

Ultrasound Characterization of Patients with MAGI (Male Accessory Gland Infection): Importance of the Topic

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Short Communication

MAGI (Male Accessory Gland Infection) represent a main cause of male infertility. The use of ultrasound evaluation in this condition is very controversial. This article summarizes the possible clinical interpretations (mainly obtained in our clinical experience) related to ultrasound images of these patients with repercussions in different specialist areas: laboratory, microbiology, endocrinology, urology, sexology, internal medicine. The US (Ultrasound) characterization of patients with MAGI (Male Accessory Gland Infection) is routinely performed through evaluation of epididymis, prostate and seminal vesicles (the last two preferably with transrectal scan). In the clinical practice the usefulness of US is controversial. The use of US is widespread, however, the specificity and sensitivity of this diagnostic tool is not considered very high for these specific conditions [1]. AIUM (American Institute of Ultrasound in Medicine) suggests use of TRUS (Transrectal Ultrasound) for evaluation of prostate-vesicular tract in all infertile patients. Other indications are represented by: a. echo-guided biopsy for prostatic suspicious nodules (with the digital rectal examination), or for elevated values of PSA (Prostate Specific Antigen) and/or suspect magnetic resonance imaging; b. calculation of the prostate volume before surgical procedures and/or radiotherapy, and for calculation of PSA density; c. a guide for positioning of the needles in the course of radiotherapy; d. evaluation of functional disorders associated with LUTS (Lower Urinary Tract Symptoms); e. study of morph structural congenital anomalies; f. hemospermia; g. recurrent disease in patients with previous prostatectomy [2]. The guidelines of the EAU (European Association of Urology) admit the use of TRUS only for patients with suspected obstructive azoospermia. In particular, these guidelines suggest to identify azoospermic patients with low-volume of ejaculate. US evaluation of epididymal tract should be

limited to patients with suspicious signs of obstruction: dilation of the rete testis, cystic dilation of the cephalic tract, suspected absence of the vas deferens [3]. In particular, a recent study of Pezzella et al. [4] showed that the detection of a longitudinal diameter >10.85 mm of the cephalic tract combined with serum FSH levels <7.8 IU/ml it is suggestive of obstructive azoospermia (sensitivity=58.8%; specificity=91.4%). A recent systematic review of the scientific literature, carried out by the Florence University, showed that the US evaluation of epididymal and of the prostate-vesicular tract (transrectal scan) is useful in the clinical evaluation of patients with chronic inflammation of these anatomical sites, favoring the ability to detect US criteria associated with inflammation, and therefore suggesting the use of this diagnostic tool in various inflammatory steps that characterize the course of MAGI [5]. This interpretation is more consistent with the clinical practice; in fact, MAGI represent a nosographic category responsible for male infertility. The first classification was proposed on 1980 [6], subsequently WHO (World Health Organization) (1993) illustrated diagnostic criteria [7], and finally it was recognized in current EAU guidelines among the causes of male infertility [3]. As the mechanisms that could determine alterations of conventional sperm parameters are different, rather than only the obstruction of the ejaculatory ducts, however well evaluated by US [8], but also concerns other pathophysiological aspects, such as: oxidative stress and imbalance of cytokines, impaired secretory capacity of sex glands, direct microbial damage. US evaluation of epididymis, prostate and seminal vesicles, contributes to clinical interpretation of main clinical and translational aspects which are summarized below [9]. Previously, have been reported US criteria suggestive for P (prostatitis), PV (prostate-vesiculitis), PVE (prostate-vesiculico-epididymitis), summarized in (Table 1) [10].

Prostatitis is suspected in the presence of >2 of the following ultrasonographic signs:

1) asymmetry of the gland volume; 2) areas of low echogenicity ; 3) areas of high echogenicity; 4) dilatation of peri-prostatic venous plexus; 5) single or multiple internal similar cystic areas, 6) area/s of moderate increased of vascularity (focal or multiple).

Vesiculitis is suspected in the presence of >2 of the following ultrasonographic signs :

1) increase (>14 mm) anteroposterior diameter mono or bilateral; 2) asymmetry >2.5 mm (normal 7-14 mm) compared to the controlateral vesicle ; 3) reduced (<7 mm) anteroposterior diameter mono or bilateral; 4) glandular epithelium thickened and/or calcified; 5) polycyclic areas separated by hyperechoic septa in one or both vesicles; 6) fundus/body ratio >2.5; 7) fundus/body ratio <1; 8) antero-posterior diameter unchanged after recent immediately ejaculation.

Epididymitis is suspected in the presence of >2 of the following ultrasonographic signs:

1) increase in size of the head (cranio-caudal diameter >12 mm) and/or of the tail (cranio-caudal diameter >6 mm) (finding single or bilateral); 2) presence of multiple microcystis in the head and/or tail (finding single or bilateral); 3) low echogenicity or high

echogenicity mono or bilateral; 4) large hydrocele mono or bilateral; 5) enlargement in superior part of the cefalic tract and superior/inferior part ratio >1; 6) unchanged antero-posterior diameter of tail after ejaculation.

Table 1: Ultrasound criteria of MAGI.

The importance of these criteria is attributable to understanding of a different extension of the chronic inflammatory process, proportionate with severity of alteration of the sperm parameters [9] and of the symptoms [11], higher in PVE vs. PV and P, as well as in PV vs. P.

Laboratory Aspects

Patients with US criteria of PVE have seminal concentrations of IL-10 (interleukin 10), among the anti-inflammatory cytokines, significantly lower compared patients with US criteria of PV and P and seminal concentrations of IL-6 (interleukin-6) and TNF-alpha (tumor necrosis factor), among the main pro-inflammatory cytokines, significantly higher compared to PV and P [12]. PVE patients have lower seminal concentrations of fructose compared to patients with P, and ROS (oxygen free radicals) levels of leukocyte origin appear to be significantly increased in PVE compared to P. However the seminal concentrations fructose and ROS do not differ between patients with mono or bilateral inflammatory (amicrobic) PVE, confirming the importance of US evaluation [13]. A flow cytometric evaluation on semen of patients with MAGI showed a significant increase of the percentage of spermatozoa with fragmented DNA, without significant differences between patients with inflammatory or microbic form [14]. The US criteria suggestive for inflammation of the prostate (increase of parenchymal peak systolic velocity, presence of macro calcifications, and hyperemia) are associated with an increased percentage of spermatozoa with fragmented DNA [15]. In particular an increase of the percentage of spermatozoa with brighter fragmented DNA (sum of viable and non-viable spermatozoa, highly oxidized). Patients with US signs suggestive for testicular pathology showed a significant increase in the concentration of spermatozoa with dimmer fragmented DNA (non-viable sperm whose concentration in semen is associated with the quality of conventional sperm parameters) [15]. Finally, the progressive anatomical extension of inflammation assessed by US (P-PV-PVE), is associated with a proportional increase of the viscosity values of the seminal plasma evaluated with the original method of measurement through viscometry and expressed in centipoise (PVE>PV>P) [16].

Microbiological Aspects

The presence of micro and/or macro calcifications in the prostate tissue, the presence of signs suggestive for acinar ectasia and the detection of polycyclic endoluminal areas in the seminal vesicles represent US criteria associated with persistence of bacteriospermia [17]. After pharmacological treatment with levofloxacin (first choice in patients with microbial MAGI) the percentage of eradication is significantly lower in PVE patients compared to PV and P. Moreover bilateral PVE is associated with lower rate of eradication after pharmacological treatment compared to unilateral PVE [18]. In patients with human papillomavirus infection, [19] the detection of suggestive US criteria for P concentrated in the periurethral and transitional region of the prostate, represent a diagnostic element which helps to confirm this diagnostic hypothesis [20]. TRUS could improve the specificity of the bacteriological examination performed on prostatic secretion obtained after massage. Therefore, this test,

traditionally known in the clinical practice as Meares and Stamey Test [21], could be supplemented by TRUS with the aim to identify before of the prostate massage, the parenchymal areas with acinar ectasia and/or micro and macro calcifications that are worthy of examination [22]. Conventionally the microbiological evaluation is required for patients with leukocytospermia (leukocytes>1 million/ml) [23], however, the presence of US criteria suggestive for persistent inflammation of the prostate and of the seminal vesicles, might suggest to integrate the assessment of the leukocytes, with the use of monoclonal antibodies, such as CD45 for the characterization of other lymphocyte sub-populations, expression of chronicity of the inflammatory process with the transformation of the initial functional response of neutrophils in lymphocytes [22].

Endocrinologic Aspects

In the experimental model hypogonadism represent a risk factor for the progression of prostatic inflammation, however also in the clinical practice lower concentrations of TT (total testosterone) are associated with higher frequency of symptoms referable to chronic prostatitis [24,25]. Moreover with US evaluation was reported a reduced frequency of bilateral PVE in patients with normal serum concentrations of TT [26], suggesting a protective role of androgens on the greater extension of the inflammatory process. At the same time, the eugonadal patients had a reduced frequency of fibro-sclerotic variant of MAGI, that represent an US form associated with persistent low quality of sperm parameters after pharmacological treatment (Figure 1) [26,27].

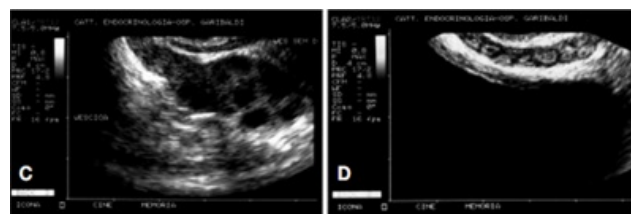


Figure 1: Dilated seminal vesicle vs. seminal vesicle with reduced thickness [27]; On the left dilated seminal vesicle with increased anteroposterior diameter (threshold: 14 mm) and polycyclic intraluminal areas. On the right seminal vesicle with a reduced anteroposterior diameter (threshold value: 7 mm) and inhomogeneous intraluminal space. The image on the left represent an ultrasound sign of "hypertrophic-congestive MAGI" associated with possible improvement of sperm parameters after therapy. On the right the image represent an ultrasound sign of "fibro-sclerotic MAGI" generally not associated with significant modification of sperm parameters after pharmacological treatment.

In patients with type 2 diabetes, the seminal vesicles are characterized by minimal or absent changes in the anteroposterior diameter after ejaculation and altered anatomical ratio between proximal and distal portion of the glandular body. These

characteristics are associated with clinical criteria attributable to the presence of autonomic neuropathy, suggesting the possible use of TRUS in the early diagnosis of this complication [10,28-30].

Systemic Aspects

Patients with IBD (Irritable Bowel Disease) have a higher frequency of MAGI compared to controls [31], in particular patients with chronic bacterial P associated with IBD have an higher frequency of MAGI compared to patients with chronic bacterial P without IBD [32]. In these patients the main US characteristic suggestive of MAGI is represented by the dilation of the periprostatic venous plexus [33].

Urological Aspects

Patients with varicocele, frequently have a concomitant dilation of periprostatic venous plexus detected with TRUS. It has been reported that these patients after surgical correction, maintain high levels of seminal viscosity (associated with reduced sperm motility), compared with controls (varicocele, without dilation of the periprostatic venous plexus), suggesting a less effective correction of varicocele on sperm parameters in these patients [34].

Sexual Aspects

Patients with acquired premature ejaculation, with a significant increase in the anteroposterior diameter of the caudal tract of epididymis and of the seminal vesicles have a linear relation between these parameters and scores of the Premature Ejaculation Diagnostic Tool [35]. The administration of selective inhibitors of V phosphodiesterase, commonly used for the treatment of erectile dysfunction, is associated with US modifications of the prostate-vesicular tract, which include: increased difference of the anteroposterior diameter of the seminal vesicles detected before and after ejaculation, increase of the ejection fraction of the seminal vesicles. These US changes correlate with increased seminal concentration of fructose [36].

Conclusions

US evaluation of the epididymal and of the prostate-vesicular tract in patients with MAGI is important for the following aspects: Evaluation of anatomical site of inflammation; Distinction between mono and bilateral form; Prognostic evaluation before pharmacological treatment; Evaluation of the possible persistence after pharmacological treatment; Additional criteria for differential diagnosis of MAGI associated with papillomavirus.

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