

Brief report

A case of the intrauterine fetal death (IUFD) in 27-weeks of gestation induced by the mutation of myocardial Na⁺ pump α subunit gene SCN5A

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Background : Concerning the intrauterine fetal death of unknown etiology, we discussed the cardiac sudden death by the genetic study.

Case report : The formalin-fixed placenta (FFPE) was examined by followings : (i) routine pathologic study, (ii) infection by PCR and immunostain, (iii) chromosomal pattern by fluorescence in situ hybridization (FISH), (iv) myocardial Na⁺ pump α subunit gene SCN5A mutation by polymerase chain reaction-single strand conformational polymorphism (PCR-SSCP). Positive examination results were mosaic XY/XXY, mutation of exon 20 in SCN5A, cytomegalovirus infection (CMV), marginal insertion of umbilical cord, and intrauterine growth retardation (IUGR).

Conclusion : IUFD was directly induced by genetic mutation of SCN5A.

Key words : placenta, intrauterine fetal death (IUFD), genetic analysis, myocardial Na⁺ pump α subunit gene SCN5A mutation, cardiac sudden death, gene mutation, polymerase chain reaction-single strand conformational polymorphism (PCR-SSCP), immunostain, intrauterine growth retardation (IUGR), pathology, method

Introduction

In IUFD 25% of causes and background factors were unclear(1). Routine placental analysis often failed to disclose the cause of IUFD. We have tried to investigate the true causes with genetic studies ; FISH, PCR, and PCR-SSCP. Genetic mutation of cardiac sudden death was suggested and reported in this paper.

Case report

Placenta of IUFD in 27-weeks of gestation was pathologically examined and its FFPE specimen was genetically analyzed (1-3). Genetic analysis was followings : (i) macroscopic and microscopic analysis (1-3), (ii) infection of CMV, Ebstein-Barr virus (EBV), Herpes sim-

plex virus (HSV) by PCR with both the reagent, usual PCR method and SYBR method of Mx3000P Real-Time QPCR System, Agilent Technologies (Japan branch office) with SYBR Premix Ex Taq (Tli RNaseH Plus), Takara (Japan), and (4) (iii) chromosomal pattern of # 13, 18, 21, and XY by fluorescence in situ hybridization (FISH) (4), (iv) myocardial Na⁺ pump α subunit gene SCN5A mutation by polymerase chain reaction-single strand conformational polymorphism (PCR-SSCP) (5),.

Pathologic findings were as followings : IUGR (660g, male), marginal insertion of umbilical cord, suggesting intraplacental fetal circulatory disturbance (Table 1). Genetic examination showed mosaic XY/XXY, mutation of exon 20 in SCN5A, and intrauterine infection with CMV (Table 1). SCN5A mutation suggested cardiac circulatory disturbance (Table 1).

Conclusion

IUFD was induced by genetic mutation, including SCN5A.

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和 文 抄 録

症例報告

心筋ナトリウムポンプ SCN5A 遺伝子変異による在胎 27週の子宮内胎児死亡の 1 症例

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背景：原因不明の子宮内胎児死亡（IUFD）の死因検索として、心筋ナトリウムポンプ遺伝子の変異を検討した。

症例内容：ホルマリン固定の胎盤に関して以下の検討を加えた：(1)FISHによる染色体検査、(2)PCR-SSCPによる心筋ナトリウムポンプSCN5A遺伝子変異、(3)PCRと免疫染色による感染症の有無、そして(4)病理検査が実施された。その結果、モザイクXY/XXY、SCN5Aエクソン20の変異、サイトメガロウイルス感染、子宮内胎児発育遅延（IUGR）、および臍帯辺縁付着が指摘された。

結論：本IUFDの直接原因として、心筋ナトリウムポンプ遺伝子等の変異が指摘された。

キーワード：子宮内胎児死亡（IUFD）、遺伝子検査、心筋ナトリウムポンプ遺伝子SCN5A変異、心筋性突然死、遺伝子変異、ポリメラーゼ連鎖反応——本鎖高次構造多型法（PCR-SSCP）、免疫染色、子宮内胎児発育遅延（IUGR）、病理検査

Table 1. Examination results

study and method		result
chromosome study by FISH	13	N
	18	N
	21	N
	XY	XY > XXY
SCN5A PCR-SSCP	exon 12-1	N
	exon 12-2	N
	exon 18	N
	exon 20	mutation
infection by PCR	CMV	+
	EBV	-
	B19V	-
Pathology	fetus	IUGR
	placenta	marginal insertion of cord

Table 2. Abbreviation

?	probably
B19V	Parvovirus B16
CMV	cytomegalovirus
EBV	Ebstain-Barr virus
FFPEs	formalin-fixed paraffin-embedded sections
FISH	fluorescence in situ hybridization
IUFD	intrauterine fetal death
IUGR	intrauterine growth retardation
N	normal
PCR-SSCP	polymerase chain reaction-single strand conformational polymorphism
SCN5A mutation	myocardial Na ⁺ pump α subunit gene SCN5A mutation
TORCH syndrome	toxoplasma, others, rubella, cytomegalovirus, herpes infection

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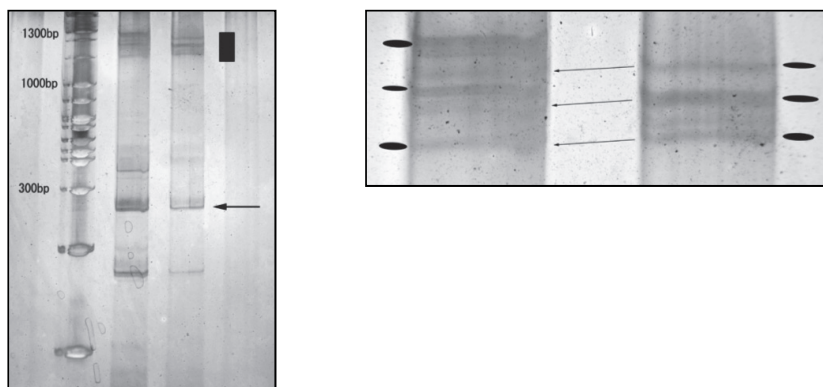


Figure. exon 20 of SCN5A in PCR-SSCP study
left : left lane : marker, middle lane : control, right lane : sample,
right : magnified figure of closed rectangle in left one
← : original PCR band,
straight bar : SSCP bands

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