Case studies in physiology: Training adaptation in an elite athlete after breast cancer diagnosis

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Running head: Athlete's running performance during breast cancer treatment.

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ABSTRACT

The aim of this study was to evaluate the capacity to return to competition of a 28-year-old female 400m hurdle elite athlete after a diagnosis of breast cancer. The study lasted 14 months after diagnosis. She was tested four times (T1–T4) to measure body mass (BM), body mass index (BMI), percentage of total fat mass (TFM%), total fat-free mass (TFFM%), bone mineral density (BMD), one-repetition maximum (1RM) and maximal power (MP) in bench-press and half-squat, maximum oxygen uptake, 400m dash and hurdles. T0 (baseline time) was established with values prior to diagnosis. BM and BMI increased from T0 to T1 (5.3% and 5.2%) and remained stable. BMD experienced no change. TFM% values decreased from T1 to T4 (3.5%). TFFM% values increased from T1 to T3 (0.9%). During T1–T2, the athlete presented a global decline from T0 in $1RM_{Squat}$, $1RM_{Bench}$, MP_{Squat} and MP_{Bench} (32.6%, 27.2%, 37.5%, 27.6%, respectively). Results during T3–T4 were also lower for these parameters from T0 (23.3%, 20.6%, 23.4%, 11%). During T1–T2, the VO_{2max} declined, compared to T0 (1.8% and 6.4%), showing a small increase at T3 (+1%) and reaching the lowest level at T4 (9%). During T1–T2, the time record of 400 m dash (8.3%) and hurdles (7.4%) increased. However, a slight improvement was found at T3 (1.3% and 0.6%, respectively). The results of this case study reflect that exercise training improved body composition, maintained BMD and TFFM, but could not completely reverse the worsening of the cardiorespiratory, muscle strength and power, and running performance levels.

Keywords: breast cancer; athlete; sport; exercise; body composition

NEW AND NOTEWORTHY

This case study follows an elite athlete and measures her performance during cancer treatment. It improves the knowledge on applied physiology showing the details of her training program and demonstrating the strong ability of the athlete to continue training and competing at a high level during antineoplastic treatment. Exercise training improved body composition, but failed to restore previous cardiorespiratory, muscle strength and power, and running performance levels.

INTRODUCTION

Breast cancer (BC) is the most common cancer in women worldwide, with an incidence rate in 2020 of 24.5% (1). In 2020, the five-year prevalence of BC in Spain was over 144,233 cases (2). Some side effects can be expected in patients with BC, including reduction of fitness capacity, lymphedema, cardiotoxicity, fatigue, bone loss, sarcopenia, dynapenia, body image concerns and mental health issues, among others (3, 4). Exercise has shown to be an effective tool to reduce these treatment-related side effects (5–8), improve health, quality of life and reduce risk of recurrence (9). In addition, it has been observed that patients with BC who remain active have better survival rates compared to those with sedentary lifestyles (9).

Research on the incidence of cancer in elite athletes is limited. In a meta-analysis conducted by Garatachea et al. (10), elite athletes, mostly men, had a lower risk of cancer (five studies provided cancer information for 12,119 athletes). Furthermore, available data have suggested that former female athletes would be protected from suffering from BC. Wyshak and Frisch (11) found that the odds ratio (OR) for the 15-year BC incidence was 0.605 (95% confidence

interval [CI] = 0.438–0.835) in these women. Due to the lack of information, it was of interest to follow a female elite athlete with a diagnosis of BC, who, after 14 months of follow-up, returned to compete at a high level after completing part of the adjuvant treatments. The purpose of this study was to evaluate the physical condition and capacity to return to competition of a 28-year-old female 400 m hurdle elite athlete, during adjuvant chemotherapy and radiotherapy, and while on endocrine therapy (ET), after the diagnosis of a hormone receptor (HR)-positive/human epidermal growth factor receptor 2 (HER2)-negative BC.

MATERIALS AND METHODS

Patient

A 28-year-old elite athlete participated in this study. Two years prior to diagnosis with BC, she competed in 400 m hurdle national championships, obtaining the second position with a final time of 60.45 s. In April 2015, without a previous family history of BC, this athlete was diagnosed with ductal carcinoma of the left breast (stage IA, according to the seventh edition of the American Joint Committee on Cancer [AJCC] TNM classification). The size of the mass was 19 mm x 15 mm; HR+, HER2-, 30% proliferation index Ki67 with non-affected axillary lymph nodes.

Design

This was an observational, prospective study of a case of an elite athlete diagnosed with HR-positive/HER2-negative BC. She was free of known cardiovascular, respiratory, and circulatory dysfunction. Data were obtained from the tests performed at the laboratory of

exercise physiology as her usual practice as an elite athlete. Before participation, she was informed of the risks and stresses associated with the protocol, and she gave her written voluntary informed consent for the tests and public reporting of her results. The present study was performed in agreement with the standards set by the Declaration of Helsinki and was approved by the Ethics Committee of the Universidad Politécnica of Madrid.

Therapy and treatments

The patient underwent a quadrantectomy and axillary lymph node dissection. After surgery, she received eight weekly cycles of paclitaxel and four three-week cycles of cyclophosphamide, epirubicin and fluorouracil. After chemotherapy, she was treated with 20 radiotherapy sessions. During these treatments, she remained active, training five days per week, adapting the intensity to her health status, and resting in weak moments due to the treatment side effects.

After completing the chemotherapy and radiotherapy treatments, the patient started ET (tamoxifen), which is associated with changes in body composition, lower caloric expenditure, osteopenia/osteoporosis, cardiovascular events, headaches, and menopausal symptoms (12, 13).

Training intervention

The main components of the training regimen focused on the competition in 400 m flat and hurdles are technique, resistance training, plyometrics, sprint training, anaerobic training, and aerobic power.

Within each performance quality, different types of training were alternated according to the different season periods. Also, different loads were employed at each period to ensure the correct adaptations and improve performance in the official events and training test. During the week, the different components were worked on in two types of sessions: type A, which consisted of warm-up, technique, plyometrics, sprint training and anaerobic training; and type B, which comprised warm-up, resistance training and aerobic power. In the season before starting the treatment (Sep 2014–May 2015), two type A and B sessions were each carried out weekly. (A more detailed description of the training program is available in the supplementary file).

From the beginning of the BC treatment (June 2015) to June 2017, one weekly session was reduced due to work incompatibility (i.e., athletic children trainer in attendance); then one week was alternated with one B and two A sessions, and the next week with one A and two B sessions. This training schedule permitted better recovery between high intensity sessions. In addition, during this treatment period, the following adaptations were made: 10% intensity reduction in aerobic power to maintain work volume, 10–20% volume reduction in anaerobic training to maintain work intensity and change of some upper body strength exercises due to discomfort around the surgical area. The remaining components were not modified, permitting the patient to follow a plan quite similar to the one developed previously to the BC diagnosis.

Daily adjustments in the training load were made to avoid physical and mental stagnation. Thus, in each training session, a limit of 10% loss in performance (i.e., speed, power, time), or the loss of execution technique, they were established in order to control and modify the training load.

Timeline

The present follow-up study started one year after BC diagnosis, when the patient had been on ET for six months (since May 2016), and it coincided with the seasonal performance peak. The study lasted 14 months and was completed in July 2017. During this time, the elite athlete was measured four times, correlating with the most important moments of the season: T1: May 2016, seasonal performance peak; T2: September 2016, after seasonal break; T3: April 2017, seasonal performance peak; and T4: July 2017, at the end of the season. A time T0 was established, based on the athlete´s values prior to diagnosis, to serve as baseline reference for comparison with the other four measurements.

MEASUREMENTS AND ASSESSMENTS

The patient visited the laboratory on five separate occasions to carry out the following tests:

Body composition

Dual energy X-ray absorptiometry (DXA) was used to measure body mass, percentage of total fat mass (TFM%), total fat mass (FM), total fat-free mass (TFFM) and bone mineral density (BMD). The tests were carried out using the GE Lunar Prodigy DXA system (GE Healthcare, Madison, Wisconsin, USA), and scan analyses were performed using the GE Encore 2002 software v 6.10.029.

Muscle Strength and Power

A progressive loading test was employed in the half squat and bench press exercises using a linear position transducer (Chronojump, Barcelona, Spain) to obtain the theorical maximal power (MP_{Bench} and MP_{Squat}) and one-repetition maximum load ($1RM_{Bench}$ and $1RM_{Squat}$) based on the load-velocity relationship (14).

The best of three attempts of 10 horizontal jumps (10HJ test), with previous 5 m flying start running, were employed to assess the plyometric performance, measuring the distance from the starting line to the subject's closest heel (15).

Maximal oxygen uptake test

Maximum oxygen uptake (VO_{2max}) was measured with an incremental running exercise test until exhaustion on a computerized treadmill (H/P/COSMOS 3PW 4.0, H/P/Cosmos Sports & Medical, Nussdorf-Traunstein, Germany). Expired gases were measured breath-by-breath with a gas analyzer (Jaeger Oxycon Pro, Erich Jaeger, Viasys Healthcare, Hoechberg, Germany). Heart response was continuously monitored with a 12-lead Jaeger® electrocardiogram (Erich Jaeger, Hoechberg, Germany).

Hematological tests

Erythrocytes, hemoglobin, and platelets were recorded during each testing session.

Running Tests

The best training times were recorded for the distances of 500 m and 200 m in an official track and field stadium. In both cases, manual times were recorded by an experienced coach with the same stopwatch to the nearest 0.1 s. The times of the 400 m flat and hurdles in each period are included in Table 1.

RESULTS

The anatomical, physiological, hematological and performance variables across pre-diagnosis (T0) and the subsequent four testing sessions (T1–T4) are presented in Tables 1 and 2, and Figures 1 and 2.

BM and BMI increased from T0 values to T1 and stayed stable during the remaining testing sessions. During ET, BMD experienced little or no change. TFM and TFM% values decreased slightly from T1 to T4. On the other hand, TFFM and TFFM% values increased from T1 to T3.

Table 1. Anatomical and hematological variables across the five testing sessions

	T0	T1	T2	T3	T4
Body mass (kg)	60.2	63.4	63.2	64.4	64.0
% Change from T0		+5.3	+5.0	+7.0	+6.3
BMI (kg/m^2)	20.61	21.68	21.61	22.02	21.89
% Change from T0		+5.2	+4.9	+6.9	+6.2
BMD (g/cm^2)	N/A	1.283	1.281	1.275	1.286
TFM (kg)	N/A	13.66	13.52	13.40	13.31
TFFM (kg)	N/A	46.90	46.91	48.08	47.78
TFM%	N/A	21.55	21.39	20.81	20.79
TFFM%	N/A	73.97	74.22	74.66	74.65
Erythrocytes (x10e^{6}·µL^{-1})	4.70	4.43	4.42	4.57	4.46
% Change from T0		-5.7	-6.0	-2.8	-5.1
Hemoglobin (g·dL^{-1})	14.40	13.40	13.30	13.60	13.50
% Change from T0		-6.9	-7.6	-5.6	-6.3

Platelets (x10e^{3}·µL^{-1})	223.00	203.00	204.00	219.00	211.00
% Change from T0		-9.0	-8.5	-1.8	-5.4

T0: pre-diagnosis; T1: May 2016; T2: September 2016; T3: April 2017; T4: July 2017; N/A: not available. Abbreviations: BMI, body mass index; TFM, total fat mass; TFFM, total fat-free mass; BMD, bone mineral density.

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Table 2. Muscle strength and power, and performance variables across the five testing sessions.

	T0	T1	T2	T3	T4
$1RM_{Squat}$ (kg)	123.0	111.0	82.9	94.4	93.6
% Change from T0		-9.8	-32.6	-23.3	-23.9
$1RM_{Bench}$ (kg)	53.0	43.5	38.6	42.1	42.5
% Change from T0		-17.9	-27.2	-20.6	-19.8
MP_{Squat} (W)	1443.0	1097.0	902.0	1106.0	1163.0
% Change from T0		-24.0	-37.5	-23.4	-19.4
MP_{Bench} (W)	254.0	222.0	184.0	226.0	230.0
% Change from T0		-12.6	-27.6	-11.0	-9.4
10HJ (m)	25.1	24.10	23.50	24.10	24.30
% Change from T0		-4.0	-6.4	-4.0	-3.2
200 m flat (s)	25.61*	27.4	29.9	28.2	27.6
% Change from T0		+7.0	+16.8	+10.2	+7.8
500 m flat (s)	78.0	91.2	85.8	84.0	82.2
% Change from T0		+16.9	+10.0	+7.7	+5.4
400 m hurdles (s)	60.71*	66.04	65.2	64.84	65.15
% Change from T0		+8.8	+7.4	+6.8	+7.3
400 m flat (s)	56.15*	61.04	60.8	60.0	61.34
% Change from T0		+8.7	+8.3	+6.9	+9.2

T0: pre-diagnosis; T1: May 2016; T2: September 2016; T3: April 2017; T4: July 2017; N/A: not available. *Official competition time. Abbreviations: 1RM, one-repetition maximum; MP, maximal power; 10HJ, 10 horizontal jumps.

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189 During T1, the athlete presented a global decline from T0 values of $1RM_{Squat}$, $1RM_{Bench}$,
190 MP_{Squat}, MP_{Bench} and 10HJ test. The test results continued to worsen from pre-diagnosis values
191 during T2. The results at T3 and T4 were also lower from T0 values, but globally better than T1
192 and T2.

193 During T1 and T2, the VO_{2max} declined compared to T0 values, showing a small increase
194 on T3, and decreased again in T4. The percentage of VO_{2max} in VT_1 behaved similarly to VO_{2max},

195 decreasing in T1 and T2, reaching values close to T0 in T3 and decreasing again in T4. The
196 percentage of VO_{2max} in VT_2 decreased slightly at T2 and T4, while at T1 and T3, it showed higher
197 values than those reached at T0. On the other hand, the velocities reached in VT_1 and VT_2 showed
198 a different behavior. The velocity reached in VT_1 decreased at T1, T2 and T3 and recovered
199 minimally at T4. In the case of VT_2, velocity decreased slightly at T1, was maintained at T2 and
200 T3, and decreased again at T4. At no time were the T0 values recovered.
201 Erythrocyte, hemoglobin, and platelet levels decreased during the four evaluation
202 sessions, representing a minimal diminution during the intervention, but in a normal range.
203 At T1, the times of all the events increased from T0 values. During T2, worsening in the
204 times of all the events continued. Results showed a slight improvement at T3. Unfortunately, the
205 baseline values were not reached. Nevertheless, it should be noted that there is a similar
206 difference between 400 m hurdles and 400 m flat across T1-T4 sessions (~4 s).
207

208 **DISCUSSION**

209 The purpose of this study was to evaluate the changes in different variables (e.g., VO_{2max},
210 strength, hematological and performance variables) assessed in an elite athlete who continued
211 training during the recovery phase of BC.
212 Body weight and BMI increased from T0 values during the four testing sessions. Despite
213 this situation, TFM decreased from T1 to T4 and TFFM increased from T1 to T3 and was
214 maintained in T4. In the study conducted by Freedman et al. (16), patients with BC showed no
215 significant changes in body weight; however, fat mass increased while fat-free mass decreased.
216 These results show that the increase in body weight and BMI can be explained, at least in part,

by an increase in fat-free mass. On the other hand, BMD hardly underwent any changes and even increased slightly. According to Kim et al. (17), women diagnosed with BC can lose up to 6.9% of BMD. In addition, ET is associated with a loss of BMD in pre-menopausal women (18). Our athlete, however, was able to maintain her BMD, TFFM and TFM, probably in part due to strength training, which has shown to have a protective effect on bone and muscular mass in patients (19).

In the study by Courneya et al. (20), patients with BC who followed a resistance training protocol improved muscular strength by 25–35%. In our case, test results worsened until T2, during which the lowest values were reached. Subsequently, an improvement in the values was reflected, although the T0 values were not reached. It has been previously shown that anticancer treatment induces loss of muscle mass and muscle strength (21). In the present clinical case we were not aware of the TFFM values prior to diagnosis, but there may have been a loss of muscle mass that was not fully recovered during treatment. During hormone treatment, %TFFM values remained almost unchanged, with a range between 73.97% and 74.65%. This data could indicate that there had not been a higher loss of muscle mass. Nevertheless, muscle strength and power levels did not recover to baseline levels. Another possible explanation beyond the loss of muscle mass, could be the cancer treatment itself. In this sense, taxane use has been associated with the accumulation of intramuscular adipose tissue (IMAT)(22), and with peripheral motor neuropathy (23), which could impair both the muscle quality and lead to muscle dysfunction (22). Moreover, doxorubicin intake could decrease muscle strength levels due to altered calcium metabolism (24). In addition, our athlete had not completed the ET and during this period, training volume was reduced by 10–20% which could represent an insufficient stimulus for the athlete. All these factors could have impeded the recovery of muscle strength and power levels.

Comentado [ASJ1]: REVIEWER 2: "For example, it is clear that your athlete lost some muscle mass from T0 but what is puzzling is the relationship between total fat free mass and squat and bench. Fat free mass is less at time point T1, however both squat bench and are higher at T3 and T4. Why? There is little attempt to explain these findings into an integrated whole, which is a pity. This is but one example, and there are many more in the manuscript"

Comentado [ASJ2R1]: Thank you very much for your comment. We have tried to look for possible explanations to the process you have pointed out.

VO_{2max} decreased in all measurements, compared to T0 values, with T4 being the lowest value. Although the drop in VO_{2max} between T1 and T2 (1.0%) could be explained by the variability of the analyzer itself (<2.0%), the gain between T2 and T3 (3.5%) and the loss between T3 and T4 (3.4%) could not. The moment of the training season in which it was done the test might be another explanation of some of the observed data. In this sense, the gain between T2 and T3 (September 2016 to April 2017), could be produced by the training planification, with the objective of the highest performance at the end of the competitive season (i.e., June), Further, the loss between T3 and T4 might be explained by the late measurement made in T4 (July 2017), after all the summer competitions (June and early July 2017), and with a decline of the performance. These results disagree with those found by other investigations. In a case study of a female athlete with BC, VO_{2max} decreased at the beginning of treatment and returned to baseline levels at the end of treatment (25). In this case, the athlete had lower pre-diagnosis VO_{2max} values to our athlete (50.1 $ml \cdot kg^{-1} \cdot min^{-1}$ and 55.0 $ml \cdot kg^{-1} \cdot min^{-1}$, respectively), and 11 months after diagnosis had a 9.9% reduction in VO_{2max}, whereas our athlete, after 12 months, had a decrease of 11.8%. The fact that our athlete had not yet completed her treatment, while the athlete in the study by Savage, Dittus and Lakoski (25) had completed it, may be one of the reasons that could explain why our athlete did not recover to baseline VO_{2max} values. Moreover, our athlete had a 10% reduction in intensity of aerobic power training, and, due to her high pre-diagnostic values, this reduction in intensity could be an insufficient stimulus to recover her VO_{2max} levels (Figure 1). The velocities associated with VT_1 and VT_2 showed a decrease with respect to pre-diagnostic values, although the decrease in velocity in VT_2 was less than half that experienced in VT_1. Regarding the % VO_{2max} in VT_1 and VT_2, the behavior is very similar to that of

Comentado [TPB3]: REVIEWER 2: "Some consideration should be given to the amount of measurement variability inherent in some of these measures. For example, while the difference between T0 and the remainder of the time points for VO2 max is probably real, the difference between the remaining timepoints is within the limits of day-to-day measurement variability even for the very best labs."

Comentado [TPB4R3]: Your comment is greatly appreciated. We have added a sentence about the measurement variability of our gas analyzer.

Comentado [ASJ5]: REVIEWER 2: "Some of these data would be better presented as figures rather than in table form.".

Comentado [ASJ6R5]: Thank you very much for your suggestion, we have added two figures in relation to cardiorespiratory variables (lines 264-266):
- Figure 1 with the VO_{2max} values and the percentage of change between tests.
- Figure 2 with the percentage of VO_{2max} at VT_1 and VT_2, and the velocities reached at VT_1 and VT_2.

the velocities, in VT_1 the decrease is much greater than in VT_2 (Figure 2). Unfortunately, we have not found other studies showing these parameters to compare them with ours. Further, echocardiographic data (e.g., ejection fraction, myocardial strain) were not available, and this limitation could have helped us to better understand this issue.

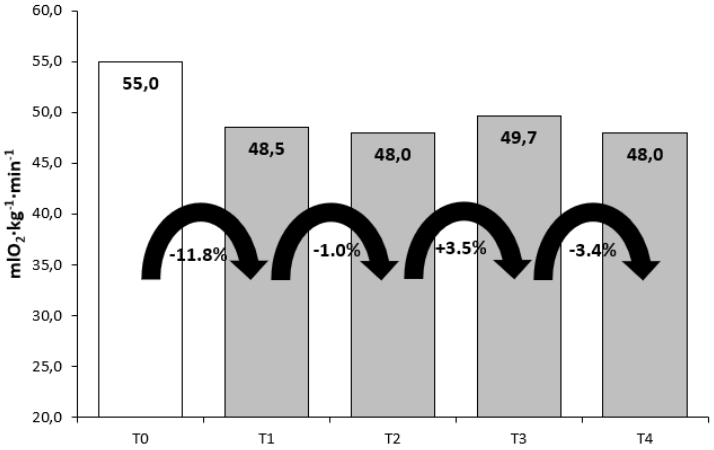

Fig 1. Maximal oxygen uptake (VO_{2max}) across the five testing sessions. T0: pre-diagnosis; T1: May 2016; T2: September 2016; T3: April 2017; T4: July 2017.

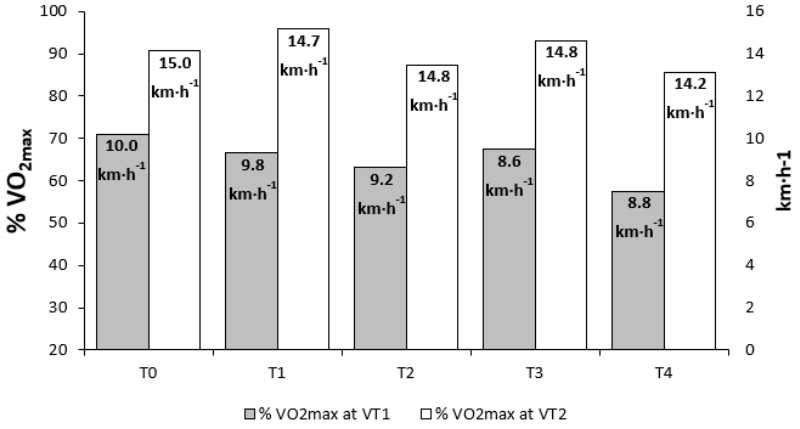

Fig 2. Percentage of VO_{2max} and velocities associated to VT_1 and VT_2 across the five testing sessions. T0: pre-diagnosis; T1: May 2016; T2: September 2016; T3: April 2017; T4: July 2017.

During T3, the results for erythrocytes, hemoglobin, and platelets improved and were maintained in the final measurement. Despite this improvement, T0 values were not reached, contrary to what occurred in the case study of Savage, Dittus and Lakoski (25), in which the athlete recovered her initial hemoglobin levels after the end of treatment. Our results agree with those reported by Grey et al. (26), who showed in their research that women with BC treated with ET suffered hemodilution, presenting significantly lower erythrocyte and hemoglobin values than the control group. The fact that our athlete was still in treatment with ET could explain the results at a hematological level. It should be noted that the athlete in the study by Savage, Dittus and Lakoski (25) did not receive ET, so the impact on hematological variables could have been lower.

In relation with the running performance, we did not find other study analyzing the effects of cancer treatment to compare with. As mentioned above, there is a difference of ~4 s between

400 m hurdles and 400 m flat over the four measurements. Based on these results, the decreased performance on 400 m hurdles may be caused by a lower physical performance with a maintenance of the technique. Our results could be explained by the decrease in muscle strength and power levels, VO_{2max} and hematological values due to anticancer treatment.

From diagnosis to the end of the follow-up period, we observed that the athlete was able to develop a similar training program, with minor adaptations. However, she presented lower results in the follow-up compared to T0 levels in muscle strength and power, VO_{2max}, and running performance. These differences could be explained by several factors: a) the athlete was coping against the deleterious late effects of chemotherapy and radiotherapy treatments; b) she was still under ET with its catabolic late effects; and c) d the training adaptations in volume (-10% to -20%) and intensity (-10%).

In conclusion, the data from this case study describe the effects of BC treatment on different anatomical, physiological, hematological and performance variables in an elite female athlete. In this case, exercise training improved body composition and maintained BMD and TFFM, but could not completely reverse the worsening cardiorespiratory, muscle strength and power, hematological. and running performance levels.

AUTHOR CONTRIBUTIONS:

A.B.P. and S.C. conceived and designed the experiments; M.A., S.B., M.P., and A.B.P. applied for ethics committee approval; P.G.F., A.B.P., and S.C. recruited the subject and realized the informative session before the starting of the study; L.G., P.G.F., A.B.P., and S.C. performed the experiment; T.P.B., A.F.S.J., L.G., P.G.F., A.B.P., and S.C. extracted the data; T.P.B., M.A., A.F.S.J., S.B., M.P., P.G.F., A.B.P., and S.C. analyzed the data; T.P.B., A.F.S.J., and A.B.P. elaborated tables;

T.P.B., M.A., A.F.S.J., S.B., and A.B.P. wrote the original draft of the manuscript; T.P.B., M.A., A.F.S.J., S.B., M.P., P.G.F., A.B.P., and S.C. revised the manuscripts; T.P.B., M.A., A.F.S.J., S.B., L.G., M.P., P.G.F., A.B.P., and S.C. approved the final version of the manuscript.

AKNOWLEDGEMENTS

We thank the athlete, C.S.A, and our colleagues physicians A.A., L.C., and M.A.S.P., for their contribution and commitment to this case study. We also thank our colleagues M.A.J.L. and M.C.C.M. for their support on all documents required for the start-up process and regulatory approval.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

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