THE OFFICIAL BULLETIN

ACADEMY OF PEDIATRICS • VADODARA

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Working with 'small' miracles everyday

August

CORRESPONDENCE

Dr. Ashutosh Singh Rathore

Secretary, Academy of Pediatrics, Vadodara

SUMANDEEP HOSPITAL

Opposite Govt press, Anandpura, Kothi, Vadodara - 390 001.

Mobile : +91 99099 52293 • E-mail : aop.vadodara@gmail.com • Website : www.aopvadodara.org

ACADEMY OF PEDIATRICS, VADODARA

Diseases that Masquerade Neurology

Dr. Sarbani Raha

drsarbaniraha@rediffmail.com

A 'masquerade' is a pretence, a false show. When I decided to pursue neurology, I presumed I would have to try and get into the depths of brain and brain only. I was proven wrong more than once and only after many years did I acquire the wisdom to realise that it may be the brain that is giving rise to symptoms but the problem may not necessarily lie there. On some occasions, the neurological manifestation is part of a multisystem involvement and on others, it may only suggest acute decompensation. I shall attempt to discuss, and in the process learn more about such cases in the present and in subsequent issues of the journal.

Presentation

A 3 year old boy presented with history of two episodes of seizure, one year apart. I asked all the right questions to confirm that it was indeed a seizure (unresponsive, rapid eye blinking, jerking of limbs distally). Both the episodes had occurred out of sleep and in the early morning hours. The child was admitted during the events, and it had taken him almost 12 hours to recover completely. A well grown boy with normal development, he did not seem to have any other signs or symptoms and I thought I was dealing with idiopathic focal epilepsy which is an age related focal epilepsy with seizures occurring out of sleep, 'Benign Rolandic epilepsy" being the most common one.

Of course, the history took a different turn, when the parents revealed that they had lost a 2 and half year old daughter to a similar episode of early morning seizure. They had another healthy 6 year old daughter and were not consanguineous in marriage.

Early morning seizures may represent hypoglycemic seizure following night time fasting and I made enquiries about the RBS (random blood sugar) levels during the two events and also whether the child appeared sweaty and cold to touch during the episode. Parents revealed that the RBS was indeed 22 and 17 mg/dl respectively during the episodes and the baby was cold and 'lifeless'.

While many times we attribute seizure to hypoglycaemia, we may associate a seizure to hypoglycaemia only in presence of a history of fasting and RBS levels lower than 40mg/dl in non- neonatal non-diabetic population. Hypoglycemia frequently leads to confusion, stupor, coma and seizures are not as common as assumed.

The boy had a normal weight for age and head circumference for age, no abnormal neurological or systemic examination findings except that his lips were dark (like that of a smoker!). I asked the mother whether the boy was getting 'darker' and the surprised mother confirmed that she did think so and also mentioned that her daughter was getting 'darker', before she succumbed to a seizure.

Well, the history had unravelled many points so I summed them up for myself- non-consanguinity, 2 children affected, one died; early morning hypoglycemic seizure, hyperpigmentation, normal neurology. I realised this was an autosomal recessive endocrine condition with probable adrenal insufficiency.

Good sense did tell me that I should immediately refer the patient to an Endocrinologist and be done with it. But the child was on Valproate 400mg/day and the parents insisted that I should treat for seizures. In the past (when I was less wise) I have sent such a child to the respective sub speciality only to be called up and interrogated about my reasons for not treating epilepsy and I have proven myself a fool by not providing evidence for/against epilepsy or neurological disease.

Investigations

Hence I decided to collect evidence for what I suspected and then refer for management.

It did not seem pragmatic to wait for another episode and delay testing so I advised admission for inducing fasting hypoglycaemia and critical sample testing.

The child was admitted. After dinner at 10 pm parents were asked to allow only clear water. RBS by glucometer was tested starting at 6 am, every hour till RBS dropped to 50mg/dl, after which it was tested every 30 minutes. At 11am (13 hours of fasting), RBS was 41mg/dl and critical samples were collected.

Critical sample testing in hypoglycaemia

- Plasma glucose
- serum electrolytes
- serum ammonia
- serum lactate
- serum C peptide
- serum Growth hormone
- serum insulin
- serum cortisol
- 3, beta hydroxyl butyrate(BOHB)
- TMS(tandem mass spectrometry)

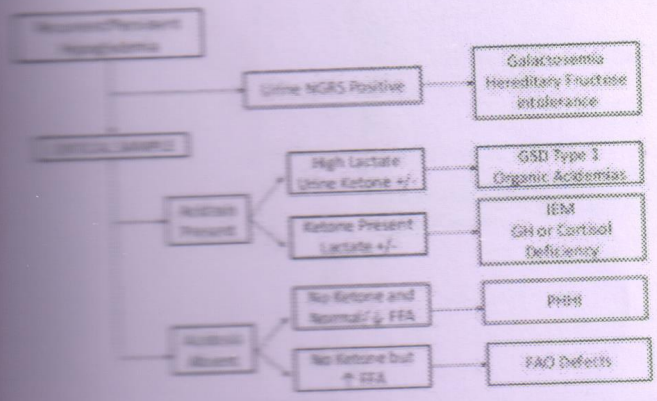
In this boy, I was expecting high levels of ACTH (adrenocorticotrophin hormone) hence I requested for ACTH levels also. One may argue that an early morning cortisol, ACTH, 17-OHprogesterone, Renin, LH (Leutinizing hormone) and FSH (follicle stimulating hormone) could have probably be enough and a critical sample testing, which is cumbersome may not have been required; but that would mean I had started thinking like an Endocrinologist, which I definitely had not!

The results poured in to reveal a plasma glucose at 22mg/dl, cortisol <0,16mcg/dl, ACTH >1250pg/ml (range 9-52), BOHB 18.8 mg/dl (range0.1 to 3.0), serum insulin 0.2, plasma bicarbonate 16mEq/L (range 22-30) ; rest normal.

On correlating the investigations with the patient I realised that a low cortisol had failed to give a negative feedback to the anterior pituitary thus raising the ACTH and leading to hyperpigmentation; it was also leading to failed gluconeogenesis and thereby reduced plasma glucose.

I realised I could not go further for obvious reasons and I had collected enough evidence to say that we were dealing with hypoglycemic seizures secondary to cortisol deficiency which was familial.

I referred the child to an Endocrinologists, stopped the Valproate and reassured the parents that it should be possible to reach a confirmed genetic diagnosis, avoid hypoglycaemia and ensure that this boy lives his life to the fullest by maintaining a regular follow up with the Endocrinologist.



Disease	OMIM	Gene
Congenital adrenal hyperplasia		
21-Hydroxylase deficiency	201910	Cyp21
11β-Hydroxylase deficiency	202010	Cyp11B1
3β-Hydroxysteroid dehydrogenase deficiency	109715	HSD3B2
17α-Hydroxylase deficiency	202110	Cyp17
Lipoid adrenal hyperplasia	201710	STAR
Congenital adrenal hypoplasia	300200	NR0B1 (DAX-1)
	300473	NR5A1 (SF-1)
Familial glucocorticoid deficiency		
Type 1	202200	MC2R
Type 2	609196	MRAP
Type 3	609197	unknown
Triple A syndrome	202110	AAAS
X-linked adrenoleucodystrophy	300371	ABCD1
Autoimmune polyglandular syndrome type 1	240300	AIRE

Above mentioned are a flow chart and table for anyone who wants to pursue the diagnosis in a child presenting with hypoglycaemia beyond the neonatal period. The table enlists the genes responsible for the non-metabolic, so to say endocrine disorders that may present with hypoglycaemia.

Conclusion: History still forms the mainstay in reaching the diagnosis. It pays to start with an open mind to avoid bias. Hypoglycemia and seizure are cause and effect in a select group of patient who then require targeted investigations to confirm the diagnosis and treat accordingly.

Feedback : drsarbaniraha@rediffmail.com