HIGH LEVEL OF WHITE BLOOD CELLS IN SEMEN

*Leucospermia*

The presence of more than one million of white blood cells in 1 millimeter (mL) of ejaculate.

♀ Symptom ♂ Male

About High level of white blood cells in semen

High level of white blood cells (over one million of white blood cells in 1 millimeter (mL) of ejaculate), or leukocytes, in the semen, is an abnormality of semen quality, and can be indicative of a disease of the male genital tract (Pic. 1).

Elevated amount of white blood cells in semen may be associated with the presence of bacteria in semen (bacteriospermia), genital or urinary tract infections, which could cause pain, alterations in accessory sex gland functions, tubal occlusion and fertility problem including decreased sperm motility and count. Another condition strongly associated with high level of white blood cells in the semen is varicocele (enlarged veins in the scrotum).

Leukocytes (polymorphonuclear neutrophils and macrophages, Pic. 2) have an important effect on male fertility as they are implicated in reactive oxygen species (ROS) production. ROS are highly reactive molecules that cause damage to various cell components, most importantly to DNA and cell membrane. Spermatozoa membrane and nuclear DNA damage caused by increased ROS with defective antioxidant defect could play a role in development of poor sperm quality including motility and fertilizing ability. Leukocytes and abnormal sperms are considered major sources of ROS in semen. In a state of inflammation, the white blood cell count in the semen is elevated and may affect sperm quality. Even if the condition is not caused by
infection, impaired fertility can occur.

The diagnosis of leukospermia has contradicting effects on pregnancy rates in natural pregnancies, intra-uterine insemination (IUI) and in vitro fertilization (IVF) with or without intra-cytoplasmic sperm injection (ICSI). Before assisted reproduction techniques (ART) treatment, the spermiogram of the man should be carefully evaluated. If any pathological components of the ejaculate, such as leukospermia, are found, the couple should first undergo treatment of the condition before the fertility treatment can be planned.

Generally, for the treatment of leucospermia, a 4-6 week course of extended spectrum antibiotics, such as erythromycin, trimethoprim-sulfamethoxadole, doxycycline, azithromycin, ofloxacin, or a quinolone, is recommended. Antibiotics treatment is associated with a reduction in the concentration of leukocytes and improved fertilization rate. Generally, the female partner is also treated. Recommended follow-up includes semen analysis three months later the antibiotics treatment.

Leucospermia may be associated with several conditions, including:

**Bacteriospermia**

Bacteriospermia is the presence of bacteria in the semen. It is usually associated with bacterial genitourinary tract infection, which can remain asymptomatic, but already produce significant bacteriospermia. The immune reaction of the organism leads to inflammation and can cause concurrent leucospermia, as the leukocytes aim to destroy and phagocytose (devour) the bacteria. Bacteriospermia affects the normal fertility process by any of these following mechanisms: deterioration of spermatogenesis, decreased sperm motility, altered acrosome (a vesicle present on the head of the sperm cell) reaction, altered morphology, formation of reactive oxygen species leading to increased DNA fragmentation index, formation of antisperm antibodies, and genital tract obstruction due to inflammation and fibrosis (scar tissue formation).

**Genital tract infection**

Infectious agents can interfere with the reproductive function in both sexes. Infections of male genital urinary tract account for about 15% of the case of male infertility. Different sites can be affected in the male reproductive system, such as the testis, epididymis, and male accessory sex glands. Spermatogenesis itself can be affected by urogenital infections at different levels of development, maturation, and transport of spermatozoa. These infections can be both sexually transmitted and non-sexually transmitted. Among the most common microorganisms involved in sexually transmitted
infections, thus interfering with male fertility, are the Chlamydia trachomatis and Neisseria gonorrhoea. Less frequently, male infertility may be due to nonsexually transmitted epididymo-orchitis, mostly caused by Escherichia coli. Infections of the lower genital tract seem to have little importance. However, such infections, as well as those involving other parts of the male genital urinary tract, may cause a microbial colonization of the semen. Moreover, the infection-induced inflammation causes an elevated count of leukocytes, and can lead to leukospermia.

**Varicocele**

An abnormal enlargement of the pampiniform venous plexus in the scrotum (Pic. 4). Varicocele is a common abnormality with the following andrological implications: failure of testicular growth and development, symptoms of pain and discomfort, male infertility. Varicocele is frequently diagnosed when a patient is 13–30 years of age, and rarely develops after the age of 40. Overall, it occurs in 15-20% of all males. There are significant decrease in semen quality and significant increase in seminal leukocytes count in varicocele. Even subclinical varicocele (causing no symptoms to the patient) induces seminal and spermatozoal subclinical inflammatory response in the form of low-level leucospermia, leading to increased spermatozoal ROS production, oxidative stress, and DNA fragmentation.

**Prognosis**

The association between seminal leukocytes and semen quality is still a matter of debate in the literature. Leukocytospermia, defined by the World Health Organization (WHO) as more than 1 million leukocytes per millilitre, has an incidence of 10-20% in the general population and is especially common in infertile men. However, lower concentrations of seminal leukocytes (0-1 × 10^6/mL) are still more widespread, and are seen even in the absence of infection.

However, the results of more recent studies suggest that leukocytes negatively impact on semen quality as a result of the presence of reactive oxygen species (ROS), which are primarily produced by leukocytes. It is believed that ROS are harmful to spermatozoa. Aziz et al. reported a positive correlation between leukocytospermia and sperm tail defects, acrosomal damage and high sperm deformity index scores.

However, in another study, Ziiyyat et al. reported an increase in sperm motility in semen samples with moderate leukocytospermia (defined as seminal leukocytes <1 × 10^6/mL), but observed a paradoxical decrease in sperm motility in semen samples exceeding a threshold of 1 × 10^6 leukocytes/mL.
Similar results were found for semen samples classified as having normal morphology (sperm deformities were not described in this study). In support of this finding, Lackner et al. have shown that leukocytospermia may not necessarily have a negative impact on outcomes following assisted reproductive techniques. They reported similar fertilization rates for non-leukocytospermic samples and leukocytospermic samples (63.4% vs. 64.3%, P = not significant). Corresponding pregnancy rates also did not differ significantly between the two groups.

Considering the results from these reports, it is possible that leukocytes in semen samples may have a dual effect on semen parameters.
An illustration of varicocele. The veins of the scrotum, so-called pampiniform plexus, are significantly enlarged.

Sources

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