Thiamine-responsive megaloblastic anemia: a rare presentation of an uncommon disease !

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Background

- Thiamine-responsive megaloblastic anemia syndrome (TRMA) is characterized by a triad of megaloblastic anemia, progressive sensorineural hearing loss, and diabetes mellitus (DM).(1)
- It is a rare autosomal recessive disease due to mutation in SLC19A2 gene, encoding a high-affinity thiamine transporter 1.(2)
- Only about 80 cases have been reported worldwide so far.(3)
- We herein report an extremely rare case of TRMA without megaloblastic anemia, with associated stroke, and optic atrophy.

Case summary

- A 1-year-old girl born to consanguineous parents presented with right focal convulsions, hemiplegia, and photophobia. She was diagnosed with left-sided stroke and epilepsy. Her thrombophilia profile was normal.
- Hyperglycemia was accidentally discovered. She was diagnosed with DM, with low C-peptide 0.1 ng/ml (N. 2.83-9.93), and HbA1c 7%.
- Her fundus examination revealed bilateral optic atrophy.
- Audiometry was done showing profound sensorineural hearing loss at high frequencies.

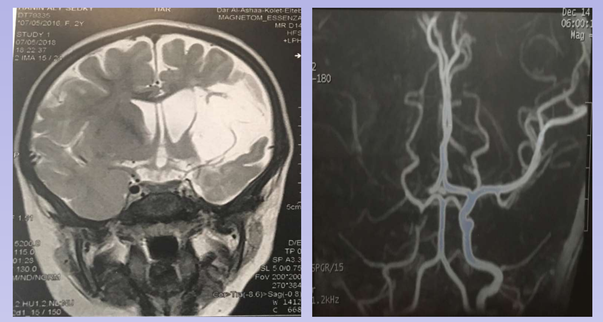


Figure 1: Extensive non-hemorrhagic ischemic insult in left cerebral hemisphere.
Figure 2: MRA brain showing markedly attenuated left-sided internal carotid artery and lost tracing of main trunk of the left middle cerebral artery with occlusion of the main trunk of the ipsilateral left anterior cerebral artery.

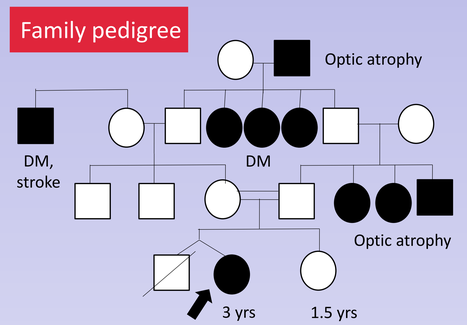
- At the age of 3 years, she presented with fever, and pallor.
- She had mild hepatosplenomegaly and purpuric spots all over her body. Her weight was 15 Kg (+0.17SD), and height 89 cm (-1.7SD).
- Her complete blood count showed pancytopenia.

Investigations	Result
Total bilirubin Direct bilirubin	0.8 mg/dl 0.2 mg/dl
LDH	742 U/L (N. 340-550)
DAT	Negative
Renal, Liver functions	Normal
Urine analysis	SG 1010, no urobilinogen

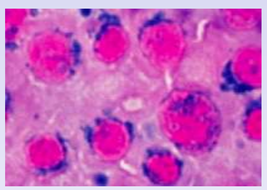
Investigations	Result
Triglycerides, Cholesterol	Normal
PT, PTT, D-dimer	Normal
FDP	Negative
C_3, ANA, Antids-DNA	Negative
HIV, EBV, Hepatitis B, C	Negative

LDH: Lactate dehydrogenase, DAT: Direct antiglobulin test, SG: Specific gravity, FDP: Fibrin degradation products, ANA: Antinuclear antibody, Antids-DNA: anti-double-stranded DNA.

- Cytomegalovirus-induced pancytopenia was suspected to be the cause with positive CMV IgM 6.5 U/ml (N. ≤1), IgG 2.6 U/ml (N. ≤1).
- Although her hematological findings started to improve, it deteriorated again.
- Pancreatic autoantibodies were negative confirming non-type 1 DM.



- Bone marrow with Prussian blue stain revealed sideroblastic anemia with ringed sideroblasts confirming the diagnosis of TRMA.



- Echocardiography, and thyroid function tests were normal.
- On thiamine therapy (50 mg/day), her hematological findings, HbA1c normalized (5.6%), and her insulin requirements decreased to 0.5 U/Kg/day.
- Her genetic testing confirmed the diagnosis with homozygous mutation for a pathogenic non-sense variant of SLC19A2 gene.

- Patient's hematological findings:

Parameter (Reference range, unit)	At diagnosis	After PRBCS	On follow up	After thiamine therapy
Hb (g/dl)	6	9.5	8.5	10.5
MCV (76-96 fl)	81	86	84	81
MCH (26-32 pg)	26	26	26	26
MCHC (32-36 g/dl)	32	32	33	32
WBCs (/uL) ANC (N.>1500)	7.360 700	9.000 1.700	7.000 1300	10.600 4.450
Platelets (150.000-450.000/ul)	15.000	201.000	150.000	400.000
Retic count (1-2%)	3.6%	1.5%	3%	1.4%

Conclusion

- TRMA syndrome should be kept in mind in the differential diagnosis of DM with deafness.
- BM with Prussian blue stain demonstrating ringed sideroblasts is helpful in diagnosis-even if no megaloblastic anemia is present.

References

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