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P-086 AZF Microdeletions: A New Look at Past Paradigms

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Study question: To elucidate whether AZF screening is indicated in men with proven non-obstructive azoospermia (NOA) or severe oligozoospermia ($<5x10^6$ sperm/mL) who concomitantly harbor chromosomal abnormalities.

Summary answer: Some chromosomal aberrations are concomitant with AZF microdeletions, and hence Y chromosome microdeletion (YCM) screening is necessary for these patients.

What is known already: In the era of assisted reproduction, finding cost-minimization strategies in infertility clinics without affecting the quality of diagnosis and treatment is becoming one of the top-priority topics for future research. Formulating definitive guidelines concerning the indications for paraclinical testing could be one of the strategies. Accordingly, definitive guidelines for AZF screening do not exist especially in men who also have chromosomal abnormalities. The current clinical practice is to decide per case whether to pursue further molecular testing, with the accompanying added psychological and socio-economic burden.

Study design, size, duration: An observational retrospective cohort study of 10,388 consecutive cases from a tertiary infertility referral center (Royan institute, Tehran, Iran) over the last 12 years. A comprehensive literature review was also performed to summarize scientific evidence.

Participants/materials, setting, methods: The study recruited the largest cohort of men with primary infertility (NOA or severe oligozoospermia) ever presented who underwent screening for cytogenetic abnormalities and YCMs using sequence-tagged sites-polymerase chain reaction (STS-PCR) with a primer set covering the AZF regions according to the EAA/EMQN guidelines, as part of the infertility workup prior to ART.

Main results and the role of chance: In total, one-third of men with YCMs concomitantly had an abnormal karyotype (excluding those with heteromorphisms) (169/565; 29.9%, 95% CI: 26.3-33.8). In respect to the frequency of YCMs, our findings suggest that the cases diagnosed with 46,X,add(X) with incidence of 1.8% (3/169; 95% CI: 0.6-5.1); 45,X and mosaic forms: 45,X/46,X,inv(Y)(p11.2q12); 45,X/46,X,del(Y); 45,X,der(Y;Autosome); 45,X/46,X,idic(Y)(p11.2); 45,X/46,XY,r(Y); and 45,X/46,X,idic(Y)(q11.2) (19/169; 11.2%, 95% CI: 7.3-16.9); and inv(Y)(p11.2q12) (2/169; 1.2%, 95% CI: 0.3-4.2) should also be referred for AZF deletion screening, as data suggests they are accompanied with YCMs.

Limitations, reasons for caution: The extension of the outcomes beyond the described population could introduce concerns on appropriate medical management. Confirmatory studies in other geographic/ethnic groups are still necessary to reach a consensus regarding the outcomes.

Wider implications of the findings: It has been recommended that all men with NOA who have chromosomal abnormalities, except those with 46,XY/45,X karyotype, do not need AZF testing. The results reflect a crucial need for reconsidering whether YCM testing is indicated in the population of men with certain karyotypic abnormalities.

Trial registration number: Not Applicable