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LETTER TO EDITOR

Increased exfoliation of immature germ cells detected in semen analysis routine and its clinical significance

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To the Editor,

Currently, semen analysis is the unique test to evaluate men's fertility potential. Semen analysis provides valuable information on sperm production and quality. In addition to the conventional assessment of the sperm characteristics in a basic semen analysis routine, performing a differential diagnosis of leukocytes and sperm precursors *immature germ cells* (IGC) is also pivotal (1-3), due to adding valuable and clinically suitable information to the semen report. While increased leukocyte count may indicate infections (4), increased exfoliation of IGC from seminiferous tubules suggests abnormal spermatogenesis (5, 6). Even the inflammation could induce exfoliation of IGC from seminiferous tubules (7). In semen analysis, a global and differential count of all seminal round cells can improve the diagnosis (8) and treatment options to achieve a successful pregnancy (9). A high count of IGC in semen would represent different seminal and reproductive alterations and would be an essential indicator for detecting testicular alterations (6). Therefore, an index could be developed comparing IGC count/mL *vs.* sperm count/mL. In some instances, this index would be paramount for estimating, for example, the negative impact of varicocele on the germinal epithelium in increased exfoliation of IGC in semen. The normal is to find one IGC for every 40 spermatozoa, values between 20/1 and 40/1 are indeterminate, and values lower than 20/1 indicate increased exfoliation of IGC, which suggests a loss of integrity of the germinal epithelium. Occasionally, ratios greater than 1/1000 are also found, mainly in ejaculate with high sperm count (*Andrade-Rocha FT, Unpublished data*). The lower this index, the worse is the integrity of the germinal epithelium. The cells are sloughed off before completing the spermatogenesis process and spermatozoa production. For example, the conventional semen parameters routinely evaluated in a 32 years old man in *Lisa Andrology Lab* (*Petrópolis, RJ, Brazil*) for investigating male infertility showed the ratio was six IGC for each sperm; it was even worse, showing an inversion in the index (Table 1 and Figure 1) show a representative aggregate of IGC in the semen specimen.

Table 1.
Patient semen characteristics and lower reference limit.

Parameter	Outcomes	Lower reference limit – percentile 5th (11)
Semen volume	6.1 mL	1.4 mL
Sperm count/mL	317 000	16 x 10^6/mL
Total sperm count	1 931 710	39 x 10^6 per ejaculate
Vitality	20%	54%
Total motility	10%	42%
Progressive motility (a)	0	30%
Slow/irregular motility (b)	9%	-
Non-progressive motility (c)	1%	1%
Immotile (d)	90%	20%
Normal morphology	0.53	4%
Amorphous sperm	11%	-
Tapered sperm	7%	-
Sperm immature germ cells *vs.* sperm	1/6	1/40
Hypo-osmotic swelling	18%	58%
pH	8.2	> 7.2

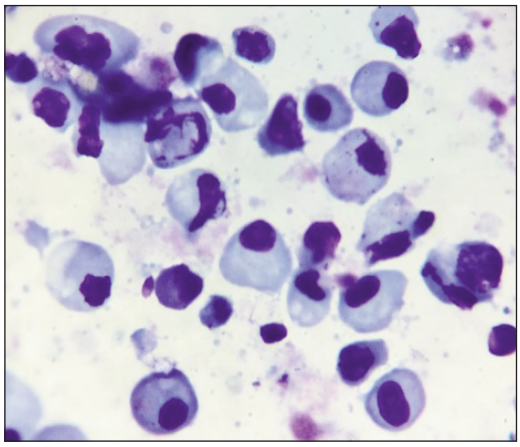

Figure 1.
Unequal aggregation of immature germ cells regarding to sperm. The semen smear used for the microphotograph shown in this editorial was made with concentration to show the proportionality between IGC and sperm in the analyzed semen specimen.

No conflict of interest declared.

This assessment measures the intensity of the famous seminal stress pattern that *John MacLeod* proposed in the 1960s (10). According to MacLeod, the stress pattern is characterized by an increase of amorphous and tapered and exfoliated IGC in semen and is usually diagnosed in some varicocele men. Unlike previous observations by *MacLeod* (10), it has been observed that varicocele men can cause structural changes in sperm, like amorphous and tapered sperms, increased exfoliation of sperm precursors and both.
Therefore, further studies are needed to expand knowledge on this issue, which is practically unexplored in clinical and laboratory practice.

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