studies should be made as to their differences.

Regarding the mechanism by which syndrome malin is produced, the theory that psychotropic drugs might possibly exert a toxic effect directly on the central nervous system, particularly, the mesencephalon, diencephalon and medulla oblongata is becoming popular[11].

However, the idea of placing emphasis on the impairment of metabolic mechanism of the cell membrane of the muscle, as the mechanism of development in the case of malignant hyperpyrexia, is also considered worthy of studying in syndrome malin.

## SUMMARY

We have reported on one case of syndrome malin which took a typical course.

Serum CPK and LDH showed high values, and changes in them were in agreement with the course of the clinical symptoms. Furthermore NPN and urea N also showed abnormally high values, but they were transient.

It is highly possible that deterioration of general conditions and instability of the autonomic nervous system will lead to the development of this syndrome, with parenteral mass-dose administration of psychotropic drugs as a cue. Hence, there is a need to exercise utmost care in this respect.

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