

Psychogenic polydipsia: a mini review with three case-reports

Polidipsia psicogena: una breve revisione della letteratura con tre casi clinici

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Summary

Background

Psychogenic polydipsia or primary polydipsia (PPD) is a disorder characterized by excessive thirst and compulsive water drinking. It may occur in both nonpsychiatric and psychiatric patients. PPD is a poorly understood, underdiagnosed disorder in patients with mental disorders. It is associated with reduced life-expectancy in patients with schizophrenia, independently from psychiatric diagnosis, because of the many, and often serious, clinical complications.

Case reports

We present three cases of psychogenic polydipsia in psychiatric

patients with long-term psychiatric mental illness and exposure to neuroleptics. PPD onset is associated with somatic delusions, dry mouth, and stressful events, respectively; those symptoms and events are broadly described in the literature. The first is a case of PPD with an episode of SIWI (self-induced water intoxication), the second is a case of simple polydipsia, and the third is a case of PPD associated with the syndrome of inappropriate secretion of antidiuretic hormone (SIADH). We briefly discussed risk factors for PPD.

Key words

Psychogenic polydipsia • PPD • SIADH • Hyponatremia • Psychosis

Riassunto

Premesse

La polidipsia psicogena o primaria (PPD) è un disturbo caratterizzato da sete eccessiva e ingestione compulsiva di acqua. Essa può verificarsi sia in pazienti psichiatrici che non psichiatrici. La PPD è un disturbo poco compreso e sotto diagnosticato in pazienti con disturbi mentali. Si associa a ridotta speranza di vita in pazienti con schizofrenia, indipendentemente dalla diagnosi psichiatrica, a causa delle molte e, spesso, serie, complicanze cliniche.

Casi clinici

Presentiamo tre casi di polidipsia psicogena in pazienti psichiatrici con malattie mentali ed esposizione a farmaci neuro-

lettici, entrambe di lunga durata. L'esordio della PPD si associava, rispettivamente, a deliri somatici, xerostomia ed eventi stressanti; tali sintomi ed eventi sono ampiamente descritti in letteratura. Il primo è un caso di PPD con un episodio di SIWI (*self-induced water intoxication*, intossicazione idrica auto indotta), il secondo è un caso di polidipsia semplice, mentre il terzo è un caso di PPD associata a sindrome da secrezione inappropriata dell'ormone antidiuretico (SIADH). Abbiamo brevemente discusso sui fattori di rischio della PPD.

Parole chiave

Polidipsia psicogena • Polidipsia primaria • Sindrome da secrezione inappropriata dell'ormone antidiuretico • Iponatremia • Psicosi

Introduction

Psychogenic polydipsia or primary polydipsia (PPD) is a disorder characterized by excessive thirst and compulsive water drinking¹. It may occur in both nonpsychiatric and psychiatric patients. The prevalence in the latter group ranges between 6% to 20%, and is usually higher in patients with schizophrenia²⁻⁴.

The water intake is conventionally over 4 l/day, while the daily urinary output exceeds 2 l⁵.

Primary polydipsia results in PPHS (primary polydipsia-hyponatremia syndrome) (natremia less than 135 mEq/l)

only in 10% to 20% of patients⁵ owing to high maximum renal clearance capacity⁵.

PPHS is usually asymptomatic in chronic hyponatremia⁶, an electrolytic modification that develops gradually, but clinical signs and symptoms are frequent in the case of quick decline of serum sodium levels (i.e. in SIWI, self-induced water intoxication)^{6,7}.

In less than 48 hours, a cerebral edema may develop because of acute hyponatremia; the central nervous system dysfunction and/or low plasma sodium concentration can lead, depending on the severity of hyponatremia, to nau-

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TABLE I.

Polyuria: the main causes (adapted from Moore et al., 2003)¹⁶.
Poliuria: le cause principali (adattato da Moore et al., 2003)¹⁶.

1) Abnormal thirst:
• compulsive water drinking
• psychogenic polydipsia (excessive thirst + compulsive water drinking)
• hypothalamic disease (i.e. sarcoidosis, craniopharyngioma, trauma, postencephalitis)
2) Cranial diabetes insipidus:
A) primary:
• family hypothalamic- X-linked or dominant autosomic mutation
• pregnancy (placental vasopressinase)
• adipsic hypothalamic
B) secondary:
• trauma (brain injury)
• tumors (pituitary, craniopharyngioma, glioma, lymphoma, metastases)
• iatrogenic (post-hypophysectomy, radiotherapy)
• autoimmune/lymphocytic hypophysitis
• granulomatous/Infiltrative (sarcoid, histiocytosis, hemochromatosis)
• infections (meningitis, encephalitis, HIV)
• vascular (Sheehan's syndrome, gastro-intestinal bleeding)
3) Nephrogenic diabetes insipidus:
A) primary:
• hereditary (X-linked, recessive autosomic mutation)
• idiopathic
B) secondary:
• chronic renal disease
• metabolic disease: hypokaliemia, hypercalcemia
• drugs: lithium, AVP antagonists, tetracyclines, amphotericine B, demeclocycline
• smotic diuresis: glycosuria (i.e., poorly controlled diabetes mellitus)
• systemic disease: amyloidosis, sickle-cell disease, myelomatosis

sea, vomiting, disorientation, headache, agitation, confusion, hallucinations, impaired mental function, incontinence, seizures, and coma^{2 6 8-10}.

There are several organic disorders clinically characterized by polyuria and/or polydipsia, with or without hyponatremia (Table I).

On the other hand, both in psychiatric and in nonpsychi-

atric patients, hyponatremia may be not related to polydipsia. This is the case of the syndrome of inappropriate antidiuretic hormone secretion (SIADH), which is another metabolic disease often associated with psychosis. The functional relationship between inappropriate vasopressin secretion and psychosis is unclear. A permissive vasopressin release, despite reduced plasma osmolality, is the core of the syndrome; normal renal and adrenal functions are also cardinal findings. Low plasma osmolality (< 280 mOsm/kg), hyponatremia, high urinary osmolality (related to plasma osmolality) and hypernatremia (> 30 mmol/l) are frequent in SIADH^{6 7 11}.

Besides schizophrenia, several psychotropic drugs (i.e. antipsychotics, antidepressants, and mood stabilizers) may cause SIADH. See reviews for more detailed information^{6 12-14}. We summarized, in Table II, the most useful tests in differential diagnosis among PPD, DIN, DIC, SIADH and PPD + SIADH.

We report here three cases of PPD with several complications.

Case report 1 (A)

Mr. A is a 40-year-old man affected by DSM-IV-TR Disorganized Schizophrenia.

His family history is positive for schizophrenia.

When A. was 14, insomnia, withdrawal from the social context, incoherent thoughts and behaviors appeared, followed by paranoid thoughts, auditory hallucinations and psychomotor agitation. He has been treated with oral haloperidol, 6 mg/day, orphenadrine and chlordesmethyldiazepam. Despite a good pharmacological compliance, hallucinations and disorganized thinking persisted for most of the time.

In 1995, he received a formal diagnosis of "schizophrenia" and in 1996 he was admitted to a "residential facility" where he is still housed.

In 2001, clozapine treatment was administered, but soon interrupted because of "heart failure".

In 2002, when Mr. A was taking haloperidol 2 mg/day, clonazepam, and valproic acid, he started drinking water compulsively, 7 l/day, and urinating 4 l/day. The patient complained dry mouth and "an iron ball" in the bowel, but there were no signs of exacerbation of psychosis.

With time, a progressive increase in fluid intake was observed, despite psychopharmacological adjustment (clonazepam was discontinued and haloperidol was increased to 5 mg/day). Laboratory measures, physical and neurological examinations were all unremarkable, apart from urine specific gravity (1005, normal values 1010-1025), until 2008, when Mr. A started drinking 20 l/day. Urine specific gravity decreased to 1001 and natremia to 124 mEq/l. He showed mild confusion and suffered from

TABLE II.

PPD, DIN, DIC, SIADH, PPD + SIADH: differential diagnoses. *PPD, DIN, DIC, SIADH, PPD + SIADH: principi di diagnosi differenziale.*

	Polydipsia	Polyuria	ADH ser.	Na ser.	Na ur.	Osm pl.	Osm ur.	WDT
PPD	Present	Present	Normal	Normal or low*	Normal or low*	Normal or low	Low or very low	Normal
DIN	Present	Present	Normal	High	Low	High	Low	Abnormal
DIC	Present	Present	Very low	High	Low	High	Low	Abnormal
SIADH	Absent	Absent	High	Low	High	Low	High	-
PPD + SIADH	Present	Present	High	Very low	Normal	Very low	Normal	Normal

PPD: psychogenic polydipsia; DIN: nephrogenic diabetes insipidus; DIC: cranial diabetes insipidus; SIADH: syndrome of inappropriate antidiuretic hormone secretion; *If sodium concentration in the serum is low, the syndrome is called PPHS (primary polydipsia hyponatremia syndrome); ADH ser.: serum ADH concentration (normal values 0.5-7.6 pg/ml); Na ser.: serum sodium concentration (normal values 135-145 mEq/l); Na ur.: urinary sodium concentration (normal values 40-200 g/l); Osm. pl.: plasma osmolality (normal values 280-295 mOsm/kg); Osm. ur.: urine osmolality (normal values 50-1290 mOsm/l); WDT: water deprivation test (this test is performed in absolute liquid deprivation, included coffee and alcohol for at least 6-8 hours, until 18 hours. The patient is not allowed to smoke during the test). It is better to start WDT in the morning. The test is normal if urine osmolality and urine specific gravity progressive increase in consecutive collections: Osm > 800 mOsm/kg and urine specific gravity > 1030).

nausea and vomiting, yet the psychopathological picture was stable so that we could restrict his access to fluid intake to 3 l/day. One month later, urine specific gravity increased to 1004, natremia to 137 mEq/l, and neurological examination returned to the normal range.

Since fall 2008, Mr. A had been drinking approximately 7 l of water a day – sometimes more than 10 l – and urinating approximately 3 l/day.

In July 2009, Mr. A underwent more laboratory examinations that were all normal, including natremia, plasma osmolality, and ADH serum, except for urine specific gravity (1004).

His case history included occasional urinary incontinence. The more Mr. A is concerned about his constipation and foreign bodies in his bowel, the more water he drinks.

Year after year, the time free from bizarre behaviors, odd and non-structured delusions with disorganized thinking, progressively decreased.

Case report 2 (B)

Mr. B is a 61-year-old man diagnosed with DSM-IV-TR Paranoid Schizophrenia. His family history is negative for mental disorders. He smokes 40 cigarettes/day.

At the age of 25, social withdrawal, avolition, apathy and paranoid ideation emerged. In 1979, he was admitted in a psychiatric hospital because of visual and auditory hallucinations and psychomotor agitation. Discharged with a diagnosis of "Psychosis", he was prescribed haloperidol and orphenadrine. The clinical picture improved partially, but auditory hallucinations and interpretative thoughts persisted.

In 1996, he was diagnosed with "Paranoid Schizophrenia" and was admitted to a residential facility, where he

is currently housed. Mr. B states he began drinking more water than usual in 1992 owing to dry mouth. His psychopharmacological therapy at that time was pimozide, orphenadrine and benzodiazepines (BDZs).

His daily water intake gradually increased: in October 2007, when he was drinking 6 l of water/day, natremia fell to 130 mEq/l and urine specific gravity to 1002. He was asymptomatic, with unremarkable physical and neurological examinations.

Since the beginning of 2009, when he was taking risperidone 6 mg/day and lorazepam, the patient had increased water drinking to 10 l/day. He again supported his compulsive drinking was due to dry mouth, nevertheless, social withdrawal and disturbing auditory hallucinations were stronger than usual. In July 2009, natremia, plasma osmolality, natriuria, and urine specific gravity were lower than standard. Physical and neurological examinations and serum ADH were unremarkable.

Haloperidol 1 mg/day was added and thirst decreased gradually along with restlessness and disturbing misperceptions.

Currently, Mr. B. is drinking about 3 l of water daily.

Case report 3 (C)

Ms. C. is a 34-year-old unmarried woman affected by DSM-IV-TR Bipolar Disorder, type I.

Her family history is positive for major depressive disorder. Ms. C. was a very introverted child showing little interest in looking for friends.

In 1992 insomnia, euphoria, logorrhea, hyperactivity, sexual disinhibition, and ideational acceleration appeared. Hospitalized in a psychiatric ward, Ms. C. was treated with clotiapine, haloperidol, biperiden, lorazepam, and

lithium carbonate, and then discharged with diagnosis of Manic Episode. After 6 months of good psychic health, depressed mood, social withdrawal, crying spells, and thoughts of self-harm emerged. The major depressive episode was followed by another manic episode.

She was diagnosed with Bipolar Disorder, Type I, in 1994. Atypical neuroleptics did not benefit her significantly, hence she started taking clozapine until she reached a dosage of 300 mg/day.

Her mother reported that Ms. C's body image has been distorted since 1991. She lost and gained weight regardless of mood fluctuation.

In 2002, when the therapeutic regimen was clozapine 100 mg/day, lithium carbonate 900 mg/day, valproic acid and clonazepam, with mood being relatively stable, and the form and content of thought were more regular than in the past, PPD suddenly emerged. She started drinking 8 l of water/day and urinating 4 l/day. She says that the onset of polydipsia occurred when she did not feel to be in the center of attention. She still compulsively drinks when she is sad

and/or anxious, or when she carries-out a task unwillingly. Ms. C. believes drinking decreases anxiety, frustration, and sadness and, even though she is aware her behavior is ineffective, she equally feels obliged to drink. Polydipsia and polyuria made her condition worse: in 2008, the patient drank up to 15 l/day. She was diagnosed with nephrogenic diabetes insipidus. Lithium was replaced by levomepromazine, and clozapine was increased to 125 mg/day.

Despite lithium discontinuation, PPD did not decrease.

In July 2009, she underwent more instrumental (MRI scan of the brain) and laboratory investigations (i.e., urinary sodium, specific gravity, and osmolality) that were all normal as well as physical and neurological examination, with the exception of vasopressin (ADH), that was inappropriately high (18.7 pg/ml).

Currently, her mood is neither low nor euphoric, her content and form of thought are both regular, and her anxiety is waxing-and-waning, while she still drinks 8 l of water/day and urinates 4 l/day.

Discussion

We described three cases of chronic "severe polydipsia", the first associated with an episode of SIWI (self-induced water-intoxication) and the third associated with SIADH. PPD onset occurred late in the course of mental illness, after many years of exposure to "typical neuroleptics", in all three cases reported. Chronicity^{15 16} and long course of illness^{3 9} seem to be associated with polydipsia. Schizophrenia is probably a risk factor for primary polydipsia and PPD associated with SIWI¹⁵, while the relationship between antipsychotics and primary polydipsia is unclear. We report dry mouth symptoms, somatic delusions, and stressful life events as circumstances "triggering" or contributing to PPD described in literature^{5 8 14}.

As a neurobiological and neurotransmitter explanation, the polydipsic theory of dopamine supersensitivity is a reason reported for the strong association of polydipsia and psychosis^{12 17 18}. This explanation is consistent with many years of exposure to "typical neuroleptics", with the limited efficacy of high-dose antipsychotic therapies (Case A and B) and with the exacerbation of psychotic symptoms in parallel with increased compulsive drinking (Case B).

Moreover, male gender, smoking, and white race are risk factors for SIWI, yet there is little evidence about their relationship with simple polydipsia¹⁹.

As far as therapy is concerned, behavioral and pharmacological treatments are available for psychogenic polydipsia. The former include therapeutic fluid restriction, with or without reinforcement schedules using tokens to get rewards (more feasible in inpatients), and cognitive techniques. As Mr. A. did not show clear psychosis exacerbation, but substantial cognitive impairment, we chose a partial fluid intake restriction without reinforcement schedules.

TABLE III.

Synopsis of the three case-reports. *Sinossi dei tre casi clinici.*

	Case A	Case B	Case C
Gender	M	M	F
Diagnosis	Disorganized		
Schizophrenia	Paranoid		
Schizophrenia	Bipolar		
Disorder I			
Age	40	61	34
Duration of illness	26	36	18
Duration of PPD	7	17	8
Duration of psychotropic treatment	26	36	18
CT/MRI			
Brain scan abnormality	-	Not available	± (1)
Low plasma osmolality	-	+	-
Hyponatremia	-	-	+
SIADH	-	-	+
Polyuria	++	++	++
Polydipsia	++	++	++
Dry mouth	+	++	-
Somatic delusions/ body image distortion	++	+	++
SIWI	+	-	-

M: male; F: female; -: absent; +: slight; ++: marked; N.V.: not assessable; SIWI: self-induced water intoxication; ± (1): at the lower normal threshold.

Furthermore, several drugs may improve PPD, but none had been tested in a large trial. Clozapine, low-dose risperidone, and low-dose olanzapine – all administered after long-term exposure to typical neuroleptics – may decrease dopamine receptor supersensitivity and, eventually, thirst stimulus^{14 17 18}. In our report, Mr. B increased his water intake rapidly side by side with the exacerbation of disturbing hallucinations. He was already taking Risperidone 6 mg/day, so that we administered low-dose haloperidol to reduce psychosis symptoms. Approximately 15 days after the beginning of the low-dose typical neuroleptic, hallucinations and PPD began decreasing at the same time. Other pharmacological treatments include oral clonidine 0.2 mg b.i.d and oral enalapril 10 mg b.i.d. Regarding the treatment of PPHS, demeclocycline, 600 to 1200 mg/day, and lithium carbonate inhibit the action of ADH at the level of the distal renal tubules so that they reduce urine concentration, but both these drugs are potentially nephrotoxic. “Aquaretics” (i.e. conivaptan, lixivaptan, and tolvaptan) induce diuresis without altering sodium and potassium excretion so that they increase net fluid loss and urine output while decreasing urine osmolality. Ms. C. discontinued lithium in December 2008, yet PPD currently persists. Vieweg and de Leon claim that lithium treatment can sometimes explain polydipsia, especially in bipolar patients, but do not rule out PPD^{8 20}. The gold standard of SIADH treatment is identifying and correcting the underlying disorder (see the literature for more information)^{6 12-14}. Restriction of daily fluid intake to 500 to 1000 ml helps raise serum sodium levels at a rate of approximately 2 to 3 mEq/l per day (if serum sodium levels rise too quickly, quadriparesis, pseudobulbar palsy, mutism and seizures may occur due to osmotic demyelination). Other treatment options include hypertonic saline solution and drugs that reduce the renal action of ADH (i.e. Aquaretics, see above)^{7 21}. The value of a proper diagnosis of PPD lies in the possibility of planning an appropriate therapy to contrast the reduced life expectancy associated with PPD in patients with schizophrenia, independently from psychiatric diagnosis¹⁶. As pointed-out in literature and as shown in our report of three cases, further research is needed to better understand the pathophysiology of PPD, due to the complexity of the interconnections between psychopathology, neurobiology, endocrinology, and the effects of the psychiatric drugs.

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