Y chromosome AZF deletions/duplications and spontaneous pregnancy loss

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INTRODUCTION

Spontaneous abortion (SA) is the most common pathology in obstetrics with incidence of 10-15% among clinically recognized pregnancies. The occurrence in three or more consecutive pregnancies is defined as recurrent SA with incidence of 0.5-3% in women trying to conceive. The etiology is diverse and multifactorial (uterine abnormalities, autoimmune, infectious, endocrine, and genetic factors) but still the major part of it (50-60%) remains idiopathic. Half of them are considered to be caused by the male factor. Gene defects, Y chromosomal abnormalities and microdeletions are implicated in male infertility but have been poorly evaluated in SA.

AIM OF THE STUDY

The aim of this study was to investigate the possible association of Y chromosome AZF deletions/duplications with spontaneous pregnancy loss.

MATERIALS AND METHODS

One hundred and seven men from couples experiencing two or more SA, and 116 fertile men were enrolled in this study. DNA extracted from whole blood was tested for presence of sex chromosome aneuploidies, AZF deletions, partial AZFc deletions and duplications using 13-plex quantitative fluorescent (QF) PCR and subsequent capillary electrophoresis on ABI 3130 Genetic Analyzer. (Life Technologies, USA). Schematic view of the AZF locus and AZF deletions are given in Figure 1, while the electrophoreograms of the 13-plex QF-PCR representing partial AZFc deletion and duplication are shown in Figure 2.

RESULTS

The results from our study are presented in Table 1.
In total, three partial AZFc deletions (1 gr/gr and 2 b2/b3) and 21 AZFc duplications (12 b2/b4 and 9 b2/b3) were detected. Partial AZFc deletions were slightly more frequent among male partners from couples experiencing SA (1.87%) in comparison to control fertile males (0.86%). The AZFc partial duplications were more frequent among control fertile males (12.07%) than in among male partners from couples experiencing SA (6.54%). None of the male partners from couples with SA and controls had any sex chromosome aneuploidy or complete AZF deletions.

Table 1. Y chromosome rearrangements among male partners from couples experiencing SA in comparison to control fertile males.

Y chromosome AZFc rearrangements		SA patients n=107 n (%)	Controls n=116 n (%)	*p*
Duplications	b2/b3	5 (4.67%)	4 (3.45%)	*p=0.642*
	b2/b4	2 (1.87%)	10 (8.62%)	***p=0.026***
	Total	7 (6.54%)	14 (12.07%)	*p=0.158*
Deletions	gr/gr	0	1 (0.86%)	*p=0.520*
	gr/gr+b2/b4	0	0	*0*
	b2/b3	2 (1.87%)	0	*p=0.229*
	b2/b4	0	0	*0*
	Total	2 (1.87%)	1 (0.86%)	*p=0.514*

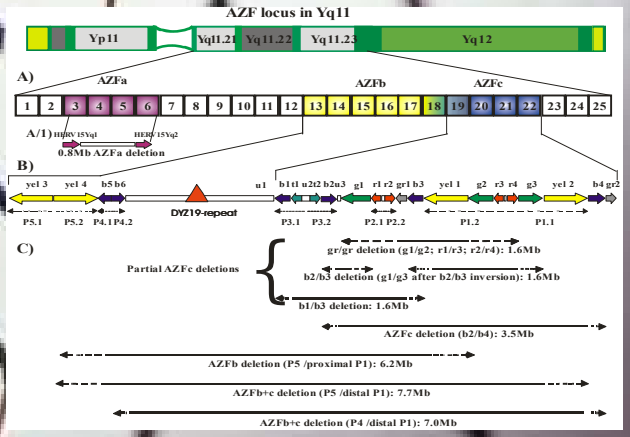

Figure 1. Schematic view of the AZF locus in Yq1. **A)** Deletion map of AZF locus: 25 intervals (D1-D25) and three AZF regions (AZFa, AZFb and AZFc). **A/1)** Complete AZFa deletion, caused by recombination of two homologous HERV 15Yq1/q2 blocks; **B)** Structural organization of the different amplicons in the AZFb and AZFc regions belonging to five palindromic structures (P1-P5); **C)** Partial and complete AZFc, AZFb and AZFb+c deletions caused by recombination between different amplicons.

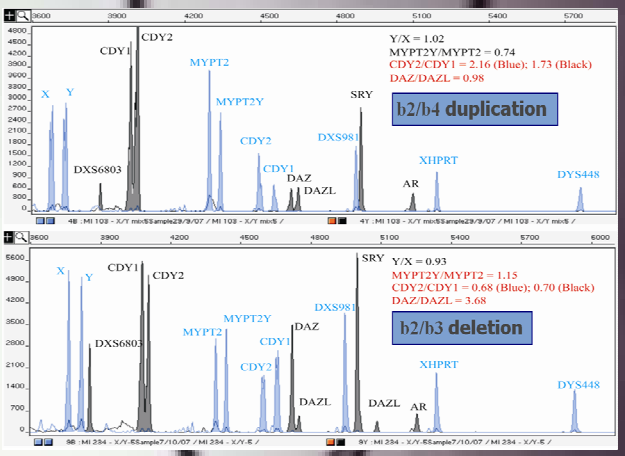

Figure 2. A representative electrophoreograms of 13-plex PCR results from SA patients with AZFc b2/b4 duplication and AZFc b2/b3 deletion.

CONCLUSION

In conclusion, our study suggests that partial AZFc deletions might represent a male risk factor for SA, while partial AZFc duplications might have a protective role.

ACKNOWLEDGMENTS

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