Gonad evaluation in male dermatomyositis. A pilot study

Sirs,

Gonad evaluation was studied in 10 post-pubertal male dermatomyositis (DM) patients (Bohan and Peter criteria) (1) and 10 age-matched healthy controls. None of them had history of testicular abnormalities. Disease activity and damage scores were assessed concomitantly to gonadal evaluation (same day) using various tools (2-4). Clinical examination of the genitalia (including penis length/circumference and testicular volumes) and ultrasound (including *plexus pampiniformis* or spermatic plexus) were performed. Sperm analysis was carried out according to World Health Organisation (WHO) guidelines (5) and Kruger criteria (6), and the presence of antisperm antibodies by direct Immunobead test® (Irvine Scientific). Luteinizing hormone (LH), FSH, prolactin and total testosterone were determined by DELFIA time-resolved fluoroimmunoassay kits (Wallac). Data were compared by *t*-test, Mann-Whitney U-test, Pearson's chi-square test or Fisher's exact test.

The median of current age and age at spermarche were similar in DM patients and controls [42.5 *vs*. 42.5 years, p=0.909; 13 *vs*. 12.5 years, p=0.477]. Sperm abnormalities according to WHO or Kruger criteria occurred in 100% DM patients compared to 30% in controls (p=0.0031). DM patients had a lower median sperm concentration (42.5 *vs*. 120.05 x 10^6/ml, p=0.016), total sperm count (48.45 *vs*. 242.5 x 10^6, p=0.008), total motile sperm count (30.25 *vs*. 160.95 x 10^6, p=0.008), normal sperm morphology by WHO criteria (8.5% *vs*. 26%, p=0.005) and by Kruger (1.5% *vs*. 7.25%, p=0.004) compared to controls. Likewise, the median testicular volumes by Prader orchidometer were lower in DM versus controls (right p=0.033 and left p=0.017). The median of *plexus papiniformis* in left testicle by ultrasound was higher in DM patients compared to controls [0.2 (0.2–0.25) *vs*. 0.2 cm, p=0.03]. No differences were observed in the frequency of antisperm antibodies and median of penis length and circumference. A trend of a high median elevated FSH and LH levels and a low median total testosterone was evidenced in DM patients *versus* controls (5.35 *vs*. 3.65 IU/litre, p=0.055; 6.15 *vs*. 3.6 IU/litre, p=0.075; 310 *vs*. 442 ng/dl, p=0.049; respectively). Primary hypogonadism (low FSH and LH with elevated total testosterone) was observed in only one DM patient that presented azoospermia and in none of the controls (10% *vs*. 0%, p=1.0). Sperm abnormalities occurred in all 10 DM patients (Table I).

To our knowledge, this is the first systematic evaluation focused on testicular dysfunction in DM patients and revealed that gonad function is severely affected with universal sperm abnormalities probably associated with disease activity and/or immunosuppressive treatment. Reinforcing the possible role of inflammation, we have previously described one case of subclinical orchitis in active JDM (7). Furthermore, increased *plexus pampiniformis,* observed in 3 of our DM patients, may be a consequence of an underlying inflammation in spermatic veins. On the other hand, the testis is also highly susceptible to the toxic effects of chemotherapy (8, 9). In fact patients who had decreased testicular volumes and elevated FSH and LH levels were those who received immunosuppressive medication, particularly those more frequently used in

Table I. Demographic data, clinical features, muscle enzymes levels, scores, treatment and gonadal function parameters of 10 DM patients.

Patients	1	2	3	4	5	6	7	8	9	10
Demographic data, yrs										
Disease onset	42	41	43	41	23	38	20	32	37	31
Disease duration	6	1	3	13	1	7	9	11	1	4
Current age	48	42	46	54	24	45	29	43	38	35
Clinical features										
Cutaneous	+	+	+	+	+	+	+	+	+	+
Muscular	+	+	+	+	+	+	+	+	+	+
Articular	+	+	+	–	+	–	+	+	–	+
Cardiopulmonary	–	–	+	+	–	+	–	+	+	–
Gastrointestinal	–	–	–	–	–	–	–	–	–	+
Muscle enzymes										
CK IU/liter	45	540	420	550	80	55	390	200	68	450
AST IU/liter	23	61	28	21	29	25	28	27	19	44
ALT IU/liter	23	100	14	13	57	23	13	18	24	69
Aldolase IU/liter	7	8.2	5	7.7	10.5	5	4	5	4	7
LDH IU/liter	456	675	485	314	342	280	317	431	454	384
Scores										
DAS (0-20)	0	13	9	0	15	0	10	0	8	19
VASP (0-10)	3	4	4	1	2	0	4	2	3	5
VASPH (0-10)	1	5	5	1	4	0	5	2	4	5
Global MITAX (0-1)	0.4	0.7	0.7	0.4	0.7	0.3	0.5	0.4	0.5	0.7
MYOACT-A (0-10)	3	3	2	1	0	0	2	0	0	2
MYOACT-M (0-10)	1	4	1	0	0	0	3	0	0	6
MYOACT-C (0-10)	2	6	4	2	7	1	4	2	3	9
MMT (0-80)	79	62	78	80	80	80	72	80	80	47
MDI (0-1)	0.05	0.13	0.1	0.02	0.13	0.05	0.15	0.1	0.05	0.1
Treatment (use/current dose, mg/cumulative dose, g)										
Prednisone	+/10/45	+/50/10	+/15/5	+/-/81	+/50/37.2	+/-/30	+/50/12.6	+/-/55.8	+/15/4.5	+/10/39.3
Methotrexate	+/10/3	+/15/0.6	-/-/-	+/25/1.8	+/-/0.2	-/-/-	-/-/-	+/-/4.8	-/-/-	+/-/2.9
Azathioprine	-/-/-	+/-/18	+/150/17	+/-/1.26	+/100/24	-/-/-	-/-/-	+/150/32.4	+/-/15	+/150/40.5
IVCYC	-/-/-	-/-/-	-/-/-	+/-/12	-/-/-	-/-/-	-/-/-	+/-/12	-/-/-	-/-/-
Gonadal function										
Sperm abnormalities	Terato	Azo	Oligo, Terato	Azo	Terato	Terato	Oligo, Terato	Terato	Terato	Astheno Terato
Decreased TV	–	+	+	+	–	–	–	+	–	–
Elevated FSH-LH	–	+	+	+	–	–	–	–	–	–
PH	–	+	–	–	–	–	–	–	–	–

DM: dermatomyositis; + positive; – negative; CK: creatine kinase (39-308 IU/L); ALT: alanine aminotransferase (24–49 IU/L); AST: aspartate aminotransferase (10–36 IU/L); LDH: lactate dehydrogenase (240 – 480 IU/L); aldolase (<7.6 IU/L); DAS: Disease Activity Score; VASP: visual analogue scale of patient; VASPH: visual analogue scale of physician; MITAX: myositis intention to treat activity index; MYOACT: myositis disease activity assessment visual analogue scales; A: arthritis; M: myositis; C: cutaneous; MMT: manual muscle testing; MDI: muscle damage index (5); IVCYC: intravenous cyclophosphamide; mg: milligram; g: gram; TV: testicular volume by Prader; FSH: follicle-stimulating hormone; LH: luteinizing hormone; PH: primary hypogonadism; yrs: years; azo: azospermia (no spermatozoa); terato: teratozoospermia (abnormal sperm morphology); oligo: oligozoospermia (low sperm concentration); astheno: asthenozoospermia (low sperm motility).

this disease, such as azathioprine or methotrexate. Moreover, cyclophosphamide was rarely associated with sperm abnormalities probably due to the small DM patients in the present study. In contrast, an evident association of semen alterations and this immunosuppressive drug was reported by us in systemic lupus erythematosus patients (9) and in one case of juvenile DM (10).

In spite of the limitations of this pilot study (small number of patients, the heterogeneous disease activity and range of years of patients), we have identified severe sperm abnormalities in DM patients, supporting the notion that testicle may be a potential target organ by disease activity and immunosuppressive drugs. Serial semen analyses are necessary to determine the reversibility of these abnormalities.

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