A case of ACTH resistance with generalized hyperpigmentation at birth

Sasaki Takako[1)], Amano Naoko[2)], Narumi Satoshi[2)] , Hasegawa Tomonobu[2)], Tomita Mai[1,3)], Okada Junichiro[3)], Hisano Tadashi[3)] , Yatsuga Shuichi[1)], Koga Yasutoshi[1)]

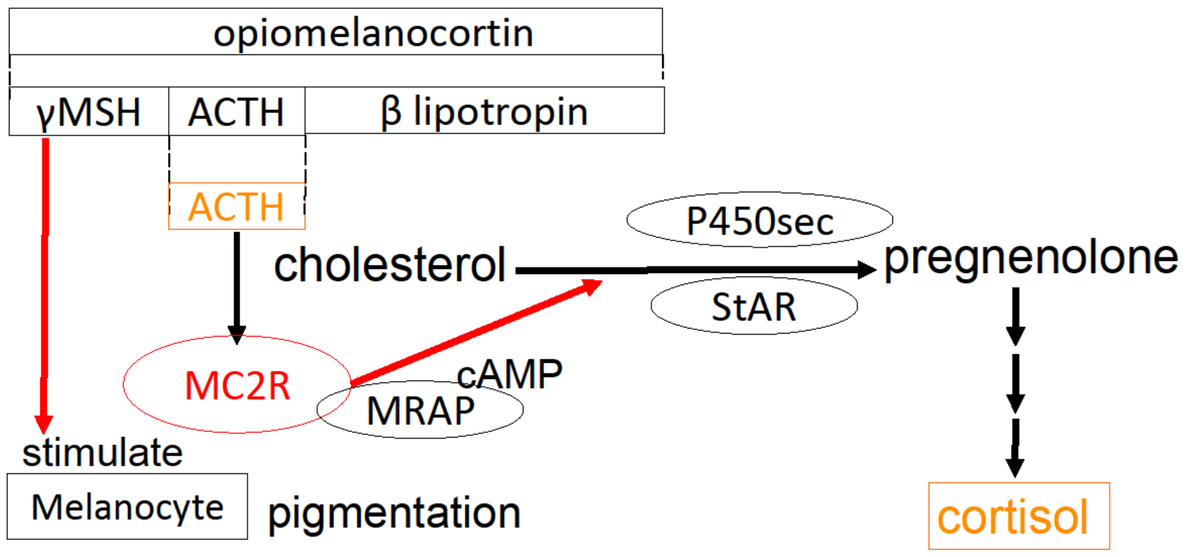
1)Department of Pediatrics and Child Health, Kurume University School of Medicine, Japan
2)Department of Pediatrics, School of Medicine, Keio University, Japan
3)Department of neonatal care unit ,St Mary's Hospital, Japan

Nothing to declare

1. Introduction

Cholesterol becomes pregnenolone. The MC2R gene (*MC2R*) encodes the receptor for ACTH, and *MC2R* mutations cause ACTH resistance.

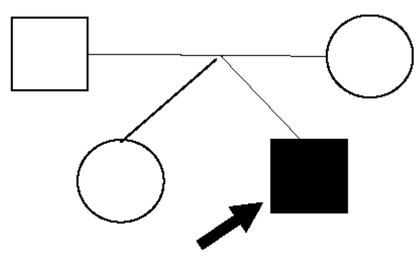
We describe a *MC2R* mutation-carrying ACTH resistance patient, who exhibited generalized hyperpigmentation at birth.



ACTH adrenocorticotropic hormone, MC2R Melanocortin 2 receptor-associated protein, MRAP melanocortin 2 receptor accessory protein , StAR steroidgenic acute regulatory protein, MSH melanocyte-stimulate hormone

2. Case Report

0 day of age, male
birth at 37 week of gestation
birth height 48 cm (+0.10 SD)
birth weight 2,112 g (-0.64 SD)



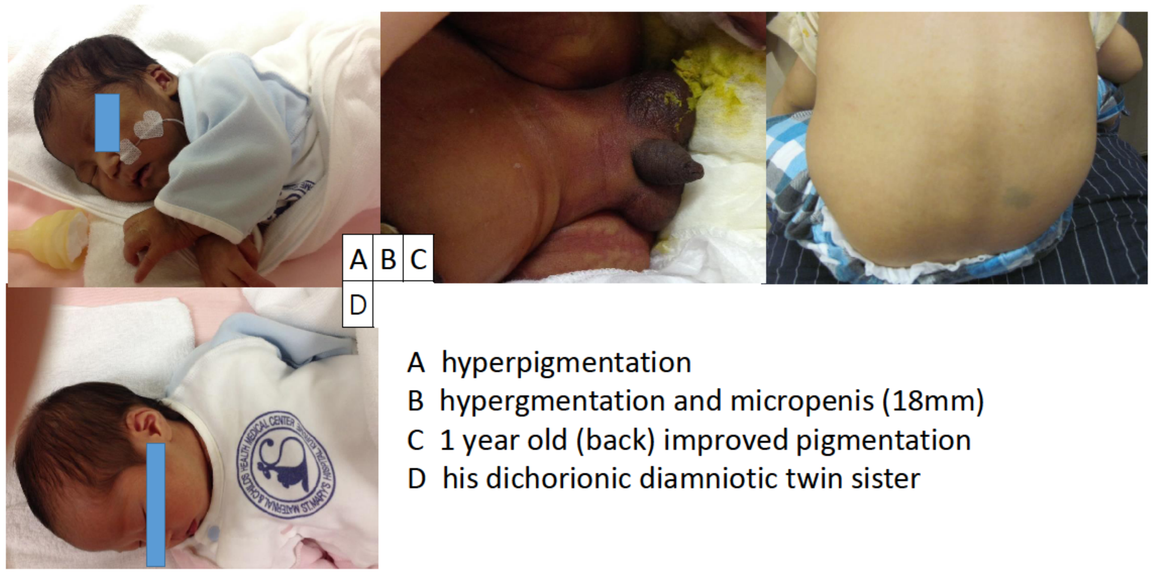
BT 35.9 C, BP mean 25 mmHg,
HR 70 /min, RR 70/min, SpO_2 99% (O_2 3L)
Apgar score: 4/7
(Appearance 0/0 Pulse 2/2, Grimace1/2, Activity 0/1, and Respiration 1/2)

generalized hyperpigmentation (especially armpit, penis)
micropenis (stretched penile length, 18 mm), testis palpable
pH 7.135, $PaCO_2$ 58.7mmHg, HCO_3^- 18.9 mmol/L,
BE -11.2 mmol/L, Lac 7.7 mmol/L, AG 13.2meq/L

Na	136	mEq/L,	renin activity	100	ng/kg/h,
K	4.6	mEq/L,	aldosterone	1.6	pg/dl,
Cl	104.7	mEq/L,	LH	<0.1	mIU/L,
ACTH	2,719	pg/dl,	FSH	0.46	mIU/L
cortisol	1.4	μg/dl,			

<steroid profile in urine>
Cortisol, and aldosterone metabolites: within normal range
17OHP metabolites: slightly high level
<chromosome> 46,XY
<abdominal CT> normal size of adrenal gland
<head MRI> normal size of pituitary

An artificial respirator was needed because of dyspnea, acidemia, and low blood pressure, and dopamine (0.05γ) was injected. Primary adrenal insufficiency was suspected due to the physical findings, and glucocorticoid was administered at birth.
His general condition improved, and respirator was turned off at 5 days of age.

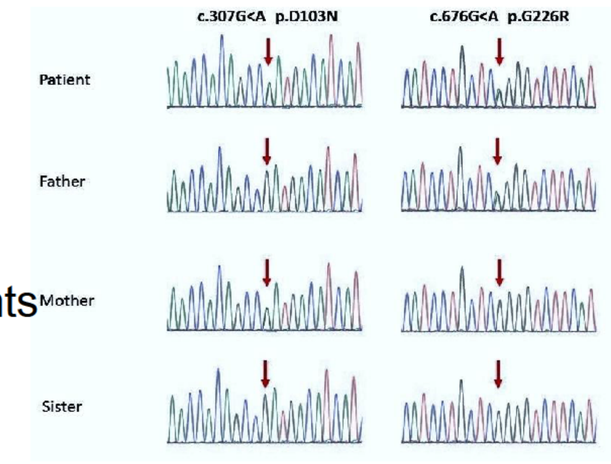


A hyperpigmentation
B hypergmentation and micropenis (18mm)
C 1 year old (back) improved pigmentation
D his dichorionic diamniotic twin sister

3. Methods & Results

Methods: Known genes associated with primary adrenal insufficiency were screened with use of next-generation targeted sequencing. The identified *MC2R* mutations were validated by conventional PCR-based sequencing.

Results:
Compound heterozygous mutations: p.Asp103Asn and p.Gly226Arg
(previously reported in patients with ACTH resistance)



4. Discussion

There are many causes of adrenal insufficiency in neonates, such as congenital adrenal hyperplasia, X-linked congenital adrenal hypoplasia, and 21-Hydroxylase deficiency. Adrenal insufficiency occurred at birth in this case. Normal serum electrolytes, and serum aldosterone level were normal. Serum cortisol level was low, and serum ACTH level was high, indicating ACTH resistance caused by *MC2R* mutations.

MC2R mutations have been described as having common episodes, such as seizure, hypoglycemia, severe infection, and tall stature/failure to thrive[(1,2)] . The patients' height is related to *MC2R* mutations and ACTH level[(3)].

Some MC2R mutation cases were treated as adrenal hypoplasia. They were treated with unnecessary fludrocortisone[(2)] .

This case was treated with hydrocortisone (~15 mg/m^2 /day), there are no common episodes and he does not have tall stature (-1.3 SD at 18 months). Appropriate diagnosis is important for *MC2R* mutation .

5.Conclusion

A neonate presenting symptoms suggesting adrenal insufficiency and/or hyperpigmentation should be considered as an *MC2R* mutation.

References (1)Elias, et al. Clin Endocrinol 2000,
(2) Lin, et al. Clinical Endocrinology2007,(3) Inamine, et al. Tohoku J Exp Med, 2005,

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