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ORIGINAL ARTICLE

Sexual Function

Acquired premature ejaculation and male accessory gland infection: relevance of ultrasound examination

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We have previously demonstrated a high frequency of premature ejaculation (PE) among patients with male accessory gland infection (MAGI). The aim of this study was to evaluate the ultrasound (US) features of patients with MAGI and acquired premature ejaculation (APE) associated (MAGI-APEpos). US evaluation of 50 MAGI-APEpos patients compared to 50 patients with MAGI without PE (MAGI-PEneg) which represent the control group. The diagnosis of APE was made through the evaluation of Intravaginal ejaculation latency time (IELT) and confirmed with the questionnaire PEDT (Premature Ejaculation Diagnostic Tool). The main outcome measure was represented by the frequency of US criteria suggestive of P (prostatitis), V (vesiculitis), and E (epididymitis) in MAGI-APEpos and MAGI-PEneg patients. MAGI-APEpos patients showed a total number of US criteria significantly higher compared to MAGI-PEneg patients. MAGI-APEpos showed a higher frequency of US criteria of V and E (complicated forms of MAGI). Finally, in MAGI-APEpos group, it was found a positive relationship between the anteroposterior diameter (APD) of the caudal tract of the epididymis and the APD of the seminal vesicles, as well as between both diameters and the PEDT score. MAGI-APEpos patients have a peculiar US characterization compared to MAGI-PEneg patients. According to these results, US evaluation of the epididymal and of the prostato vesicular tract should be considered in the practical clinical approach of patients with MAGI and APE. In particular, it could be a support for a possible pathophysiological interpretation of this clinical problem in these patients.
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INTRODUCTION

Recently, it has been proposed a unified definition of both acquired and lifelong premature ejaculation (PE) as a male sexual dysfunction characterized by a reduction of latency time, inability to delay ejaculation, and negative personal consequences.[1] However, acquired premature ejaculation (APE) has peculiar characteristics (demographic differences: men with APE are usually older, presence of comorbidities and greater Intravaginal ejaculation latency time [IELT]) including the frequent association with the urogenital tract inflammations.[1] Previously, we reported that patients with male accessory gland infection (MAGI) have a high frequency of sexual dysfunction, detectable through the application of a dedicated questionnaire (SI-MAGI = structured interview about MAGI) and PE represents one of these dysfunctions.[2] Usually in the literature, it has been reported the association between APE and chronic *P* (prostatitis),[3] however, the *P* represents only one of the three diagnostic categories of MAGI: *P* (prostatitis), PV (prostato- vesiculitis), PVE (prostato-vesciculo-epididymitis).[4] A low number of evidences concerning the frequency of PE in patients with epididymitis[5] and chronic vesiculitis,[2] this aspect appears in contrast with some important physiological aspects, such as: the contractile function of the epididymis[6] and the role of the seminal vesicles in the production of the seminal plasma.[7] Chronic inflammation of the epididymis and seminal vesicles can also be evaluated through US (ultrasound) examination and in the past our group has published the US criteria for the diagnosis of MAGI.[8] On the basis of these premises, the aim of this study was to evaluate the presence of peculiar US features in patients with MAGI and APE associated (MAGI-APEpos) compared to patients with MAGI without PE (MAGI-PEneg).

MATERIALS AND METHODS

Of a consecutive series of 1000 patients which referred to Andrology Center of Catania University during the period between January 2012 and January 2014 for the clinical counseling of andrological disorders, we selected 50 MAGI-APEpos patients. The diagnosis of MAGI and the US evaluation was performed according to criteria previously published,[4,9,10] summarized in **Box 1**. For all patients, the US examination was carried out few minutes before and 5 min after ejaculation. All patients examined had 4 days of sexual abstinence. All ultrasound examinations were performed by the same investigator. The study was approved by the Internal Institutional Board, and all examined patients signed an informed consent to the processing of personal data.

All selected patients reported the appearance of PE after a period of normal ejaculatory latency that was present from the first sexual experience. The duration of the APE has been assessed by the

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Box 1: Clinical and US criteria applied in the clinical practice for the diagnosis of MAGI

Clinical criteria

a. History of urogenital infection and/or abnormal rectal palpation

b. Significant alterations in the expressed prostatic fluid and/or urinary sediment after prostatic massage

c. (1) Uniform growth of more than 10 (3) pathogenic bacteria, or more than 10 (4) nonpathogenic bacteria per ml, in culture of diluted seminal plasma
(2) Presence of more than 10 (6) (peroxidase positive) leucocytes per ml of ejaculate
(3) Signs of disturbed secretory function of the prostate or seminal vesicles

The diagnosis is accepted if either of the following combinations if found:
a+b
a+c (1 or 2 or 3)
b+c (1 or 2 or 3)
c1+c2
c1+c3
c2+c3

Prostatitis is suspected in the presence of >2 of the following ultrasonographic signs
Asymmetry of the gland volume
Areas of low echogenicity
Areas of high echogenicity
Dilatation of peri-prostatic venous plexus
Single or multiple internal similar cystis areas
Area/s of moderate increased of vascularity (focal or multiple)

Vesiculitis is suspected in the presence of >2 of the following ultrasonographic signs
Increase (>14 mm) anteroposterior diameter mono or bilateral
Asymmetry >2.5 mm (normal 7–14 mm) compared to the controlateral vesicle
Reduced (<7 mm) anteroposterior diameter mono or bilateral
Glandular epithelium thickened and/or calcified
Polycyclic areas separated by hyperechoic septa in one or both vesicles
Fundus/body ratio >2.5
Fundus/body ratio <1
Antero-posterior diameter unchanged after recent immediately ejaculation

Epididymitis is suspected in the presence of >2 of the following ultrasonographic signs
Increase in size of the head (cranio-caudal diameter >12 mm) and/or of the tail (craniocaudal diameter >6 mm) (finding single or bilateral)
Presence of multiple microcystis in the head and/or tail (finding single or bilateral)
Low echogenicity or high echogenicity mono or bilateral
Large hydrocele mono or bilateral
Enlargement in superior part of the cefalic tract and superior/inferior part ratio >1
Unchanged antero-posterior diameter of tail after ejaculation

MAGI: male accessory gland infection, US: ultrasound

SI-MAGI.[2] This questionnaire is divided into four domains relative to urinary disorders, spontaneous and/or ejaculatory pain and/or discomfort, sexual disorders and quality-of-life. Question 5 of Section 3 (sexual disorders) is related to the presence and duration of PE.[2] The presence of APE was assessed through the evaluation of IELT[11] and confirmed with the questionnaire PEDT[12] (Premature Ejaculation Diagnostic Tool). According with these criteria, IELT <3 min[1] and PEDT score >11[12] identifies patients with APE.

Psychological or relationship problems, erectile dysfunction (evaluated through the administration of International Index of Erectile Function (IIEF-5)[13] and structured interview on erectile dysfunction (SIEDY),[14] hypogonadism, hyperthyroidism. Fifty patients with MAGI without PE (MAGI-PEneg), evaluated in the same period represented the control group.

Statistical analysis

Results are reported as mean ± s.e.m. throughout the study. The data were analyzed by *t*-Student test. Correlation analysis was conducted by Pearson correlation test. The software SPSS 9.0 for Windows was used for statistical evaluation (SPSS Inc., Chicago IL, USA). A statistically significant difference was accepted when the $P < 0.05$.

RESULTS

MAGI-APEpos had a mean age 25.0 ± 8.0 years and a mean duration of APE 18.0 ± 6.0 months. The control group had a similar mean age 24.0 ± 6.0 years. The total number of US criteria suggestive for MAGI was significantly higher in MAGI-APEpos patients compared to MAGI-PEneg (**Table 1**). MAGI-APEpos patients showed a significantly higher frequency of the following US criteria: increase of the APD (anteroposterior diameter) of the seminal vesicles detected BE (before ejaculation), internal polycyclic areas and lower reduction of APD of the seminal vesicles detected after ejaculation. Finally, increase of the APD of the cephalic and/or caudal tract of the epididymis, presence of multiple microcystis in the head and/or tail, and impaired reduction of the APD of the caudal tract of the epididymis detected after ejaculation (**Table 1**).

MAGI-APEpos patients showed a mean value of the APD of the caudal tract of the epididymis detected BE and APD of the seminal vesicles detected BE significantly higher compared to MAGI-PEneg patients (**Figure 1**). In MAGI-APEpos patients, the correlation analysis showed a positive linear relationship between PEDT score and the APD of the caudal tract of the epididymis detected BE (**Figure 2**) and APD of the seminal vesicles detected BE (**Figure 3**). Finally, in MAGI-APEpos patients, the correlation analysis showed a positive linear relationship between the APD of the caudal tract of the epididymis detected BE and the APD of the seminal vesicles detected BE (**Figure 4**).

DISCUSSION

The original aspect of these results is represented by the peculiar US characterization of patients with MAGI and APE associated. In fact, these patients have a significantly higher number of US criteria suggestive for MAGI and in particular, a higher frequency of US findings suggestive for chronic epididymitis and vesiculitis compared to patients with MAGI without PE that represented the control group. Another original aspect is represented by the positive relationship between the APD of the caudal tract of the epididymis and of the seminal vesicles that might suggest a particular US phenotype associated with PE in these patients. We can speculate that these US features may reflect an accelerated ejaculation secondary to increased volume of ejaculate. Therefore, in summary, the importance of the study can be summarized in two points:

1. The importance in the clinical practice of US evaluation for the patients with MAGI and APE associated
2. The possible presence of a peculiar US phenotype associated with the appearance of APE among patients with MAGI.

Usually, in the literature is reported the association between *P* and PE, however, *P* represents only one of the three diagnostic categories of MAGI: P, PV, and PVE. The results of this study suggest the importance of the anatomic extension of the inflammation in the epididymis and seminal vesicles as a possible determinant of APE. We believe that the importance of the results is represented by the inclusion of an additional variable to be evaluated in the clinical management of patients with PE and urogenital tract inflammation in addition to other reported by previous studies in the literature. About this aspect, it seems useful to analyze the main findings regarding the clinical variables to be considered for the patients with *P* and PE associated. The presence of PE was detected in 15% of men that have been evaluated in an Andrology Center for the couple's infertility. The severity of PEDT score was positively associated with the severity of prostatitis symptoms and with semen concentration of interleukin-8.[15] The presence of varicocele correlates with the severity

of the prostatitis symptoms that represents a factor associated with a higher frequency of PE.[16]

Another variable to consider is represented by the different response to antibiotic therapy that usually improves the severity of PE in patients with P, but the improvement is associated with the reduction of prostatitis symptoms.[17] However, it is also important to evaluate the predictive factors of response to therapy, including the number of leukocytes in the prostatic secretion, Zohdy suggests that the presence of 19 or > leukocytes pcm has a diagnostic sensitivity 85.6% and a diagnostic specificity 70.7%.[18] The study of Trinchieri and colleagues showed that the frequency of PE in patients with a leukocytes count between 10–30 (36%) and >30 (32%) is significantly higher than patients with leukocytes count <10 in the urine obtained after prostate massage.[19] The negativity of cultures in treated patients represents a protective factor for recurrence of PE.[20]

The persistence of MAGI in elderly might be associated with the appearance of LUTS that is associated with high prevalence of PE 16%.[21] The increase of the age in patients with LUTS does not represent a protective factor for PE, in fact, another study conducted on 1779 men with a mean age 56 years and a mean IPSS score (International prostate symptoms score) = 7.96 points, showed a prevalence of PE 41%.[22] In young patients with P, the frequency of PE seems to be increasing among the younger patients as demonstrated by the study of Qiu: 42.9%, 37.0%, and 35.7% in the 18–30, 30–40, and 40–57 years age groups, respectively.[23]

Table 1: US features of MAGI-APEpos patients compared to MAGI-PEneg patients

US criteria	*n=50 (%)*	
	MAGI-APEpos	*MAGI-PEneg*
P (prostatitis)		
P 1	25.0 (50)	25.0 (50)
P 2	5.0 (10)*	25.0 (50)
P 3	20.0 (40)	20.0 (40)
P 4	10.0 (20)	20.0 (40)
P 5	5.0 (10)*	15.0 (30)
P 6	5.0 (10)*	15.0 (30)
P 1–6	12.0 (24)*	20.0 (40)
V (vesiculitis)		
V 1	40.0 (80)*	10.0 (20)
V 2	10.0 (20)	2.0 (4)
V 3	5.0 (10)	10.0 (30)
V 4	10.0 (20)	2.0 (4)
V 5	25.0 (50)*	10.0 (20)
V 6	10.0 (20)	10.0 (20)
V 7	10.0 (20)	10.0 (20)
V 8	25.0 (50)*	2.0 (4)
V 1–8	17.0 (34)*	7.0 (14)
E (epididymitis)		
E 1	45.0 (90)*	5.0 (10)
E 2	45.0 (90)*	2.0 (4)
E 3	10.0 (20)	2.0 (4)
E 4	10.0 (20)	10.0 (20)
E 5	5.0 (10)	10.0 (20)
E 6	25.0 (50)*	10.0 (20)
E 1–6	23.0 (46)*	7.0 (14)
All US criteria		
P 1–6+V 1–8+E 1–6	17.0 (34)*	12.0 (22)

*P<0.05 versus MAGI-PEneg. P 1–6; V 1–8; E 1–8: US criteria of MAGI [Box 1]. MAGI-APEpos: male accessory gland infection and premature ejaculation associated; US: ultrasound

There are no data in the literature regarding the US features of the epididymis and seminal vesicles of patients with PE. Only the study of Trinchieri and colleagues reported that the painful ejaculation was associated with enlargement or asymmetry of the seminal vesicles.[19] The severity of PEDT score was positively associated with prostatic

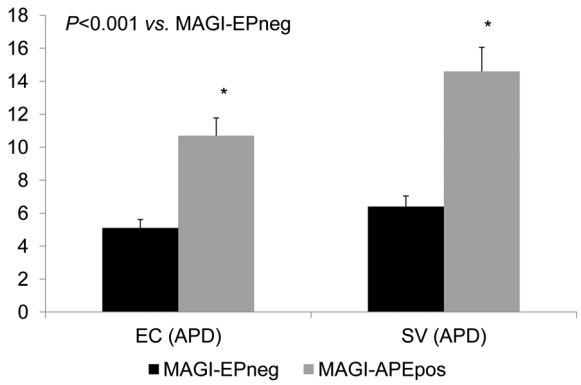

Figure 1: Anteroposterior diameter (APD) of the caudal tract of the epididymis (EC) and seminal vesicles (SV) detected before ejaculation (BE) in MAGI-APEpos patients compared to MAGI-PEneg patients.

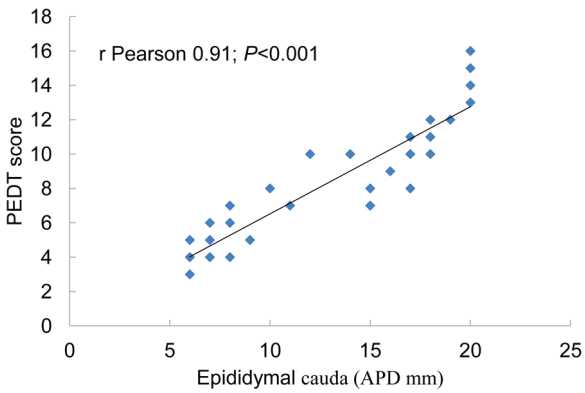

Figure 2: Correlation between anteroposterior diameter (APD) of the caudal tract of the epididymis and PEDT score (Premature Ejaculation Diagnostic Tool) in MAGI-APEpos patients.

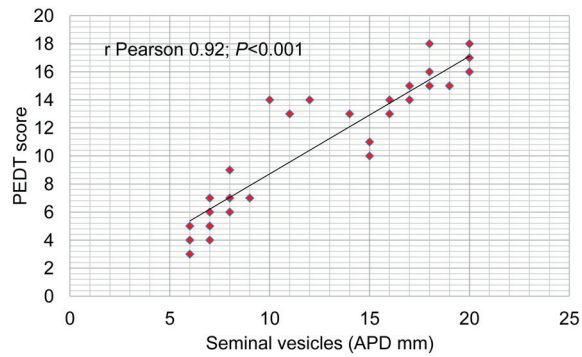

Figure 3: Correlation between anteroposterior diameter (APD) of the seminal vesicles and PEDT score (Premature Ejaculation Diagnostic Tool) in MAGI-APEpos patients.

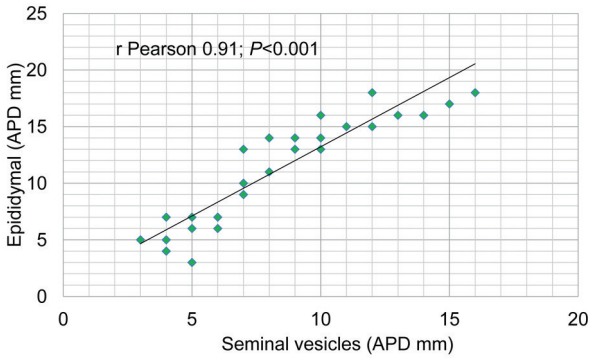

Figure 4: Correlation between anteroposterior diameter (APD) of the caudal tract of the epididymis and APD of the seminal vesicles in MAGI-APEpos patients.

artery peak systolic velocity that represents a US criterion of P.[16] Finally, in a series of 358 men with P, the presence of prostatic calcifications was observed in 49% of patients, but the results of the study showed a significant association of this US finding with erectile dysfunction but not with PE.[24]

In summary, the data of the literature suggest to consider the following possible determinants of PE in patients with P: male infertility, severity of symptoms, seminal concentration of interleukin 8, varicocele, age, and the increase of peak systolic velocity of prostatic artery. The results of this study suggest a peculiar US phenotype in patients with MAGI and APE associated, in particular the relationship between increased APD of the epididymis and seminal vesicles with the PEDT score deserves further evaluation to understand the possible mechanisms of this relationship. In particular, the US evaluation of patients with MAGI and associated PE could be a support in the clinical practice for a possible pathophysiological interpretation of this problem in these patients or suitable for idiopathic cases of PE.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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