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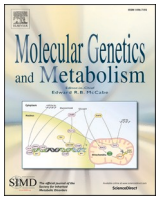

Oral D-mannose therapy during pregnancy in a woman with MPI-CDG: A case report and management review

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ABSTRACT

Mannose 6-phosphate isomerase deficiency is a rare disorder of N-glycosylation leading to impaired coagulation, enteropathy, hypoglycemia and liver disease. D-mannose is the only available treatment. We report the case of a pregnant woman with MPI-CDG and the management of D-mannose therapy during pregnancy. D-mannose was discontinued at 6 weeks' gestation, due to the potential fetal toxicity observed particularly in animal models, but severe digestive symptoms and hypoglycemia relapsed. We decided to readminister D-mannose therapy at 10 weeks' gestation although data on teratogenecity in humans are lacking. Symptoms resolved rapidly when D-mannose was resumed. Monitoring of transferrin glycoforms profile and coagulation parameters allowed to gradually increase D-mannose dosage throughout pregnancy. The patient delivered at 38 weeks' gestation after an intrauterine growth retardation was noted. The infant was 2.390 kg at birth with a low Apgar score but rapidly recovered. Low dose D-mannose treatment administered from 10 weeks' gestation could be a safe option for women with MPI-CDG.

1. Introduction

Mannose-6-phosphate isomerase (MPI) deficiency is a rare disorder of protein N-glycosylation and belongs to the group of congenital disorders of glycosylation (CDG) (1–3). The disease (OMIM: 602579) was called CDG-Ib or Lac-Saint-Jean-Saguenay syndrome in former

Abbreviations: aPTT, activated partial thromboplastin time; CDG, congenital disorder(s) of glycosylation; IUGR, intrauterine growth retardation; MPI, Mannose-6-phosphate isomerase; Trf, transferrin; WG, weeks' gestation.

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classifications (4,5). It causes enteropathy, hyperinsulinemic hypoglycemia, progressive liver fibrosis, coagulation impairment and thrombosis (2,4–11).

MPI catalyzes the conversion of fructose-6-phosphate into mannose-6-phosphate. Oral D-mannose intake can efficiently bypass the cytosolic mannose-6-phosphate deficiency *via* specific cellular transport mechanisms (12,13). Administration of D-mannose corrects enteropathy and hypoglycemia, prevents thrombosis, and normalizes transferrin (Trf) glycoforms profile (2,14–17). However, it has no effect on the progression of liver fibrosis (17–19).

Normal pregnancies have already been reported in mild MPI-CDG patients who were not treated with D-mannose (Table 1). Westphal et al. described a case of an MPI-CDG woman who delivered three healthy children. Her history was notable because she presented clinical manifestations in childhood that gradually improved in adulthood (15). Helander et al. reported a 32-year-old MPI-CDG mother who was asymptomatic. The diagnosis was made following an abnormal Trf glycoforms assay, initially performed for screening of chronic alcohol consumption (20). Close follow-up during pregnancy in a MPI-CDG patient whose D-mannose therapy was discontinued has been reported (17,21).

While multiple literature sources and the MPI-CDG guidelines agree that mannose is the specific treatment for MPI-CDG (22,23), to our knowledge, no studies have documented mannose exposure during pregnancy for patients with MPI-CDG. Nonetheless, several animal studies have demonstrated teratogenic effects following mannose exposure (24–28).

Here, we present the first case of a pregnant woman with MPI-CDG who was treated with D-mannose therapy during pregnancy. D-mannose was discontinued at 6 weeks' gestation (WG) due to concerns about potential teratogenicity. An early relapse of MPI-CDG symptoms prompted reintroduction of D-mannose at a low dose at 10 WG. Subsequently, the dosage was adjusted based on Trf glycosylation profile and coagulation parameters until the end of pregnancy.

2. Patient and methods

The 26-year-old patient was diagnosed with MPI-CDG at the age of 3 months. Her case is referred to as No. 22 in the article by De Lonlay et al. in 2001 (9). She presented hypoglycemia, chronic diarrhea and hepatomegaly. Trf glycoforms study showed a typical type 1 pattern with accumulation of 0-sialo Trf and 2-sialo Trf, consistent with CDG type 1. MPI-CDG was suspected because of the absence of neurological involvement and was confirmed by enzymatic activity measurement. Molecular analysis in *MPI* (NM_002435.3) provided double heterozygote mutation c.764 A > G (p.Tyr255Cys)/c.1193 T > C (p.Ile398Thr) (9). She was initially treated with mannose at 0.17 g/kg every 4 h during her first year. At 1.5 and 3.5 years-old, she received 6 g per day in 4 doses, later increasing to 12 g per day (180 mg/kg/day) in 3–4 doses. Compliance to D-mannose was limited during adolescence.

Her history included a liver fibrosis with shear-wave elastometry at 43 kPa (reference range: $\leq$ 5 kPa, > 13 kPa indicates compensated advanced chronic liver disease (29)), a splenic infarction of the upper pole at the age of 25 following a one-year discontinuation of oral D-mannose (patient's decision), a first-trimester spontaneous miscarriage and tobacco use.

Oral D-mannose was supplied in powder form in 1 g individual sachets and prepared by a compounding pharmacy based in Paris (Delpech pharmacy). Reimbursement by Social Security was based on the rate applicable to a reimbursable compound preparation for a rare disease.

From the start of pregnancy, the patient was monitored by monthly clinical examination, bi-weekly Trf glycoforms studies, and coagulation factor assays (antithrombin and factor XI). Follow-up was conducted at a general hospital in collaboration with the Necker Hospital metabolic disease reference center and the biochemistry department of Bichat Hospital in Paris. Trf glycoforms study was performed on a Sebia

Table 1
Overview of all published pregnancy in MPI-CDG.

Authors	Year	Age at MPI-CDG diagnosis (years)	Symptoms	Laboratory parameters	Liver fibrosis	Treatment	Number of pregnancy	Events during pregnancy	Infant outcome
Westphal et al. (15)	2001	$2^{1/2}$ years	Chidhood: diarrhea, intestinal protein loss Adulthood: none	Chilhood: antithrombin 50 % Adulthood: antithrombin low, normal liver enzyme and factors II, VII, X	No	Childhood: anticoagulation during 13 years Adulthood: none	3	None	Healthy
Helander et al. (20)	2014	32 years	None	Antithrombin, protein S, protein C slightly lowered Normal liver enzyme	No	None	2	Not known	Healthy
Girard et al. (17) Lebredonchel et al. (21)	2020	6 years	Childhood: diarrhea, hepatomegaly, hypoglycemia Adulthood: chronic anemia, recurrent phlebitis, pulmonary embolism (after delivery)	Mild liver involvement	Elastometry 6.2 kPa (<5)	Mannose since 6 year-old (poor compliance) Stopped at 8 WG Enoxaparin during pregnancy	1	Pyelonephritis, third trimester proteinuria Delivery at 39 WG (caesarean)	Healthy, 3.540 kg, Apgar 10/10
Our patient	2025	3 months	Childhood: diarrhea, hepatomegaly, hypoglycemia Adulthood: diarrhea, hypoglycemia, splenic infarction	Lowered anticoagulation factors, mild liver involvement, low platelet count	Elastometry 43 kPa (<5)	Mannose since infancy Stopped at 6 WG Restarted at 10 WG throughout pregnancy	1	Ileocolitis Pancreatitis Hypoglycemia (9 WG) IUGR 6th percentile Delivery at 38 WG	2.390 kg at birth Apgar 2–2-4 (rapid recovery) Healthy at 8 months of age

Capillarys 2 using the Sebia CDT Kit, following the manufacturer's recommendations. This technique allows for the identification and quantification of Trf glycoforms from 0-sialo to 5-sialo-Trf (30).

Routine clotting parameters including prothrombin time, aPTT, factor XI, antithrombin, and anti-Xa activity were evaluated on STA R Max^3 instruments (Stago). The complete blood count was performed with the use of a XN hematology analyser (Sysmex).

3. Results

A pregnancy was confirmed for the patient at 6 WG, when she was still taking oral D-mannose at a dosage of 12 g per day (180 mg/kg/day). D-mannose was discontinued due to concerns about potential embryonic toxicity (24–26). Treatment with enoxaparin was initiated at 130 IU/kg and dose was adjusted to achieve an anti-Xa activity between 0.4 and 0.8. Anticoagulation therapy was necessary due to the increased risk of thrombosis associated with MPI-CDG, amplified by the discontinuation of D-mannose therapy. In addition to its anticoagulation properties, heparin alone is sometimes used to treat protein losing enteropathy in MPI-CDG patient (16,31).

The patient was admitted to the hospital at 9 WG, three weeks after discontinuation of D-mannose presenting with several episodes of watery diarrhea per day and abdominal pain. Clinical examination revealed mild diffuse abdominal tenderness and 2 kg weight loss. C reactive protein level was increased (139 mg/l; reference range: <5 mg/l), as were neutrophils count (30,000 cells/µl; reference range: 1700-7500) and lipase level (410 UI/l; reference range: 13–60). Hypo-osmolar hyponatremia was also observed (Na 124 mmol/l; reference range: 136–145, osmolarity 267 mosm/l; reference range: 278–298). AST and ALT levels were increased but within the range we usually observed in our patient (AST 87 U/l; reference range: 10–35, ALT 102 U/l; reference range: 10–35). Albumin level was low (34 g/l; reference range: 40–49). Complete laboratory data are referred in Table 2. CT scan showed ileo-colitis but no arteriovenous thrombosis of the coeliomesenteric axes, slight pancreatic edema and no perforation nor abscess. She underwent laparoscopy. Intraoperative findings included hyperhemia in the small intestine, indicative of an inflammatory process without perforation. Surgical appendectomy was performed with histologic examination showing a normal appendix. Microbiologic analyses of peritoneal samples were negative. She was treated with a 7-days course of ceftriaxone and metronidazole. Abdominal pain and ileo-colitis resolved within a few days but mild nocturnal asymptomatic hypoglycemia was noted with capillary blood glucose between 50 and 60 mg/dl (reference range: 80–100). Hypoglycemia was corrected with a standard glucose infusion. Blood insulin analysis was not performed at that time. Diarrhea persisted (2 to 4 loose stools per day) and albumin level dropped to 25 g/l suggesting protein losing enteropathy.

D-mannose was resumed at 10 WG with a low dosage of 4 g per day (60 mg/kg/day) divided into 4 doses. This decision was made after discussions with the patient and her husband, who were fully informed of the potential risks to the fetus. Hypoglycemia and diarrhea improved rapidly and did not recur throughout the pregnancy. Treatment with enoxaparin was continued at a dosage of 180 IU/kg. Quantification of Trf glycoforms before and during oral D-mannose therapy is shown in Fig. 1. All parameters improved during the course of D-mannose treatment. In view of the relative degradation of the Trf glycosylation pattern (with increases of the % of 2-sialo and 0-sialo Trf) at 21 WG, the D-mannose dosage was increased to 8 g per day (120 mg/kg/day), divided into 4 doses.

Intrauterine growth retardation (IUGR) at the 4th percentile was observed at 30 WG. The patient was hospitalized for preterm labor at 33 WG. She was treated with atosiban (32) and corticosteroids.

Delivery was induced at 38 WG due to IUGR with the newborn at the 6th percentile for weight. The patient delivered a girl weighting 2.390 kg (under the 5th percentile), measuring 45 cm in length with a head circumference of 31.5 cm. The Apgar score was altered (2–2–2–4) requiring aspiration and non-invasive ventilation at birth. The infant presented with hypotonia, hyperextension movements, irritability, and a lack of suction and was classified as stage II according to the Sarnat score. Treatment in a neonatal intensive care unit included antibiotics (cefotaxime and amikacin), sedation (morphin) and therapeutic hypothermia. Brain MRI and electroencephalogram results were normal. She rapidly recovered and a normal examination was observed at day 7. Subsequently, her growth and neurological development were normal, except for a mild peripheral hypertonia (Table 3).

D-mannose was increased for the patient to 12 g per day (180 mg/kg/day) three weeks after delivery and curative anticoagulation with enoxaparin 180 IU/kg was continued for three months.

Table 2
Laboratory data before and during during pregnancy.

Weeks' gestation		1 year before pregnancy	6	8/9	10	15	19	23	25	31	35	38
Weight (kg)		64	68	66	66	65	67	69	70	71	71.5	_
Treatment												
D-mannose dosage in g per day (mg/kg/day)		12 (180)	Discontinuation at 6 WG	0	4 (60) Start at 10 WG	4	4	8 (120) Start at 21 WG	8	8	8	8
Enoxaparin dosage (IU/24 h)		_	8000 Start at 6 WG	8000	12,000	12,000	8000	8000	12,000	12,000	12,000	12,000
Coagulation	Reference range											
Prothrombin Time (%)	80–120	62	_	85	78	80	86	83	88	78	80	81
aPTT ratio	< 1,20	1.42	_	1,63	1.29	1,38	1,2	1,14	1,08	1,19	1,14	1,49
Antithrombin (%)	80–120	_	_	38	57	53	63	74	71	62	87	65
Factor XI (%)	67–196	_	_	19	54	43	54	56	61	64	92	_
Anti Xa activity (IU/ml)	1,03–1,37	<0.1	_	0,8	0,54	0,66	0,46	0,35	0,24	0,45	0,63	0,88
Aminotransferase												
AST (UI/l)	10–50	91	_	62	31	163	82	29	28	37	22	44
ALT (UI/l)	10–50	84	_	83	27	152	82	30	26	30	16	30
Hemogram												
Hemoglobin level (g/dl)	13,4-16,7	12.7	_	11.3	8.7		10,7	10,2	10,4	10,2	10,5	11,3
Platelet counts (G/l)	150–400	83	_	117	152	86	90	76	86	92	134	151

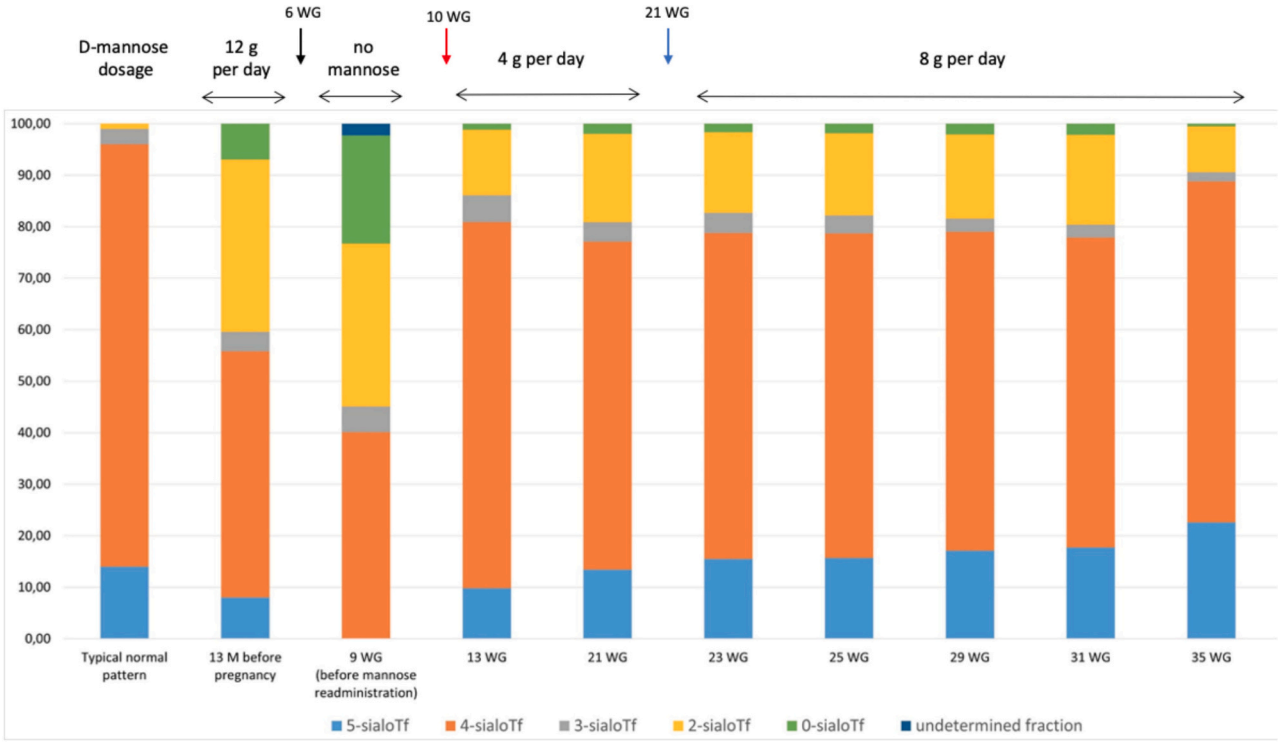

Fig. 1. Evolution of Trf glycoforms percentages in the patient.
Bar histogram showing respective % of 5-sialo to 0-Trf fractions during the follow-up of the patient. Discontinuation of oral D-mannose at 6 WG (black arrow) was associated with a worsening of Trf glycosylation characterized notably by a decrease of the 4-sialo Trf glycoforms (orange) coupled to increases of the 2-sialo (yellow) and 0-sialo Trf glycoforms (green). Readministration of D-mannose at a dose of 4 g per day (60 mg/kg/day) at 10 WG (red arrow) and at a dose of 8 g per day (120 mg/kg/day) at 21 WG (blue arrow) was associated to a clear improvement in Trf glycosylation with the increases in the 5-sialo (light blue) and 4-sialo Trf glycoforms at the expense of the 3-sialo, 2-sialo and 0-sialo hypoglycosylated fractions. The dark blue fraction corresponds to an undetermined hypoglycosylated Trf form found at 9 WG only.

Table 3
Infant outcome from birth to 8 months of age.

Age (months)	0 (birth)	1	2	3	4	5	6	7	8
Height (cm)	45	47	54	56	57	61	63	_	66.5
Weight (kg)	2.390	3.300	4.200	4.900	5.400	6.000	6.700	_	7315
Head circumference (cm)	31.5	_	36	37	38	39	40	_	41
Neurological development	Hypotonia Hyperextension movements Irritability Lack of suction	_	No hypotonia Smile	_	No hypotonia	_	_	_	Mild peripheral hypertonia Normal axial tone
Eye exam	_	-	No strabismus Normal ocular pursuit Normal pupils	_	Normal ocular pursuit	_	_	_	No strabismus
Clinical events	Antibiotics (cefotaxim, amikacin) Sedation (morphin) Therapeutic hypothermia	Gastroesophageal reflux	_	_	_	_	_	Bronchiolitis	Normal auditory test

Coagulation factors, including antithrombin, and factor XI, increased proportionally to the D-mannose dosage. The average rates of antithrombin and factor XI were 58 % and 48 % with 4 g per day (60 mg/kg/day) of D-mannose, and 71 % and 68 % with 8 g per day (120 mg/kg/day), respectively. Similarly, liver enzyme levels improved slightly with 4 g per day of D-mannose and normalized with 8 g per day. Hemoglobin levels remained stable throughout pregnancy, and platelet count improved only at 35 WG.

4. Discussion

We report the first case of a patient with MPI-CDG who received oral D-mannose therapy during pregnancy. Our patient experienced recurrent digestive symptoms and hypoglycemia when D-mannose therapy was discontinued at 6 WG due to concerns about teratogenicity. Consequently, treatment was reintroduced at gradually increased doses starting at 10 WG and continued until the end of pregnancy.

The aim of this case report is to explain our management of this

particularly rare clinical situation, characterized by uncertainty regarding the use and appropriate dosage of D-mannose and by an increased thrombotic risk due to pregnancy and D-mannose treatment interruption.

1. Benefit of D-mannose in humans despite teratogenicity in animal models

Mannose is the specific treatment for MPI-CDG and should be preferred, especially over diazoxide, which mainly treats hyperinsulinemic hypoglycemia and is contraindicated during pregnancy. D-mannose was first used in 1998 (2). It corrects coagulation defects, reduces thrombosis risk, and significantly improves clinical symptoms (2,14–17). A review in 2023 reported symptom improvement in 26 out of 30 MPI-CDG patients treated with D-mannose (33). Oral D-mannose is generally well tolerated, with rare adverse events; paradoxical reports of diarrhea and abdominal pain have been observed (31); in critically ill patient with hepatic failure, it may cause hemolytic jaundice (34). Besides being essential in severe cases, it has advantages such as low cost, oral administration, and wide availability (35). Conversely, intravenous D-mannose infusion can cause seizures due to intracellular ATP defect and impaired glucose metabolism, which can be reversed with glucose infusion (36).

However, D-mannose has been suspected of being toxic and teratogenic. D-mannose passes through placenta by specific transport mechanisms and simple diffusion (37,38). Toxicity has been observed in honey bees since 1928 (39). Excess mannose inhibits glucose and fructose phosphorylation and leads to an accumulation of mannose-6-phosphate which interferes with glycolysis (27,40). *In vitro* rat embryos exposed to mannose exhibit growth retardation, cerebral malformations, and faulty neuraltube closure (25,28). Supporting this, intravenous administration of D-mannose to pregnant rats induced dysmorphic features and abnormalities of brain or neural tube development (24). In a MPI-null mouse model, mannose supplementation during pregnancy resulted in embryonic death, growth retardation, and placental hyperplasia (27). Similarly, in an MPI knockout mouse with residual enzyme activity close to that of human MPI-CDG, dose-dependent embryonic resorption, placental disorganization, and severe ocular damage following D-mannose administration was observed (26). In their study, Sharma et al. demonstrated that administering water containing 1 % mannose, equivalent to the therapeutic dose for children (0.8–1 g/kg/day), to pregnant mice resulted in a decrease in both the number of offspring and the size of placenta. Doses two to five times higher amplified this effect (26). However a reliable comparison between the doses of D-mannose administered in animals and humans remains uncertain. These findings highlight the potential toxicity of D-mannose in animal models and call for caution when considering its use during pregnancy (35).

Interestingly, mannose has been used for several years in the prevention of recurrent urinary tract infections in women by inhibiting bacterial adherence to the bladder wall (41). Pregnant women may be exposed to mannose themselves, as it is sold over the counter in health stores or on websites often as a medical device. However, there are no published reports of any side effects from these treatments, and data on D-mannose exposure in pregnant women are missing (42).

2. Symptoms following the discontinuation of D-mannose therapy and management

Digestive impairment. Ileo-colitis developed at 9 WG. Our first hypothesis was an intra-abdominal thrombosis of celiac vessel, but the CT scan ruled out this option. We also did not find any evidence of intra-abdominal infection. Since the ileo-colitis started 3 weeks after D-mannose discontinuation and resolved following re-administration, we should consider MPI-CDG as a potential cause with a recurrence of MPI-CDG symptoms. Indeed, diarrhea is a hallmark of MPI-CDG and can cause chronic, disabling symptoms such as edema, protein-losing enteropathy, and abdominal pain, which mimic Crohn's disease or celiac disease (18,33,43). Recurrent episodes of diarrhea and vomiting can occur early, as described in a 2 year-old girl (33), in a neonate at one week of life (17), and in 2 infants at 3 months of life, including our patient (9). Relapsing gastrointestinal symptoms following D-mannose suspension were already described by Noman et al. in an adult MPI-CDG patient (44). By contrast, pancreatitis is not typically associated with MPI-CDG, and, to date, it remains unclear whether pancreatic involvement could be related to MPI-CDG.

Increased risk of thrombosis. Pregnancy is a high-risk period for thrombosis (45). Risk of thrombosis in MPI-CDG is mediated by coagulopathy and increased platelet aggregation (23). At 6 WG, enoxaparin anticoagulation was initiated in our patient due to her history of splenic infarction and the increased thrombotic risk associated with D-mannose discontinuation (23). The enoxaparin dose was guided by anti-Xa levels targeting 0.4 to 0.8 IU/ml.

3. Reintroduction of D-mannose therapy, dosage adjustment and timing.

Reintroduction of D-mannose therapy at 10 WG, after discontinuation, was a difficult decision. It was based on an individual assessment of the benefits and risks, considering our serious concerns about the recurrence of disabling symptoms related to MPI-CDG (diarrhea, hypoglycemia) and the occurrence of ileo-colitis of uncertain etiology following treatment discontinuation.

We browsed the Reference Center on Teratogens, a French public website for healthcare professionals, but found no information on mannose (46). Additionally, a working group from the National G2m network for inherited metabolic diseases performed a bibliographic analysis on the use of mannose and other medications in pregnant women. They concluded that the use of mannose during pregnancy in MPI-CDG patients is generally discouraged due to potential teratogenicity observed in animal models and should be discussed during multidisciplinary consultations (Personal data). The consultation also involved experts from the United States and Europe (MetabERN), although no prior experience was reported. The health and well-being of the mother were prioritized in this case, in line with fundamental ethical principles.

We initiated the minimum dose of D-mannose (4 g per day) at 10 WG when the embryo/fetus had passed the most vulnerable period, as most differentiation is usually completed by this time (47). It was given in four doses due to its short half-time (16). As expected, hypoglycaemia and diarrhea rapidly subsided. The use of low-dose D-mannose during pregnancy resulted in rapid and sustained improvement in Trf glycoforms profiles (Fig. 1).

We increased the D-mannose dose to 8 g per day (120 mg/kg/day) at 21 WG, aiming to further improve the laboratory parameters. Coagulation factors increased and liver enzyme levels normalized (Table 2) but no immediate additional benefit on Trf glycosylation profile was observed (Fig. 1). Treatment adherence was considered high, as the Trf glycoforms profile and laboratory parameters gradually ameliorated throughout pregnancy.

An improvement in Trf glycosylation profile was noted at 35 WG toward the very end of pregnancy (Fig. 1). This aligns with an observation by Lebredonchel et al., who reported a spontaneous improvement in Trf electrophoresis profiles in a patient not receiving D-mannose therapy during the second and third trimesters (21).

After delivery, the dose of D-mannose was increased and maintained at 12 g per day (180 mg/kg/day).

4. Infant outcome

IUGR is not a known feature of MPI-CDG pregnancies. It has been reported in animal models following D-mannose administration during

pregnancy, as mentioned above (25–28). *In vitro* studies suggest placental accumulation of mannose and abnormal glucose metabolism (27). Currently, there is a lack of data to draw firm conclusions, as placental histology was not performed in our patient. Other environmental factors (*e.g.* smoking) could also be involved.

A low Apgar score at birth was also unexpected. Maternal medication can affect the Apgar score (48), but it remains unclear whether D-mannose was the cause.

At 8 months of age, her overall growth, weight gain, and neurological development were generally normal, with slight peripheral hypertonia.

Ophthalmological follow-up should be recommended due to ocular toxicity observed in mice (26).

5. Conclusion

This is the first individual with MPI-CDG treated with D-mannose during pregnancy. Therapy was initially stopped due to known teratogenic risks in animals but resumed at 10 WG because of relapsing symptoms and thrombotic risk. Management involved strict timing: 4 g per day (60 mg/kg/day) at 10 WG, and 8 g per day (120 mg/kg/day) at 21 WG, using the lowest effective dose to reduce teratogenicity. The treatment improved her condition. The child had intra-uterine growth retardation and low Apgar scores at birth, but links to D-mannose are uncertain. The infant was in good health at 8 months of age, despite moderate peripheral hypertonia. Further follow-up is needed. This case suggests that low-dose mannose could be a lower-risk option during pregnancy. An international or European registry, for example through the European Reference Network for Hereditary Disorders (MetabERN), could be established to monitor all pregnancies concerning MPI-CDG affected women with or without D-mannose therapy.

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Ethics

In compliance with French and European data protection regulations (including GDPR), the patient was informed during routine care that anonymized clinical data might be used for research. Non-opposition was documented in medical records. All data were anonymized and stored in a secure, password-protected database. This study was approved by the Ethics committee of the Faculties of Medicine, Dentistry, Pharmacy, Nursing Schools, Physical Therapy, Midwifery, and Hospitals in Strasbourg University (reference CE-2025-106).

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CRediT authorship contribution statement

Lionel Martzolff: Conceptualization, Data curation, Writing – original draft, Writing – review & editing. **Alexandre Raynor:** Investigation, Resources, Writing – review & editing. **Elodie Lebredonchel:** Investigation, Resources, Writing – review & editing. **Sara Marescaux:** Writing – review & editing. **Dominique Desprez:** Writing – review & editing. **Claire Douillard:** Writing – review & editing. **Laure Federici:** Writing – review & editing. **Isabelle Alamome:** Writing – review & editing. **Nathalie Trillot:** Writing – review & editing. **Jean-Meidi Alili:** Writing – review & editing. **Annie Harroche:** Writing – review & editing. **Delphine Borgel:** Writing – review & editing. **Camille Wicker:** Writing – review & editing. **Jean-Edouard Terrade:** Writing – review & editing. **Arnaud Bruneel:** Investigation, Resources, Writing – review & editing. **Pascale De Lonlay:** Conceptualization, Supervision, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare no conflicts of interest.

Data availability

Data will be made available on request.

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