Munchausen syndrome by proxy or metabolic deficit? The diagnosis requires a multidisciplinary approach

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ABSTRACT

Genetic disorders associated to mitochondrial fatty acid β-oxidation deficiency are rare autosomal recessive disorders that often appear early in childhood. Affected individuals display a wide range of symptoms that may include hypoglycemia, intermittent hemoglobinuria, muscle weakness, liver, neurological disorders and heart abnormalities. These disorders can mimic Munchausen by Proxy (MBP), a form of caregiver-induced disease. Ruling out genetic or metabolic causes is crucial in such cases to avoid misdiagnosis and potential harm to both the child and the caregiver (often the mother). In a forensic context, investigating metabolic and genetic abnormalities can aid in identifying cases of child abuse or poisoning. A case regarding a 3-year-old girl admitted to the hospital with suspected MBP due to benzodiazepines (midazolam) administration is described. The importance of a thorough evaluation is highlighted, considering that genetic testing revealed a familial mitochondrial disorder, excluding MBP as the cause of the child clinical symptoms. This case underscores the need for comprehensive assessments to ensure accurate diagnoses and appropriate interventions, especially when young children are involved.

Key words: *toxicology, munchausen by proxy, child abuse*

CASE REPORT

A Caucasian 3-year-old female was hospitalized with upper airway inflammation, accompanied by drowsiness and episodes of desaturation, rapidly progressing to a cardiac arrest. Upon awakening, the patient experienced abdominal pain and rapid loss of consciousness following airway suctioning and oxygen administration that required admission to the intensive care unit and intubation. Toxicological screening was negative for all tested substances except benzodiazepines. On the third day of hospitalization, a throat swab tested positive for *Staphylococcus aureus*. Chest X-ray revealed bronchial accentuation with right pleural effusion. During this period, midazolam, a benzodiazepine, was administered by medical staff for diagnostic and therapeutic purposes (Table 1). On the fifth day, urinary screening was positive for midazolam. Ten days after admission, a laryngoscopy was performed under midazolam sedation. The child continued to complain of abdominal pain, vomiting, and coughing, with nocturnal desaturation episodes (78% SpO_2). After a month, the patient developed thrombophlebitis of the left basilic vein, which was treated with enoxaparin. On the same day, the infant experienced epileptic seizures, and the urine screening was again positive for benzodiazepines (>1000 ng/mL). Subsequently, by order of the judge, the child was placed under guard while her mother was removed and placed in custody on suspicion of MBP. The patient's condition deteriorated, requiring monitoring for over 70 days.

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Almost daily, gas chromatography–mass spectrometry (GC-MS) analyses were performed to monitor midazolam concentration in urine (OH-midazolam) (Table 1). Because the mother had been removed from her daughter, with the serious accusation of illicitly administering the drug midazolam (MBP), the judge ordered a multidisciplinary medical evaluation of the case to verify the accusatory thesis.

A review of the medical documentation verified the number of infusions (a total of 5, all for therapeutic purposes) and the persistence of OH-midazolam levels despite the mother's absence for over 16 days.

Moreover, the mother's personality did not match the typical profile of MBP Syndrome, despite a forensic psychiatrist arguing otherwise based solely on toxicological data. Ultimately, retracing the medical examinations that the child underwent, signs of a fatty acid metabolism deficit was suspected. This was then confirmed by genetic medical counseling and additional laboratory tests listed in Table 2. Further confirmation of the diagnosis was sought by investigating the younger sister, who also showed the same metabolic deficit. MBP was then ruled out and the case was closed.

The persistence of elevated midazolam levels was due to a familial fatty acid β-oxidation deficiency causing altered pharmacokinetics. Indeed, it is known that fatty acid β-oxidation deficiencies are associated with dysfunction of many organs, including liver and kidneys, both of which are involved in various metabolic processes.

The limitations of this case report relate to the absence of blood examination during the first month at the hospital (with a negative blood test on day 31), as well as the lack of hair tests.

DISCUSSION

The MBP is a nosological entity classified within the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) under the category of factitious disorders.

Table 1
Toxicological urine tests

Days	Midazolam intravenous infusion	Toxicology
Day 3	6 mg	Not tested
Day 4	6 mg	Not tested
Day 5	2 mg	Not tested
Day 6	6 mg	urine screening positive (benzodiazepine)
Day 10	6 mg	Not tested
Day 30	None	urine screening positive (benzodiazepine >1 000 ng/mL, GC-MS OH-midazolam 5.18 µg/mL
Day 31	None	positive for zolpidem* (urine), GC-MS midazolam (blood negative)
Day 43	None	urine screening positive (benzodiazepine >1 000 ng/mL)
Day 44	None	GC-MS OH-midazolam 3.76 µg/mL
Day 49	None	GC-MS OH-midazolam 1.78 µg/mL
Day 50	None	GC-MS OH-midazolam 0.76 µg/mL
Day 51	None	GC-MS OH-midazolam 1.3 µg/mL
Day 52	None	GC-MS OH-midazolam 1.73 µg/mL
Day 53	None	GC-MS OH-midazolam 1.34 µg/mL
Day 54 (Day of mother's removal)	None	GC-MS OH-midazolam 1.53 µg/mL
Day 55	None	GC-MS OH-midazolam 0.78 µg/mL
Day 56	None	GC-MS OH-midazolam 0.96 µg/mL
Day 62	None	GC-MS OH-midazolam 0.99 µg/mL
Day 63	None	GC-MS OH-midazolam 0.79 µg/mL
Day 64	None	GC-MS OH-midazolam 0.82 µg/mL
Day 65	None	GC-MS OH-midazolam 0.59 µg/mL
Day 70	None	GC-MS OH-midazolam 0.26 µg/mL

**Zolpidem is a GABAA receptor agonist of the imidazopyridine class*

Factitious disorders are characterized by individuals simulating or exaggerating their own symptoms to assume the sick role and receive care and attention. It is essential to differentiate this disorder from outright malingering, where individuals feign illness for material gain. In MBP, as hypothesized in the present case, the affected individual induces clinical symptoms in a second person under their care, typically a child, elderly parent, or disabled relative, to garner attention for themselves (1). Mothers affected by this disorder often have a high level of education, and some of them have medical or nursing backgrounds.

They have a fascination with medicine and are comfortable in hospital settings, often collaborating with healthcare professionals. The presentation of symptoms is usually unquestioned, posing challenges for diagnosis and treatment (2). In such individuals, pathological aspects often surface, such as paranoid reactions, a manic belief that the child is truly ill, and a sociopathic personality. In our case, the mother has never presented herself as a resolving *deus ex machina*, which constitutes the dominant feature of the behavioral characteristics of MBP. In these cases, the perpetrator demonstrates a certain mastery of the situation, as it is in their interest that the object of their attention to ultimately have a

Table 2

Confirmatory laboratory tests for fatty acid β-oxidation deficiency

Serum Aminoacids (μmol/L)	Urine organic acids (mmol/mol creatinine)	Serum acylcarnitines (μmol/L)
Aspartic acid: 28 (r.v.<23)	Lactic acid: 342 (r.i. 1 – 25)	C12.1: 0.44 (r.i.0.04 – 0.20)
Glutamic acid: 212 (r.i. 10 – 133)	2-OH-isobutyric acid: 5 (r.v. <2)	C12: 0.77 (r.i. 0.04 – 0.21)
Citrulline: 58 (r.i. 3 – 47)	Adipic acid: 67 (r.v. <34.3)	C6DC: 0.13 (r.i. 0.02- 0.11)
Arginine: 137 (r.i. 12 – 133)	Pyroglutamic acid: 21 (r.v. <12)	C14.2: 0.29 (r.i. 0.003 – 0.15)
Valine: 463 (r.i. 64 – 294)	2-ketoisovaleric acid: 5 (r.v. na)	C14.1: 0.87 (r.i. 0.02 – 0.20)
Phenylalanine: 110 (r.i. 26 – 98)	Pimelic acid 10 (r.v. <2)	C14: 0.29 (r.i. 0.03 – 0.15)
Isoleucine: 171 (r.i. 31 – 86)	2-keto 3 -Me valeric acid: 5 (r.v. na)	C16.1: 0.19 (r.i 0.01 – 0.07)
Leucine: 286 (r.i. 47 – 155)	para-OH-phenylacetic acid: 49 (r.i. 6 – 28)	C16: 0.58 (r.i. 0.01- 0.23)
Lysine: 219 (r.i. 52 – 196)	Suberic acid: 40 (r.v. <10.1)	
	cis-aconitic acid: 7 (r.i. 26.87 – 189)	
	Sebacic acid: 4 (r.i. 1 – 4)	
	4-OH-phenyllattic acid: 19 (r.i. 0.003 – 3.1)	
	Stearic acid: 10 (r.i. 1.6 – 6)	
	Acetyl-tyrosine: 23 (r.v. <2)	
	4-OH phenylpyruvic acid: 18 (r.v. <2)	
	Glissolic acid: 115 (r.i. 0.29 – 16.9)	
	Tiglyglycine: 5 (v.n. na)	

r.i., reference interval; r.v., reference value; na, not available.

favorable outcome, thus enabling them to benefit from the recognition derived from their efforts toward that outcome. In this scenario, excluding metabolic and genetic pathologies may be crucial for resolving forensic cases, but more importantly, for preventing very young children, already afflicted by serious illnesses, from unjust separation from their mothers. Although in our case, the accusation of MBP lacks of methodological or scientific basis, it is a well-established fact that toxicological data must be critically evaluated considering clinical, metabolic, and genetic factors to address significant legal issues (3). The preferred methodological approach in cases of suspected MBP involves not only blood analysis to detect acute intoxication, but also hair analysis to reveal chronic substance administration (4). Adopting this approach would likely have provided clearer and earlier insights of the situation.

Excluding or confirming alternative causes to MBP within a reasonable timeframe is crucial before embarking on a diagnostic-therapeutic pathway or isolating the child. Isolation from the caregiver should aim to resolve the state of intoxication and prevent the administration of medications not included in the therapeutic plan. However, this is not always straightforward. Resolving cases of MBP may take years, involving a retrospective review of medical documentation and the engagement of different physicians (5). The largest study on the topic (involving 796 cases of MBP) confirms the complexity of the phenomenon and urges medical personnel to carefully assess the behavioral nuances of caregivers for an accurate diagnosis (6). On one hand, MBP can mimic known pathologies (7), while on the other hand, there is the possibility that known pathologies can mimic MBP. A review of MBP cases revealed that 25% of the children had renal or urological issues. The described causes were mainly urinary tract infections, hematuria, urolithiasis, proteinuria, and acute kidney failure. However, there may be situations where the mother informs medical personnel about her son's metabolic disorders to hide a genuine case of MBP (8).

The heterogeneous clinical manifestations of fatty acid β-oxidation deficiencies can appear early in the first years of life, mimicking intoxications by exogenous substances (9). This could lead unaware healthcare providers to erroneously diagnose MBP. Although the case was resolved without a creatinine examination and renal function assessment, it is known that fatty acid β-oxidation deficiencies are associated with renal dysfunction. This could explain the pattern of OH-midazolam elimination in the child. We believe that sharing this case can be useful to avoid future diagnostic errors.

Among metabolic deficiencies, examples include glutaric aciduria type II (GAII) and I (GAI). The latter metabolic disorder is already of medical-legal interest since its exclusion is routinely requested by forensic pathologists evaluating Abusive Head Trauma (AHT) in infants (10). The described case highlights the importance of excluding metabolic and genetic pathologies in forensic cases involving neonates and infants.

In conclusion, this case underscores the ongoing need for collaboration between clinical and forensic toxicology, especially regarding MBP (3). Although rare, metabolic disorders that can mimic forensic cases are not always related to known monogenic conditions but may also involve gene variants of uncertain significance (11).

Cases like this should be investigated by a multidisciplinary team (forensic physicians, toxicologists, and geneticists) to evaluate the specific pharmacokinetics of the subject while also probing the caregiver's psychological profile to ensure that rare genetic conditions are not overlooked (3), with the familial, social, financial, and legal consequences that suspicion of violence or abuse against a minor entails. The case deserves to be shared with the scientific community as it highlights the difficulty in identifying MBP in children with genetic disorders and how delayed toxicological investigations or misinterpretation of these can lead to incorrect diagnoses and dramatic effects on infants.

CONFLICT OF INTEREST

None

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