

CASE DISCUSSION

Male Infertility

LITERATURE REVIEW

- Approximately 15% of couples in the world are infertile which is approximately 50% caused by the male factors infertility
- At Cebior Laboratory, Diponegoro University since 2011 until 2022 were done 74 AZF gene analysis which found 13,51% with deletion (50% on the AZF c region, 40% on the AZF a region, 10% on the AZF a and AZF c region)

- Male infertility were caused by 2 main factor: genetic and non genetic factor
- Tiepolo and Zulffardi (1976) were the first hypothesized a correlation between the Y chromosome deletion with man infertility
- The AZF found at the Yq chromosome, may be the most thoroughly studied male sterile locus in human
- There are 4 region in AZF gene: AZF a, AZF b, AZF c, and AZF d

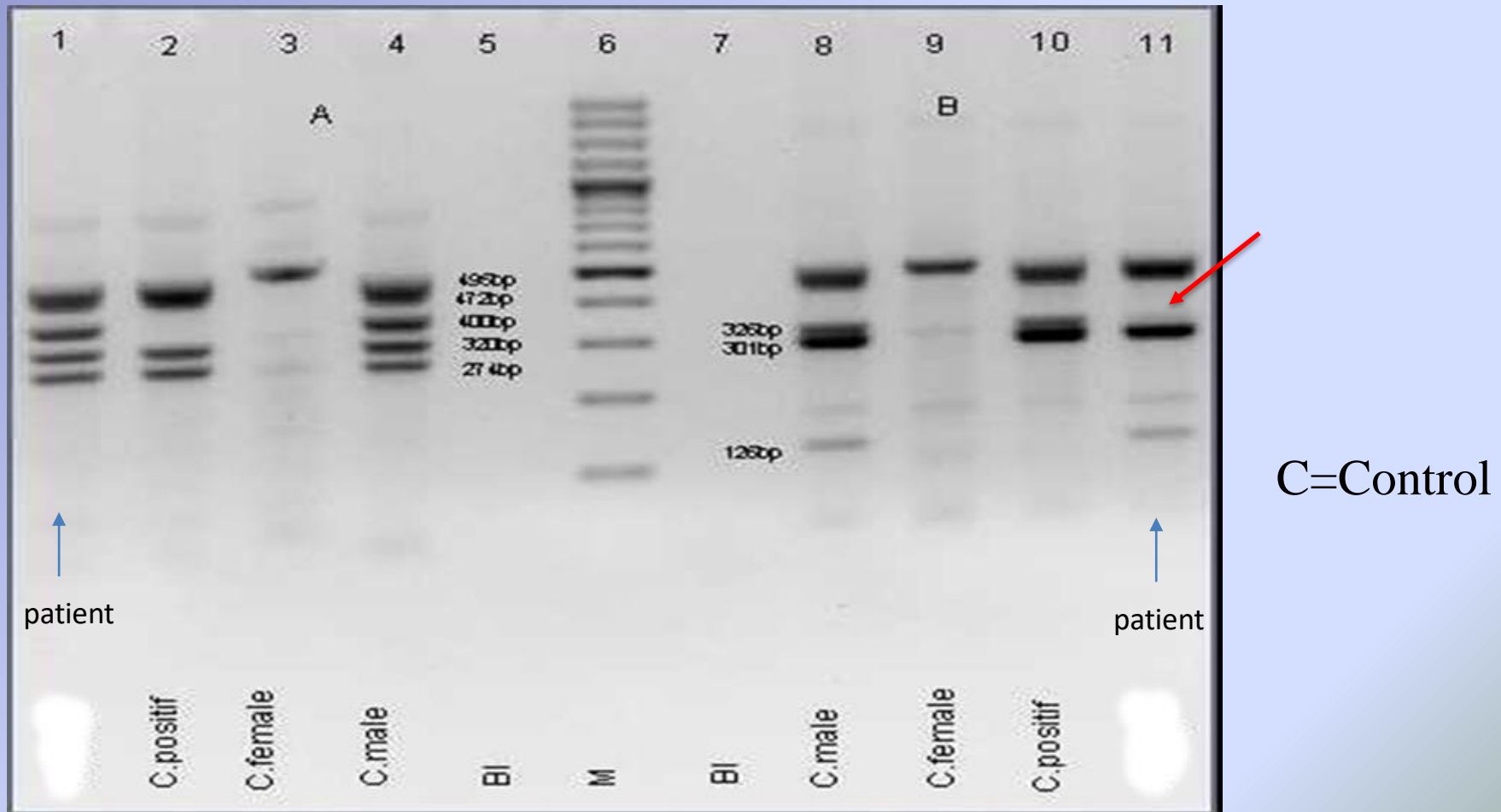
- **AZF a** → 400-600 Kb, SCO (Sertoli Cell Only Syndrome) mostly found related with this region
- **AZF b** → 1-3 Mb, micro deletion of this region may caused slight to severe oligospermia, while wide deletion may caused azospermia
- **AZF c** → 3,5 Mb, located on the distal of Y chromosome, most frequently found, 2-10% with azospermia to severe oligozopsermia, DAZ is the main gene in this region caused 13% male infertility when there is any mutation
- **AZF d** → between AZF b and AZF c, caused oligozospermia or event normal sperm account with only abnormal shape

CASE DESCRIPTION

- Young couple have been married more than 4 years, no history of pregnancies
- Diagnosed by Gynecologist with Polycystic Ovarian Syndrome → treated with hormone and metformin → increased her body weight until 100 Kg
- Consulted to another Gynecologist → suggested for sperm analysis and consultation to an andrologist

- The andrologist suggested testis biopsy and the AZF gene analysis including consultation with genetic counselor
- The biopsy confirmed azospermia
- The AZF gene analysis showed → deletion on the 326bp fragment of AZF a

Analysis of AZF/SRY gene were done with: multiplex PCR A and B



the 326bp fragment was missing confirmed AZF a deletion (red arrow)

Multiplex A	Hasil	Multiplex B	Hasil
ZFY : 495 bp	+	ZFY : 495 bp	+
SRY : 472 bp	+	SRY : 472 bp	+
sY254 : 400 bp(AZFc)	+	sY86 : 326 bp(AZFa)	-
sY84 : 320 bp (AZFa)	+	sY134 : 301 bp(AZFb)	+
sY127 : 274 bp (AZFb)	+	sY255 : 126 bp (AZFc)	+

Summary:

The DNA amplification to identified ZFY gene (identically with chromosome X) showed on 495bp fragment. The SRY gene (short arm of the Y chromosome) identified on the 472bp fragment. AZF gene identified on the 400bp, 320bp, 274bp, and 126bp fragment, the 326bp fragment was missing confirmed AZF a deletion

Conclusion: deletion on (AZF a may caused complete absent of the germ cell (Sertoli Cell Syndrome).

Mutation on the other locus could not be detected in this examination.

Notes:

- AZF a deletion caused an complete absent of the germ cell (Sertoli Cell Syndrome)
- AZF b deletion caused spermatogenesis maturation disturbance
- AZF c deletion caused oligospermia
- Deletion both three region caused complete azospermia
- SRY gene mutation caused gonadal differentiation disturbance

COUNSELING SESSION

- The couple were in denial phase when they met the counselor
- The wife refused to show the AZF gene result, even it was done in the past (3 years ago), while the husband keep silent no reaction
- She said I knew that my husband has AZF gene deletion, I do not need to show you the results. The original result is still in the lab, I did not want to take it, I only keep it in my mobile phone (this is the sign of denial and anger)
- In this situation, we give few minutes to the client to show their sadness and later she showed the results from her mobile phone
- If it was not possible to continued the counseling session, better to stop it to give more time for client to accept their conditions

- Give phone number or other contact for the client, because sometimes they'll call for help or another explanation when they ready to
- Sometimes it need a psychological counselor or meet other specialist, depend on the client condition
- Continuation of our counseling, then she was getting calm and ask: is there any possibility for us to have a child
- We informed that the possibility is:
 - Adoption
 - Sperm donor

- The ethical dilemma appear
 - Adoption: She don't want
 - Sperm donor: is not possible because it is not allowed by religion (Islam) and government rule
- Other problem the mother in law want to have grand children and keep asking her, since both of her son has no child
- Counseling could be extended that male infertility probably inherited
- Counselor gave some example: other couple with normal condition sometimes also do not have child
- How to tell to mother in law about this possibility?

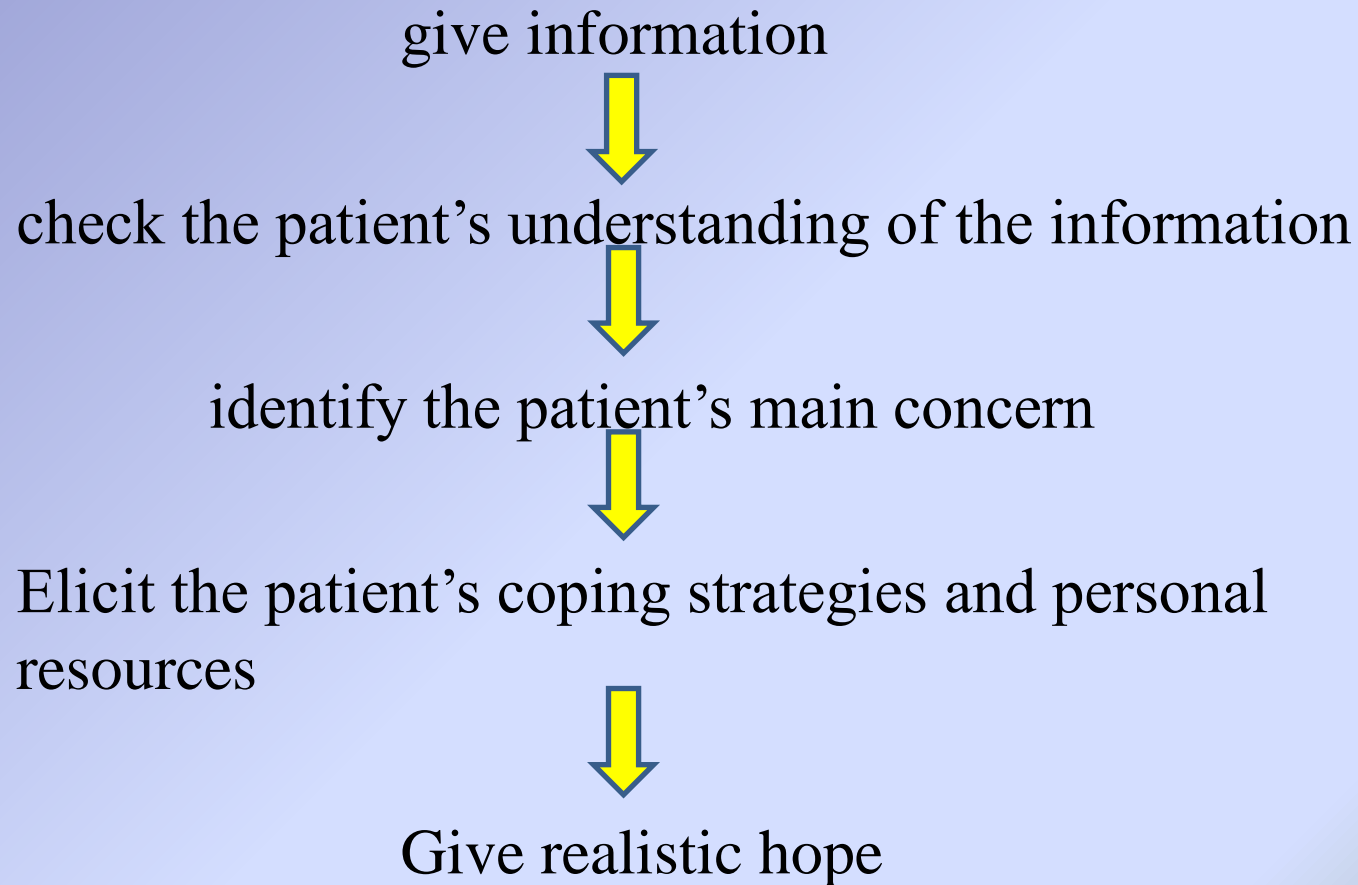
- That process may be considered in several stages: collecting genetic information and pedigree drawing; making or validating the diagnosis; estimating occurrence and recurrence risk; communicating clinical information; and supporting the family to reach a decision and take appropriate action

MORE ABOUT COUNSELING

- Genetic counseling raises special ethical issues related to confidential and privacy protection. Information about the individual, family history, carrier status, risk of genetic disease to self or offspring can be stigmatizing and hence needs to be kept confidential
- An awareness of serious psychosocial consequences must always accompany the whole process of genetic counseling, since we know genetic traits are distinctive in several aspects
- Genetic counseling has the information, education and human dimension

- The information that patients learn in the genetic counseling process has the potential to be psychologically overwhelming and to result in an emotional response
- The most common emotional responses are denial, anger, fear, despair, guilt, shame, sadness and grief.
- **Questions** → maybe vehicles for expressions of feelings, the counselee attempting to share an emotional reaction and discover the meaning of the event
- **Projective Identification** → describes a complex defense mechanism that is triggered when the meaning of an event is extremely psychologically challenging to the patient

- Lloyd and Bor (2009), summarized the process of transmitting bad news as



THANK YOU

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