INTRODUCTION

Globozoospermia syndrome is a rare teratozoospermia with an incidence below 0.1%. Presence of 100% round-headed sperm heads, absence of acrosome, and messy sperm body and tail are the main characteristics of this syndrome. The activation ability of oocytes and consequently the fertilization rate decrease due to the absence of acrosome.

The pathogenesis of globozoospermia is not clear [1-2]. Globozoospermia originates from a disturbed acrosome biogenesis and lots of studies on animal species revealed that sperm acrosomes play a role in the fertilization rate. The genetic study of familial globozoospermia led to reveal that a homozygote mutation of the gene SPATA16 linked to the globozoospermic phenotype [3].

The others genes that are associated with complete globozoospermia are autosomal recessive genetic mutation in PIK1 and DPY19L2 deletion [4-6].

There are significantly greater percentages of sperm with DNA fragmentation, increase in the frequency of sex chromosome aneuploidy and disomy 8 in cases with globozoospermia compared to normal fertile men [7-8].

The fertilization rate of these cases is low and intracytoplasmic sperm injection (ICSI) proved to be an effective therapy [9].

There are two types of globozoospermia. Total globozoospermia consists of 100% round-headed acrosomeless spermatozoa whereas partial globozoospermia contains more than 50% acrosomeless spermatozoa [2].

Patients with total globozoospermia are absolutely infertile [10] but there are some reports of successful pregnancy and live births in cases of globozoospermia with severe oligoasthenospermia after intracytoplasmic sperm injection [11-12].

The fertilization rate improves in such cases after intracytoplasmic sperm injection (ICSI) combined with assisted oocyte activation [13].

Two cases of globozoospermia with infertility are detailed in this study.

Keywords: globozoospermia, male infertility

CASE I

An infertile 29-year-old man was referred to the infertility clinic. He had been married for six years.

Hormonal analysis was normal but sperm analysis was abnormal. The infertility workup of his wife – transvaginal ultrasound, hormonal analysis, hysterosalpingography and diagnostic laparoscopy – was normal. She had regular menstruation and her cycle interval was 28-30 days.

Following these results the couple was scheduled for intracytoplasmic sperm injection.

A long protocol of ovulation induction was performed consisting of Suprefact® and Gonal F® injections. In ten cycle days the endometrial thickness was 7.8 mm and her ovaries presented 12 dominant follicles. At that time 10000 human chorionic gonadotropin units were injected and 34 hours later she underwent oocyte collection and intracytoplasmic sperm injection without oocyte activation.

But pregnancy was not achieved after three embryo transfers.

The sperm analysis just before intracytoplasmic sperm injection revealed the following:

- semen volume: 4 ml
- total sperm count: 25 million
- motility 30%.

And light microscopy showed that 100% of spermatozoa were round-headed (Figure 1).

The patient was thus diagnosed as suffering from total globozoospermia.
CASE II
A 26-year-old man married for three years and without children was referred to the infertility clinic. Hormonal analysis was normal but sperm analysis presented abnormalities. His wife had oligomenorrhea and irregular menstruation and was a known case of polycystic ovary. Her additional infertility workup included hormonal analysis and hysterosalpingography; both were normal.

The couple was then advised to undergo the intracytoplasmic sperm injection procedure.

A lengthy protocol of ovulation induction with Suprefact® and Gonal f® was performed. In 12 cycle days the endometrial thickness reached 10 mm and 10 dominant follicles developed in the ovaries. At this stage 10000 human chorionic gonadotropin units were injected and 34 hours later oocytes were retrieved. Intracytoplasmic sperm injection without oocyte activation took place at three days interval.

But pregnancy did not happen after three embryo transfers.

The sperm analysis conducted just before intracytoplasmic sperm injection revealed the following:

- semen volume: 4 ml
- total sperm count: 75 million
- motility: 70%
- 45% of spermatozoa were round-headed.

The patient was thus diagnosed with partial globozoospermia.

Among 1250 cases recorded over 10 years in our hospital, we have encountered only one case of complete globozoospermia.

DISCUSSION
The incidence of total globozoospermia is about 0.1%. [14]. We had one case of total and one case of partial globozoospermia among 250 cases (0.4%) of male factor infertility.

Roy et al. described the role of the endoplasmic reticulum resident enzyme β-glucosidase 2 (GBA2) in mice and revealed that GBA2 deficiency leaves bile acid and cholesterol metabolism intact, but causes lipid accumulation in the endoplasmic reticulum of testicular Sertoli cells, round-headed sperm, and impairs male fertility [15].

A homozygous mutation in the spermatogenesis-specific gene SPATA16 in three brothers with globozoospermia was reported by Dam et al. [16].

We recommended to our patient with total globozoospermia an evaluation of his family for this rare disease as gene mutations are recognized to cause this syndrome. Our patient had four brothers who were all fertile and had normal children.

A positive correlation between globozoospermia and higher chromosomal aneuploidies of the chromosomes 13, 16, and 21 was demonstrated by one study and suggests that there is a higher risk of creating aneuploid embryos after intracytoplasmic sperm injection in globozoospermia patients [17].

The karyotypes of our patients were normal 46,XY.

The main problem of globozoospermic cases is a low fertilization rate, and even though ICSI and oocyte activation can increase this rate, they do not necessarily achieve a pregnancy [18].

ICSI following assisted oocyte activation by electrical stimulation or oocyte activation with calcium ionophore will result in high rates of fertilization and normal clinical pregnancy [19-20].

We recommended ICSI and assisted oocyte activation in order to achieve pregnancy in the two reported cases. However, the pregnancy rate of these patients remained significantly low in spite of using these techniques.

REFERENCES
7. Brahem S, Mehdi M, Elghazel H, Saad A. Analysis of sperm aneuploidies and DNA fragmentation in patients with globozoospermia or with abnormal acrosomes.