

CASE REPORT

EFFECTS OF AEROBIC AND FLEXIBILITY TRAINING ON PHYSIOLOGICAL AND PSYCHOSOCIAL FUNCTION IN A PATIENT WITH ANAPLASTIC OLIGODENDROGLIOMA: A CASE REPORT

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Objective: Diagnoses of anaplastic oligodendrogliomas are rare. For cancer rehabilitation practitioners, anaplastic oligodendroglioma may impact on the development and maintenance of prescriptive exercise. Exercise interventions for healthy individuals and cancer patients have been shown to increase functional capacity, psychosocial functioning, and aspects of cognitive function. However, there is a lack of research into exercise interventions among patients with anaplastic oligodendroglioma. This case report of a patient with anaplastic oligodendroglioma, measures the effects of aerobic and flexibility training on physiological, psychosocial, and cognitive functioning.

Patient: A 44-year old woman diagnosed with class III anaplastic oligodendroglioma with 1p19q genetic co-deletion underwent left-frontal craniotomy, chemotherapy, and radiation treatment. Comprehensive physical, psychosocial, and cognitive assessments were completed before and after a 36-session exercise intervention.

Results: Following the intervention improvements were observed in 9 of the 14 physiological measures. Fatigue decreased by 20% and quality of life increased by almost 70%. Improvements were also observed in 6 of the 12 cognitive assessment variables.

Conclusion: The 36 sessions of aerobic and flexibility training were well-tolerated by the subject. The results demonstrate the feasibility and importance of aerobic and flexibility training for the attenuation of cancer-related decrements in phy-

LAY ABSTRACT

Patients with brain cancer represent a very small number of the overall yearly cancer diagnoses in the United States, with those diagnosed with anaplastic oligodendroglioma, accounting for nearly 30% of those diagnoses. Practitioners providing cancer rehabilitation for patients with anaplastic oligodendroglioma may find that it impacts on the implementation of exercise programming. Research has long supported the implementation of exercise for health improvements in patients with cancer. However, very little information is available regarding exercise interventions in patients with anaplastic oligodendroglioma. We report here a case of a woman with anaplastic oligodendroglioma in whom aerobic and flexibility training resulted in improvements in fatigue, depression, quality of life, aerobic fitness, and cognitive function. Aerobic and flexibility training was shown to be a feasible and tolerable intervention method in this patient with anaplastic oligodendroglioma.

biological and psychosocial variables in patients with anaplastic oligodendroglioma. The effects on cognitive function were uncertain.

Key words: rehabilitation; exercise; cancer-related cognitive impairment; brain cancer.

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Among rare brain cancers (oligodendrogliomas), Anaplastic oligodendrogliomas (AO) comprise a low percentage of this class of brain-based infiltrative neoplasm (70% oligodendrogliomas vs 30% AO, respectively). In addition, AO reportedly receive higher (III) World Health Organization (WHO) grading (I–IV), and are more prevalent in men than in women (1). Thus, practitioners providing cancer rehabilitation for patients diagnosed with AO may experience unique challenges that may affect the development and maintenance of prescriptive exercise. This case study reports significant benefits of a 36-session aerobic and flexibility intervention completed by a patient with advanced AO. More importantly, after completing the study, the current patient successfully transitioned to a standardized exercise-based cancer rehabilitation programme.

Combined surgery, chemotherapy, and radiation interventions have been shown to result in somewhat favourable prognoses and survival rates in patients diagnosed with AO (2). However, there has been limited research into the effects of exercise and the efficacy of rehabilitation in this population. In addition, there is little research detailing the common symptoms related to AO. In the current case report there were some factors that impacted on the intervention. In cancer rehabilitation, patients often present during and after treatment with a diverse array of side-effects, which must be identified and addressed when developing prescriptive exercise interventions. Our laboratory and others have demonstrated the positive impact of various forms of exercise on physiological and psychosocial variables in cancer survivors (3, 4). Specifically, Brown et al. (3) demonstrated the effectiveness of standardized, phase-based exercise on improving cardiovascular function, muscular strength, and fatigue in cancer survivors both during and after treatment.

One particular side-effect that has been recognized in the literature over the past few decades is chemotherapy- or cancer-related cognitive impairment (CRCI), which may manifest as decrements in concentration, attention, executive functioning, language, quality of life, and activities of daily living (5). While there appears to be a movement toward a more solidified consensus regarding the aetiology and presentation of CRCI in patients with cancer, the task of developing individualized and specific treatment to target CRCI remains challenging. To our knowledge, there are no published case reports regarding the effect of aerobic exercise on physiological, psychosocial, and cognitive function in a patient with AO.

CASE REPORT

The patient was a 44-year-old woman with stage III AO of the left frontal lobe. A complete timeline of the case presentation is shown in Fig. 1. Initially, the patient sought medical advice following a series of grand mal seizures that occurred in January of 2013. Magnetic resonance images (MRI) of the brain days later revealed infiltrative lesions, approximately 4.6 × 3.3 cm, in the left frontal lobe, involving cortical and subcortical white matter. Following a craniotomy (1 week following MRI) the Department of Pathology at the University of Colorado Anschutz Medical Campus confirmed earlier tumour grading. The patient also exhibited isocitrate dehydrogenase-1 mutations, and tested positive for deletions of 1p36 sequences and 19q13 sequences, but negative for the amplification of epidermal growth factor receptor sequences, tumour suppressor gene phosphatase, and tensin homolog sequences. Fig. 2 shows the pre- and post-operative MRIs of the brain. Following surgery and the provision of informed consent, the patient underwent CT

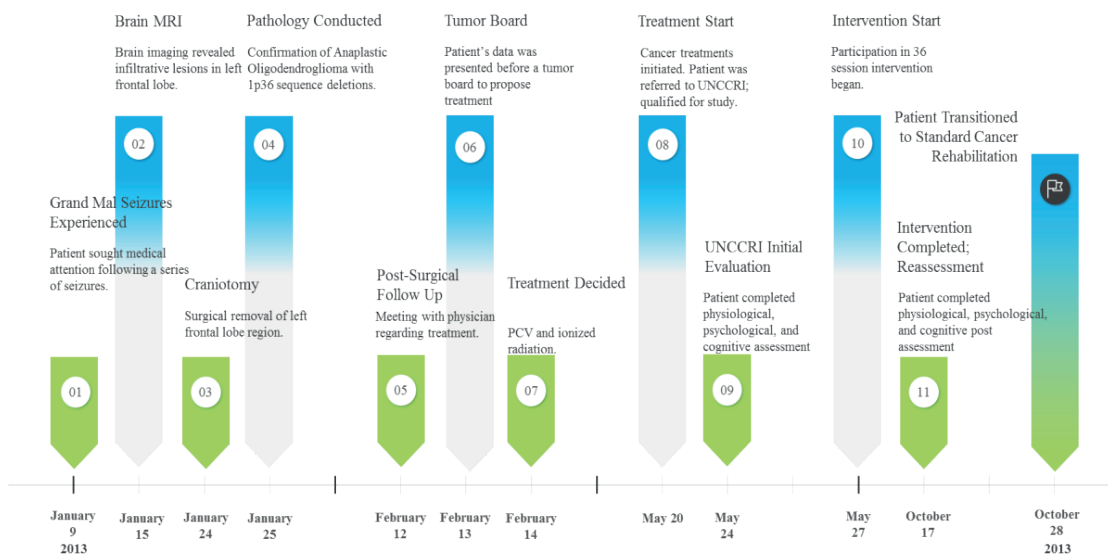


Fig. 1. Timeline of events.

simulations and preparations before radiation treatment began. Following guidelines from the EORTC-26951 clinical trial (2), a combination of procarbazine, lomustine, and vincristine sulphate (PCV) chemotherapeutic (6 dosage) regimen with ionized radiation (46 Gy followed by 14 Gy boost to the resection site and G2/FLAIR regions + temozolomide) was ordered. The patient was then referred by her oncologist in May of 2013 to the University of Northern Colorado Cancer Rehabilitation Institute (UNCCRI) and was cleared to undertake exercise by the attending physician.

The patient was experiencing fatigue, pain in her hands and feet, allodynia, hearing difficulties, blurred visual acuity in her left eye, difficulty with ambulation, chronic weakness of the lower right extremity, continual word aphasia, and hypersensitivity to loud noises. In addition, the patient did not undertake the level of daily exercise recommended by the American College of Sports Medicine, and was classified as being at moderate disease risk of cardiovascular. The subject underwent a comprehensive physiological, psychosocial and cognitive assessment prior to, and at the completion of, the 36-session exercise intervention described below. The cancer-specific treadmill protocol (6) outcome for VO_{2peak} was 28.6 ml/kg/min, which, according to current cancer-specific norms, resulted in a classification of “above average”. Strength-to-weight ratios were poor for both chest press (0.28) and leg press (0.84).

Initial psychosocial assessments revealed a severe level of fatigue (8.7; Piper Fatigue Scale), mild mood disturbance (15; Beck Depression Score), and a low level of quality of life (12.3; Ferrans and Powers Quality of Life Inventory). Cognitive data are presented below. After completing the UNCCRI physical assessments, the patient qualified for, and agreed to participate in, a study examining the impact of various training modalities on physiological, psychological, and cognitive function (7). The entire UNCCRI assessment was completed within 2 h. The University of Northern Colorado Institutional Review Board approved [573297-2] all procedures and the patient signed the informed consent form. All physiological, psychosocial, and cognitive assessment procedures and protocols have been detailed in recent publications (3, 6, 7).

Procedures

Each exercise session consisted of a 5-min warm-up, followed by 30 min of exercise at the specified target heart rate on a recumbent cycle ergometer (Motion Fitness Brain Bike®, Elk Grove Village, IL). The patient was encouraged to maintain the target heart rate for the entire session, with the exception of transient neurological changes. Following each aerobic training session the patient completed 30 min of static stretches designed to target major muscle regions throughout the body (7). Sessions

were progressive and began at 55% of heart rate reserve (HRR, Karvonen method) for weeks 1–4, progressed to 60% HRR for weeks 5–8, and finished at 65% HRR for weeks 9–12. Each training session was 1 h long.

RESULTS

Following completion of the intervention, the patient repeated the cognitive, physiological, and psychosocial assessments. The results (Table I) show reductions in both weight and body composition from pre- to post-intervention. Table II highlights the functional improvements in strength, flexibility and cardiovascular functioning. Among all physiological assessment items obtained, the patient improved in 9 out of the 14 assessments. Table III highlights improvements in fatigue and quality of life; however, the patient’s level of de-

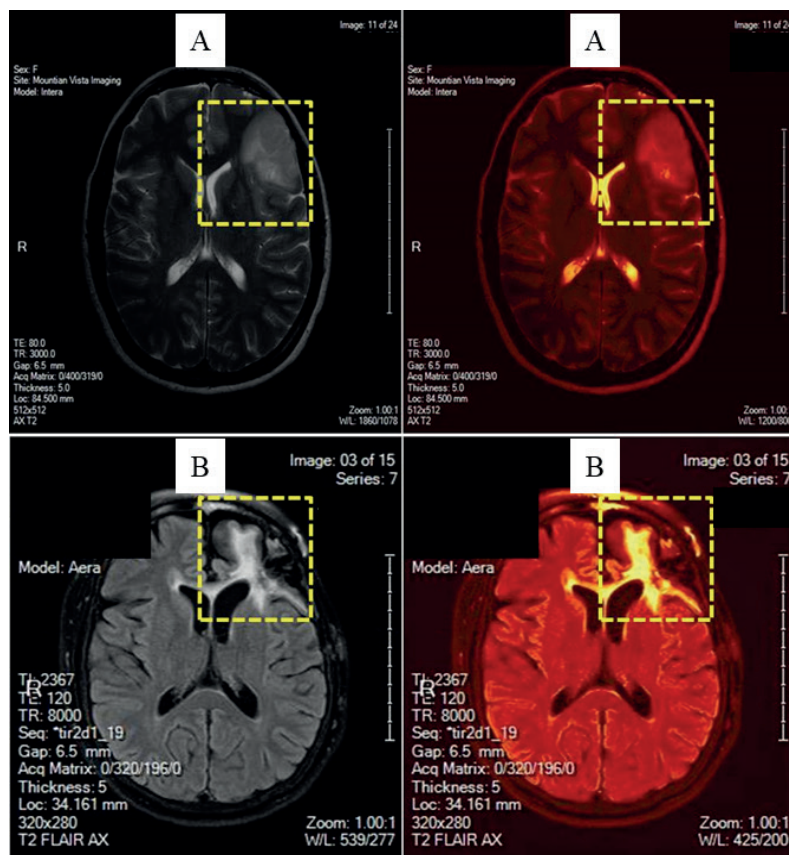


Fig. 2. Axial pre-surgical (A; 2013) and post-treatment (B; 2017) multi-planar, multi-sequence magnetic resonance images in black and white and color intravenous contrast. Dotted box indicates area of involvement. Lower left corner of individual image highlights in-depth image characteristics. Contrast color selected was “hot metal.” Note: pre and post images are close in area, but not exact.

Table I. Patient characteristics

Characteristics	Initial assessment	Reassessment	Change, %
Height, inches	62	62	~
Weight, pounds (lb)	143	126	-11.8
^a Body composition (%)	31	12.6	-18.4

^aSkinfold calliper method. height is in inches (in.); weight is in pounds (lbs.); body composition is in body fat percentage (%) and measured by skinfold caliper method

pression increased. Among cognitive function variables, the patient increased from pre- to post-intervention in 6 of 12 cognitive assessments (**Table IV**). Of note, many times throughout the aerobic training the patient stopped talking completely and slowed or ceased cycling. Her head slowly drifted downward and towards the right, and she would stop talking. While she appeared to be awake, she was completely incoherent with a blank stare. To account for these circumstances, aerobic training at the aforementioned percentages had to be reduced to a comparable rate of perceived exertion (RPE) in order to accommodate her needs while accomplishing the training objectives.

DISCUSSION

Physiological and psychosocial improvements were observed following the exercise intervention in this case, while cognitive improvements were uncertain. Abdominal endurance and shoulder strength increased by 253% and 664%, respectively, which is atypical for general trends of improvement in many cancer survivors in cancer rehabilitation. Improvements were also observed in strength measures despite any resistance training.

Thus, stationary, recumbent cycling, combined with gentle flexibility exercise, may be highly effective as an exercise modality for patients with AO, particularly in cases similar to the current one, since transient episodes of incoherence necessitated reductions in exercise workload. In addition, the patient's quality of life and cancer-related

Table II. Physiological variables measured pre- and post-assessment

Characteristics	Initial assessment	Reassessment	Change, %
VO _{2peak}	27.3	29.8	9.2
Flexibility	12	14.5	20.8
Abdominal crunches	0	60	~
Abdominal planks	17	60	252.9
STWRL	0.84	0.71	-15.5
STWRU	0.28	0.45	60.7
Leg press	131	90	-31.3
Leg extension	49	81.3	65.9
Leg curl	55	73.4	33.5
Seated row	71	84.7	19.3
Chest press	46	56.25	22.3
Shoulder press	5	38.2	664
Lat pulldown	93	78.76	-15.3
Chair test	0	50	~

VO_{2peak}: highest rate of oxygen consumed measured regardless of reaching VO₂ plateau, ml/kg/min. Flexibility determined by modified sit and reach test. STWRL: strength to weight ratio lower body; STWRU: strength to weight ratio upper body. All measures of strength were estimated using the Brzycki equation.

Table III. Psychosocial variables

Characteristics	Initial assessment	Reassessment	Change, %
Piper Fatigue Index	8.7	7.0	-19.5
Beck Depression Inventory	15.0	21.0	40.0
Quality of life	12.3	20.7	68.3

Determination of categories based on criteria defined according to the individual instrument.

fatigue also improved, although her fatigue remained in the severe category. Of concern, the patient's depression increased from "borderline clinical" to "moderate clinical". Clinicians working with patients with AO should establish strong mental health referral networks and periodically evaluate fatigue and depression. It is encouraging that 6 out of the 12 cognitive assessments in the current case resulted in improvements. This is not surprising, as exercise is known to protect against cognitive decline in the gerontological population, including those with severe cognitive diseases, such as Alzheimer's disease (8). In this case, all cognitive memory assessments (Logical Memory I, Logical Memory II, and Logical Memory %) improved by a mean of 43%, which may suggest an improvement in overall hippocampal function. Similar improvements in memory parameters have been demonstrated in a cancer rehabilitation setting (9). Rodent models have also demonstrated similar responses, particularly in memory and hippocampal function (10). However, cognitive improvements might also be a result of learning effects due to repeated assessment. The current case suggests that exercise may be an effective and feasible rehabilitative modality to attenuate some of negative neurological consequences of chemotherapy and radiation. This is particularly important for survivors of AO, as they may experience more severe and complex cognitive challenges.

While exercise-based interventions have been implemented in patients with brain tumours (11), this case report is one of the first to demonstrate the impacts of exercise and flexibility training alone in an AO cancer survivor. In addition, following completion of the study,

Table IV. Cognitive function variables

Characteristics	Initial assessment	Reassessment	Change, %
Brief Cog. Screen	56	48	-14.3
Logical Memory I	8	12	50.0
Logical Memory II	7	11	57.1
Logical Memory %	22	25	13.6
Trail Making Test A	41	64	56.1
Trail Making Test B	91.5	145	58.5
Block Design	11	12	9.1
Letter Num. Seq.	9	9	~
Coding	56	58	3.6
COWAT-G	-0.8	-2.7	237.5
COWAT-A	-0.7	-0.1	-85.7
COWAT-ED	-1.3	-1.1	-15.4

WMS IV: Weschler Memory Scale (4th edn) (BCOG: Brief Cognitive Screener [raw scores]; LMI & LMII [scaled scores]; Logical Memory delayed recall (DR) [raw scores], or cumulative percentage (CP)); TMT A or B: Trail Making Test version A or B [raw scores], WAIS IV: Weschler Adult Intelligence Scale (4th edn) (BD: block design [scaled scores]; LNS: letter number sequence [scaled scores]; CD: coding [raw scores]); COWAT: Controlled Oral Word Association Test (Z: z-score; G: gender; A: age; ED: education [scaled scores]).

the patient transitioned successfully to a standardized cancer rehabilitation programme. Brain cancers are rare, and AO cancers even rarer; thus establishing the evidence for the effects of exercise in this population is challenging. Furthermore, in this case both physiological and mild psychological improvements were demonstrated in response to exercise, supporting the use of exercise interventions in individuals undergoing treatment for brain-based cancers. In addition, the battery of physical assessments was comprehensive, assessing all of the major physiological systems of the body. This enabled an individually-targeted exercise prescription to be developed and implemented when this individual completed the initial study, thereby allowing optimal progression of exercise to occur when standardized cancer rehabilitation programming commenced.

There were, however, several weaknesses and limitations to this case report. In light of the rarity of this cancer, no appropriately matched control subject was recruited. Comparison with a non-exercised control subject would have provided greater insight into the effects of the intervention. In addition, a major limitation related to the battery of cognitive assessments that were administered; while all of the tests are validated and widely-used, they have not been widely accepted as the test battery of choice, particularly in patients with brain cancer.

Although the exercise intervention proved beneficial in this case, some questions remain. From pre- to post-assessments, overall fatigue increased, while assessments of oral word association worsened. It is possible that cancer-related fatigue played a role in some of the negative outcomes in assessment of word association. In addition, future studies should investigate this particular exercise intervention against a cognitive-only protocol in patients with AO.

Conclusion

Overall, an aerobic cycling and flexibility intervention resulted in improved physiological and psychosocial parameters in this patient with AO. However, the effects of the intervention on cognitive parameters remain ambiguous. The intervention was well-tolerated even when the cancer and its treatments resulted in transient periods of incoherence, suggesting that these modalities are effective and safe and may be translatable to other patients with AO. Exercise-based cancer rehabilitation is a growing field, and these results should encourage clinicians to incorporate exercise into a cancer survivors' rehabilitation plan, regardless of the stage or type of cancer. In addition, this case report provides evidence of the positive effects of exercise for cancer patients. Even in the rarest

of cancer diagnoses, similar to AO, many positive benefits of exercise have been shown to occur. Finally, as there are very few studies of exercise interventions that have included patients with AO, these findings may serve as the basis for further research into the physiological and psychological effects of exercise-based cancer rehabilitation for patients with AO.

The authors have no conflicts of interest to declare.

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