

# PSYCHOSIS, INTERMITTENT HYPONATRAEMIA, POLYDIPSIA AND NEUROLEPTIC MALIGNANT SYNDROME IN A PATIENT WITH SCHIZOPHRENIA

S. B. Menezes, D. A. Braganza Menezes

## ABSTRACT

The syndromes of psychosis, intermittent hyponatraemia and polydipsia (PIP) and neuroleptic malignant syndrome (NMS) are rare. Rarer still is their concomitant occurrence.

This case report describes a 44 year old, schizophrenic, Caucasian female who presented with vomiting and confusion. A subsequent seizure and fluctuating consciousness prompted rapid investigation revealing a very low sodium level. These symptoms coupled with a history of excessive water consumption in the weeks preceding admission led to the diagnosis of PIP syndrome. Intensive care led to an initial recovery, however the patient deteriorated again, developing fever and muscle rigidity. A subsequent elevated creatine kinase level led to the diagnosis of NMS and antipsychotic medication was stopped. Upon stabilisation she was transferred to psychiatric care and managed with closely monitored antipsychotic medication.

The exact pathogenesis of these two syndromes is not well understood. Neither is their potential to have a synergistic effect. Though polydipsia and hyponatraemia are well documented in psychiatric patients, whether or not there is an underlying disorder leading to excessive water consumption is unclear, as is the association between NMS and hyponatraemia. PIP is thought to be related to a dysfunction in the limbic system. In addition to this several investigators have shown that NMS is related to the degree of D2 receptor blockade. Both typical and atypical antipsychotics can lead to NMS. The co-existence of these two conditions can have important implications for their diagnosis and management.

**Key words:** Psychosis, Intermittent hyponatraemia, Polydipsia and Neuroleptic Malignant Syndrome, Schizophrenia.

## INTRODUCTION

PIP Syndrome is defined as the triad of psychosis, intermittent hyponatraemia and polydipsia. Similarly, the symptoms of fever, muscle rigidity, delirium and autonomic instability are collectively referred to as Neuroleptic Malignant Syndrome (NMS).

In terms of the aetiology of PIP syndrome, although polydipsia and hyponatraemia are well noted to be present in psychiatric patients, especially those with schizophrenia<sup>1</sup>, an underlying disorder causing compulsive water consumption in psychiatric patients remains unclear<sup>2</sup>. It is hypothesised though that impairment in central thirst regulation<sup>1,3</sup>, drug therapy<sup>4</sup> or the endogenous opioid system<sup>5</sup>, may well contribute to an

altered sensation of thirst, and result in compulsive drinking behaviour.

Neuroleptic malignant syndrome (NMS) is a rare, but serious and potentially fatal complication of treatment with antipsychotic medication. There have also been papers alluding to an association between NMS and hyponatraemia<sup>6,7</sup>, believed to be either coincidental or as a result of an undefined common pathogenesis<sup>6</sup> i.e. an acute imbalance of sodium in the central nervous system<sup>7</sup>. Others<sup>8</sup> hypothesise that acute hyponatraemia may have served as a precipitating factor for NMS.

The chances of an individual having both PIP and NMS simultaneously is quite rare, however a previous history of psychiatric illness, and subsequent treatment with psychotropic medication may provide valuable clues to the diagnosis and management of such patients.

Despite the number of reports currently in literature, there are few cases documented of both PIP and NMS concurrently. This case report describes a female schizophrenic patient exhibiting the cardinal symptoms of both PIP and NMS.

**S. B. Menezes**, MBBS DPM MRC Psych, Consultant Psychiatrist, Queen Elizabeth Psychiatric Hospital, Edgbaston, Birmingham, B15 2QZ. E Mail: Simon.Menezes@bsmht.nhs.uk

**D. A. Braganza Menezes**, University of Birmingham, Birmingham UK

**Correspondence:**

**Dr. Simon B Menezes.**

## CASE HISTORY

Miss X, a 44-year-old Caucasian female with schizophrenia, presented to the University General Hospital with vomiting and confusion. There was a history of a large volume of water consumption in the weeks preceding admission.

Soon after admission, she suffered a grand mal seizure, and on investigation was found to have profound hyponatraemia (serum sodium levels were 108mmol/L). A series of investigations were undertaken, including blood tests, CT scan, MRI and an EEG, all of which were normal.

Her condition subsequently deteriorated and she suffered respiratory arrest and became comatose. She was transferred to ITU and put on a ventilator, following which she underwent kidney dialysis to normalise her serum sodium levels.

She regained consciousness and appeared to recover, but deteriorated the next day, developing fever and muscle rigidity. She again became confused and her CK levels were found to be 58,000 Units.

Neuroleptic malignant syndrome was diagnosed following consultation by a neurologist. Her antipsychotic medication was stopped, and she was treated with Dantrolene and other supportive measures. When her condition stabilised, she was transferred back to the psychiatric hospital, where her behaviour deteriorated. She was thought-disordered, with auditory hallucinations, paranoid beliefs, incoherent speech, irritability and a lack of insight into her condition. She was started on Clozapine but as she refused oral medication, she was initially treated with Lorazepam injection and then was treated with Depixol 40 mg IM every two weeks, under close observation. When her psychiatric condition improved, she was treated with Quetiapine 150 mg per day and oral Lorazepam.

Miss X did not have any significant previous medical history, and there was no family history of mental illness. Premorbidly, her mother described her as a quiet lady who lacked self-confidence. She isolated herself and did not have many friends.

Her conclusive diagnosis was that of schizophrenia with PIP syndrome and NMS. She was monitored closely to ensure that she did not consume excessive amounts of water. Owing to management difficulties, she presented to an acute psychiatric ward, she was placed, and currently resides in, a low security private facility. Her mental state has improved but she remains thought-disordered, and lacks insight into her condition, but takes Quetiapine and Lorazepam with gentle persuasion.

## DISCUSSION

This case highlights how consumption of large amounts of water prior to admission led to a presenta-

tion of vomiting, confusion and delirium. As doctors were attempting to stabilise her electrolyte imbalance, it is evident that the possibility of developing NMS was overlooked. In this way, the presence of PIP clearly hindered the diagnosis of NMS.

PIP is thought to be caused by dysregulation of the endogenous opioid system, which in turn leads to compulsive drinking behaviour<sup>5</sup>. It is also hypothesised that there is a close link between dysfunction of the limbic system (causing psychosis) and dysregulation in hypothalamic centres manifesting in polydipsia and osmo dysregulation<sup>8</sup>. Hence one can view PIP as a neurologically-related dysregulation rather than a drug-induced condition.

Several investigators have suggested that the likelihood of an antipsychotic causing NMS may correlate with its D2 receptor blockade in the nigrostriatal tract, mesocortical pathway and hypothalamic nuclei<sup>9</sup>. Both typical and atypical antipsychotics can give rise to NMS<sup>10</sup>. The re-introduction of antipsychotics after one has had NMS and the ability of the patient to tolerate them without giving rise to the condition again, suggests that NMS is multifactorial in nature, and not solely precipitated by drugs. Advanced stages of psychotic disorders associated with catatonia can progress to exhaustion, stupor, hyperthermia and death.

Simultaneous management of the two conditions is quite complex, and it is difficult to say if there was any cause-effect relationship between the two conditions. However in this particular case, PIP was followed by NMS and delirium was the link between the two conditions. The presence of hyponatraemia may hinder the diagnosis of NMS. Hyponatraemia is a common electrolyte disturbance occurring in a broad spectrum of patients, from asymptomatic to critically ill<sup>11</sup>. There are thought to be serious neurological sequelae associated with hyponatraemia<sup>12</sup>. Miss X suffered some neurological damage, but establishing the exact nature of the neurological damage was hampered by her psychiatric condition. As part of her management we had to keep a close eye on her water intake. The quick identification and management of both the PIP and Neuroleptic malignant syndromes led to a favourable outcome.

The association of hyponatraemia and NMS that has been found may be due to an undefined common pathogenesis of NMS and PIP, or may indeed be coincidental. As delirium is common in both, the combined management of the two conditions is quite challenging. The combination of psychosis, intermittent hyponatraemia, and polydipsia (PIP syndrome), seen in the seriously mentally ill, can result in an accelerated death rate if not identified early. Although rare, it is nevertheless very important to maintain a high level of suspicion when any patient presents with fever, muscle rigidity, confusion and autonomic instability (NMS), making it essential for all doctors and nurses to be familiar with this life threatening condition.

## REFERENCES

1. Illowsky BP, Kirch DG. Polydipsia and hyponatraemia in psychiatric patients. *Am J Psychiatry* 1988; 145: 675 – 83.
2. Lydakos C, Apostolakis S, Thalassinou E, Stamataki K, Saridaki K, Basta M. PIP syndrome: A potentially threatening manifestation of a psychiatric disorder. *Int J Clin Pract* 2005; 59: 612 – 3.
3. Goldman MB, Luchins DJ, Robertson GL. Mechanisms of altered water metabolism in psychotic patients with polydipsia and hyponatraemia. *N Engl J Med* 1988; 318: 397 – 403.
4. Rao KJ, Miller M, Moses A. Water intoxication and thioridazine. *Ann Intern Med* 1975; 82: 61.
5. Nishikawa T, Tsuda A, Tanaka M, Nishikawa M, Koga I, Uchida Y. Involvement of the endogenous opioid system in the drinking behavior of schizophrenic patients displaying self-induced water intoxication: a double-blind controlled study with naloxone. *Clin Neuropharmacology* 1996; 19: 252-8.
6. Schmitz B, Trimble MR. Carbamazepine and PIP-syndrome in temporal lobe epilepsy. *Epilepsy Res* 1995; 22: 215-20.
7. Mann SC, Caroff SN, Fricchione G, Campbell EC. Central dopamine hypoactivity and the pathogenesis of the neuroleptic malignant syndrome. *Psychiatr Ann* 2000; 30:363–74.
8. Rose BD. New approach to disturbances in the plasma sodium concentration. *Am J Med* 1986; 81: 1033 – 40.
9. Millionis HJ, Liamis GL, Elisaf MS. The hyponatremic patient: a systematic approach to laboratory diagnosis. *Can Med Assoc J* 2002; 166: 1056 – 62.
10. Caroff SN, Mann SC. Neuroleptic malignant syndrome. *Medical Clinics of North America* 1993; 77: 185–202.
11. Vachharajani TJ, Zaman F, Abreo KD. Hyponatremia in Critically Ill Patients. *J Intensive Care Med* 2003; 18: 3-8.
12. Ellis SJ. Severe hyponatraemia: complications and treatment. *Q J Med* 1995; 88: 905-9.