

미세정자주입술로 임신이 된 남자태아의 Y 염색체 미세결실의 Vertical Transmission, *de novo*, 그리고 Expansion의 연구

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1,3 . 1,2,3 . 1,3 . 1,3 . 1
1 . 2 . 2 . 2

A Vertical Transmission, *de novo*, and Expansion of Y chromosome Microdeletion in Male Fetuses Pregnant after Intracytoplasmic Sperm Injection

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Objectives: Despite severe oligospermia, males with Y chromosome microdeletion can achieve conception through ICSI (Intracytoplasmic Sperm Injection). However, ICSI may not only result in the transmission of microdeletions but also the expansion of deletion to the offspring. The purpose of this study was to screen vertical transmission, expansion of microdeletions and *de novo* deletion in male fetuses conceived by ICSI.

Materials and Methods: A total of 32 ICSI treated patients with their 33 (a case of twin) male fetuses conceived by ICSI were used to make this study group. Sequence-tagged sites (STSs)-based PCR analyses were performed on genomic DNA isolated from peripheral blood of fathers and from the amniocytes of male fetuses. Ten primer pairs namely, sY134, sY138, MK5, sY152, sY147, sY254, sY255, SPGY1, sY269 and sY158 were used. The samples with deletions were verified at least three times.

Results: We detected a frequency of 12.5% (4 of the 32 patients) of microdeletions in ICSI patients. In 4 patients with detected deletions, two patients have proven deletions on single STS marker and their male fetuses have the identical deletion in this region. Another two patients have two and three deletions, but their male fetuses have more than 3 deletions which include deletions to their father's. Meanwhile, seven male fetuses, whose fathers were analyzed to have all 10 STS markers present, have deletions present in at least one or more of the markers.

Conclusions: Although the majority of deletions on the Y chromosome are believed to arise *de novo*,

in some cases a deletion has been transmitted from the fertile father to the infertile patient. In other cases the deletion was transmitted through ICSI treatment, it is likely that one sperm cell is injected through the oocyte's cytoplasm and fertilization can be obtained from spermatozoa. Our tests for deletion were determined by PCR and our results show that the ICSI treatment may lead to vertical transmission, expansion and de novo Y chromosome microdeletions in male fetuses. Because the sample group was relatively small, one should be cautious in analyzing these data. However, it is important to counsel infertile couples contemplating ICSI if the male carries Y chromosomal microdeletions.

Key Words: Y microdeletion, ICSI, Vertical transmission, *de novo*, Expansion

1976 Y 가 .¹
 azoospermia factor (AZF)
 sequence tagged sites (STS) 1.

1~55% 가 Y ICSI
 .² (Intracytoplasmic Sperm Injection, ICSI) (1) Y 46, XY
 가 가 . azoospermia
 OAT (oligoasthenoteratozoospermia)
 . AZF . ,
 germ line random *de novo*
 가 가 .
 ICSI 가 .² 2. STS markers
 가 Y sequence tag-
 ICSI 가 . ged sites (STS) marker 10 sY134. sY138.
 Y MK5 (AZFa region), sY152, sY147, sY254, sY255,
 . SPGY1, sY269, sY158 (AZFc region) (Figure 1).
 3. Genomic DNA
de novo ICSI genomic DNA gen-
 3~8 9,10 . , . omic DNA 15~23
 . genomic DNA
 . DNA
 . DNA -20
 ICSI Y 4. (Polymerase Chain Re -
 . , , *de* action, PCR)
novo . . Perkin Elmer Cyclor
 PCR .
 2% agarose gel ethidium

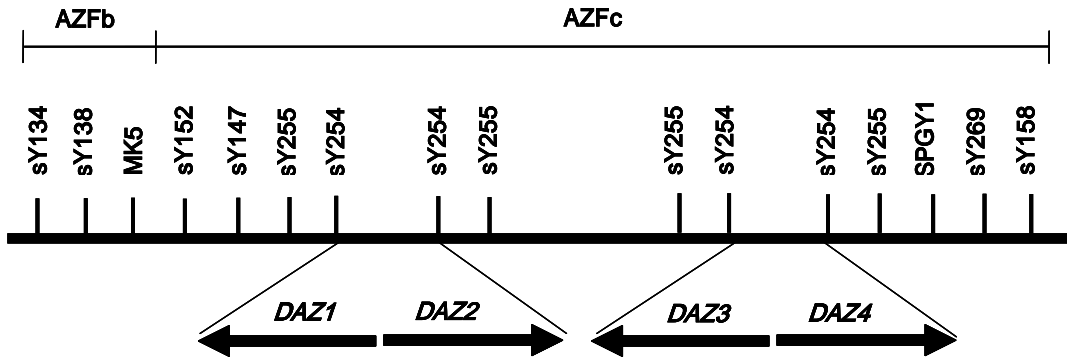


Figure 1. Y chromosome map and STS markers in AZFb and AZFc of Y chromosome long arm (Yq). 4 copies of DAZ gene are also shown.

bromide , UV (Ultra Violet)
 가 single PCR
 3
 ICSI 32 4
 12.5% (Table 1).
 Table 1 Figure 2 , 4
 2 SPGY1

Table 1. Vertical transmission, *de novo*, and expansion of Y chromosome microdeletions are presented

	Father	Fetus
Total microdeletion	4/32 (12.5%)	11/33 (33.33%)
Vertical transmission	2	2
Expansion	2	2
De novo	-	7

sY152 3-8
 (vertical transmission) 9,10가
 (Figure 2, A). 2 32 ICSI 1
 3 33 Y
 (expansion) (Figure 2, B).
 , 7 12.5%, 33.33% (Table
 (de novo) 1). , vertical transmission
 (Figure 2, C).
 Y
 , Y
 가
 Y
 가
 1994 ICSI 가 , 가
 가
 ICSI Vertical transmission 8
 Y 가 Y
 .11 de novo (de novo)

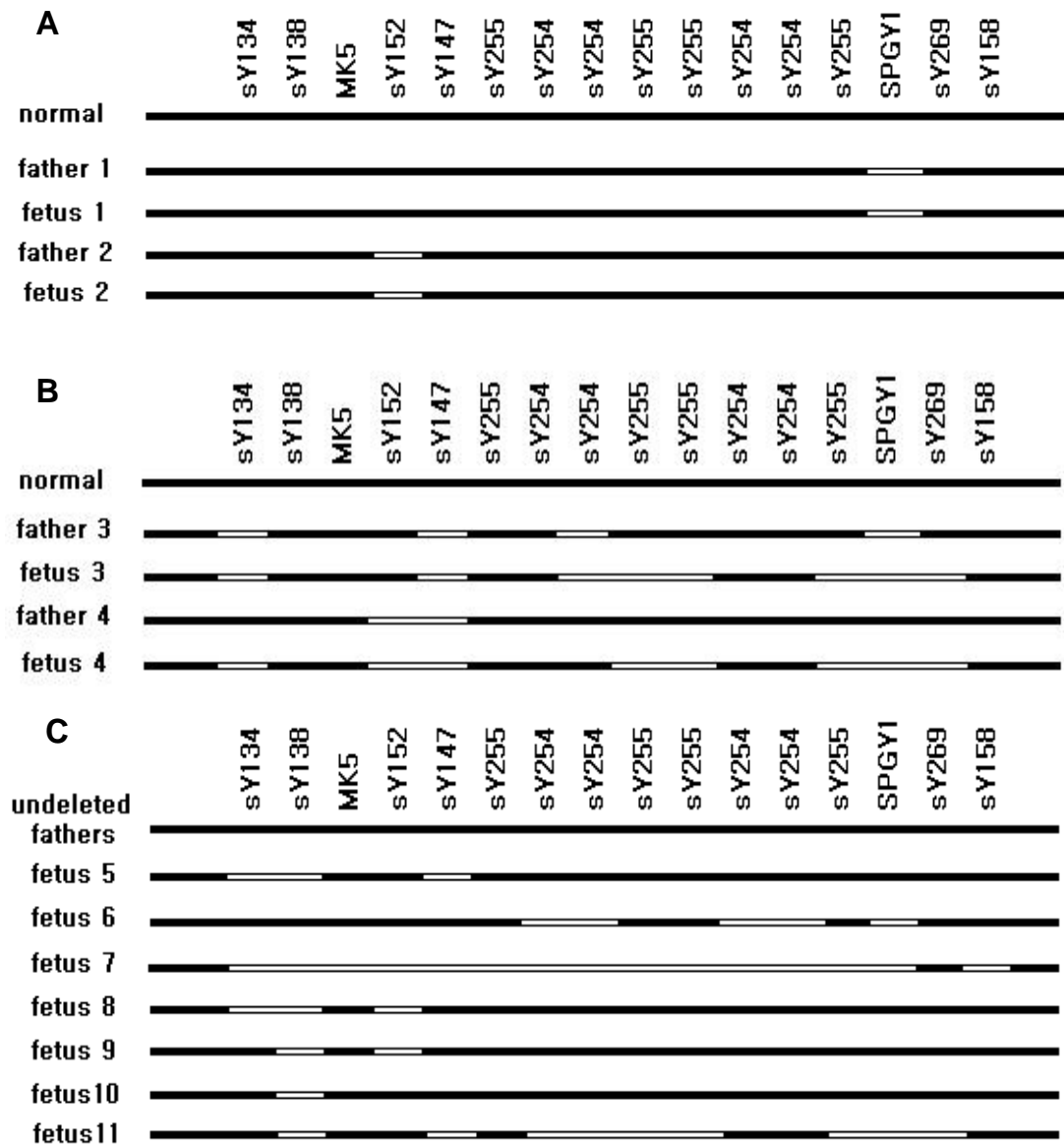


Figure 2. Schematic diagram of deletion patterns on Y chromosome long (Yq) and microdeletions in fathers and fetuses. (A) Vertical transmission, (B) expansion, and (C) *de novo*.

가 *de novo*가
가
mosaic
deletion 가
2,3,5
, primordial germ cell mosaicism morphic Y 가 poly-
ICSI expansion 가

¹² Y
 Y 가
⁹
 Y AZF region AZFa, AZFb,
 AZFc
 STS marker AZFb AZFc
 . AZFa region SCOS (Scertoli Cell Only Syndrome)
 ,
 (unpu-
 blished data). AZFb region AZFa region
 가
 maturation arrest
¹³ 가 가
 AZFc
^{14,15}
 STS marker가 AZF locus
 DAZ
 가 (Restriction
 Fragment Length Polymorphism, RFLP), DAZ probe
 Southern blot, DAZ cosmid
 (Fluorescence in situ hybridization,
 FISH)
^{4,16,17}
 , AZFb AZFc STS
 marker vertical transmiss-
 ion, *de novo* expansion 11
 가
 ,
 , ICSI
 ICSI
 가
 가

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