EFECTO DE UN PROGRAMA INTRA-HOSPITALARIO EN LA RECUPERACIÓN FUNCIONAL DE UNA PACIENTE CON MELANOMA DE CÓRNEA: UN ESTUDIO DE CASO

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TITLE: Effects of an In-Hospital Training Program on Functional Recovery in a Patient with Choroidal Melanoma: A Case Study

ABSTRACT

Objective: To evaluate the influence of a supervised in-hospital resistance training program on blood biomarkers in patients with choroidal melanoma (CM). Secondary aims involved analyzing changes in patient-reported outcomes, physical function test and training-related ocular pain levels.

Case presentation: A 69-year-old woman with inferonasal region tumor on the left eye and diagnosed of CM performed strength training sessions during isolated hospitalization. Outcome measures were evaluated at the start of the hospitalization (T0), during hospital discharge (T1) and one moth after hospital discharge (T2).

KEY WORDS: Oncology, cancer rehabilitation, uveal melanoma, hospital exercise

INTRODUCTION

Choroidal melanoma (CM) is the most usual intraocular cancer worlwide, exhibiting high mortality with cumulative metastasis rates of 25% at 5 years and 34% at 10 years (Diener-West et al., 2005), albeit with a low incidence of six to eight cases per million. (Kaliki et al., 2015; Krantz et al., 2017) It is a disorder that affects melanocytes within the tract of the eye. (Krantz et al., 2017) Disease and treatment-related visual impairments cause severe functional limitations which affect daily living activities and can also cause depression, anxiety and social isolation. (Damato et al., 2018, 2019) To date, there is a deficiency of effective supportive therapies to relieve symptoms and side effects, or to enhance the quality of life for those affected. It is suggested that general physical exercise may be able to improve overall eye health and balance in individuals with visual disabilities, (Sweeting et al., 2020; Wylęgała, 2016) albeit to date, this has been poorly demonstrated in patients with CM, with only a case study published. (Mendes Wefelnberg et al., 2024)

CM, in small and medium sized cases according to TNM classification, is usually treated with plaque brachytherapy, a specialized form of radiotherapy. (American Brachytherapy Society, 2014) This technique consists in applying radioactive sources proximal to the tumour, allowing accurate and targeted delivery radiation to cancer cells while minimizing harm to enclosing health tissues. (American Brachytherapy Society, 2014) This treatment is normally followed by a week of hospitalization in which patients cannot move from the hospital room as they are isolated. During this period, in addition to all the previously explained health issues, patients could experience a reduction in muscle strength and muscle mass due to the abrupt cessation of movement based on the decreased free movement and prolonged bed rest. (Parry & Puthucheary, 2015) As a consequence, patients could impair their musculoskeletal or cardiovascular health, physical function and, therefore, their quality of life, especially in individuals with critical illness. (Parry & Puthucheary, 2015) During these first days of bed rest, there is also a raise on inflammatory pathways with increases in C-reactive protein (CRP), interleukin-6 (IL-6), and tumour necrosis factor alpha (TNF-α), (Kehler et al., 2019) as it also induces metabolic dysregulations (decline in basal metabolic rate) (Haruna et al., 1994) and increases in oxidative stress. (Debevec et al., 2016; Rai et al., 2011) As exercise-supplemented remobilization has proved to restore muscle volume and strength after bed rest (Shur et al., 2024), strength training could be one of the tools to prevent this situation. An interesting way of implementing resistance training exercise could be by using elastic bands, which are portable, low cost and have showed to be able to reach high levels of muscle activity in upper and lower extremities when lying in a hospital bed. (Skals et al., 2018; Vinstrup et al., 2017) However, to our knowledge, no previous study has evaluated the implementation of structured exercise programs during hospitalization for CM patients, despite the potential of such interventions to reduce adverse events and enhance recovery outcomes in this vulnerable population.

Therefore, the primary aim of the study was to investigate the effects of an in-hospital resistance training program on blood biomarkers in a patient with CM. Secondary outcomes were to analyse the effects on the patient-reported outcomes, physical function tests and ocular pain intensity during training.

MATERIAL AND METHODS

Case presentation

The patient was a 69-year-old caucasian woman (left-handed; weight = 76 kg; height = 168 cm; body mass index = 26,9 kg/m^2) who was diagnosed with CM in February 2025. Her medical history was significant only for hypertension, with no other relevant medical conditions reported. She did not have any prior cancer treatment before initial examination. Informed consent was obtained from the patient before collecting data, and patient rights were maintained throughout treatment. The study was approved by the ethical committee in Hospital Universitari I Politècnic la Fe, Valencia, Spain (2024-0968-1)

Differential diagnosis

Following suspicion during an ocular examination, the patient was referred to "Hospital Universitari i Politècnic de La Fe" (Valencia, Spain), community referral hospital, for an ophthalmological evaluation where measurements were taken via ultrasound. Following assessment, the patient was referred to Oncology Department for an extension study. This was performed using a computed tomography of the chest, abdomen and pelvis. Additionally, blood tests were requested to assess potential elevations in tumor markers to determine if metastasis was present. An orbital magnetic resonance imaging was conducted to confirm and accurately measure the tumor dimensions. No metastasis was found and tumor was located in the inferonasal region of the left eye. After brachytherapy evaluation and confirmed the CM diagnostic, with a T1N0M0 grade assessed following TNM classification, the patient was scheduled for plaque brachytherapy treatment in April 2025.

Treatment

Plaque brachytherapy treatment consisted in the implementation of a COMS12 plaque containing 8 radioactive seeds, which remained in the left eye, at the tumor site, for 69 hours and 51 minutes, with a total administrated dose of 85 Gray. During hospitalization, the patient remained isolated in a room due to ocular radiation exposure. Following the prescribed treatment period, the patient returned to the operating room for surgical removal of the ocular plaque.

Intervention

To modify the standard hospital treatment protocol of isolated bed rest during hospitalization, an alternative approach involving different strength exercises was proposed. During the four days that the patient was hospitalized with the plaque brachytherapy treatment, to avoid complications due to anaesthesia, two training sessions were performed on the second and the third day, after plaque implementation and before plaque extraction.

To carry out the training sessions, elastic bands (TheraBand CLX Consecutive Loops; TheraBand, Akron, OH) with resistance graded from very low to very high (i.e, yellow, red, green, blue, black, silver ang gold) were used. On each session, each exercise started with three sets of two repetitions as a warm-up and to calculate the appropriate intensity. The targeted intensity was that at which the patient reported a perceived exertion of 5-6 of 10 at Borg CR10 scale after two repetitions. The patient selected the

appropriate band color and width to achieve the desired intensity by the end of the third set. This intensity was chosen because it corresponds to a weight that allows approximately 12-15 repetitions. (Buckley & Borg, 2011) The elastic bands were prestretched to approximately 50% of their initial length (initial length 1.9 m). The short-term intensive strength elastic training in-hospital program included the following exercises: 1) squat; 2) seated row; 3) hip abduction; 4) biceps curl; 5) shoulder abduction. For each exercise, one set was completed until task failure was achieved. All exercises, except the squat, were performed unilaterally, with two minutes of rest between them. Although, all exercises, except the row which was performed sitting, were performed in a standing position. The speed of contraction was around two seconds for each phase. Each session was supervised by a physical therapist or a physician who entered to the room wearing lead-protective attire and carrying a radiation monitor to prevent exposure, while maintaining a safe distance from the patient.

Outcome measures

Outcome measures were evaluated at the start of the plaque brachytherapy treatment hospitalization (T0) and were then reevaluated during hospital discharge day (T1), which was three days after the initial measures, and one month after hospital discharge (T2).

The primary outcomes were the blood biomarkers (including inflammatory response biomarkers, metabolic and lipidic response biomarkers, and tumor markers), which were measured in samples collected and processed by a trained nurse. Inflammatory response biomarkers analysed were CRP, procalcitonin and IL-6. Metabolic and lipidic response biomarkers were glucose, urea, creatinine, glomerular filtration rate, total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, non-HDL cholesterol, triglycerides, total bilirubin, aspartate aminotransferase (AST/GOT), alanine aminotransferase (ALT/GOT), alkaline phosphatase, lactate dehydrogenase (LDH), creatine kinase (CK), total proteins, albumin, calcium, chloride, sodium, potassium, red blood cells, hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, red cell distribution width-standard deviation, red cell distribution width-coefficient of variation, nucleated red blood cells, white blood cells, neutrophils, lymphocytes, monocytes, eosinophils, basophils, neutrophils (%), lymphocytes (%), monocytes (%), eosinophils (%), basophils (%), granulocytes, platelets, mean platelet volume, platelet distribution width, platelet-large cell ratio, prothrombin time, prothrombin time ratio, Quick index, international normalized ratio, activated partial thromboplastin time and ratio, fibrinogen, hemoglobin A1c (HbA1c) and estimated average glucose. Tumor markers analysed were carcinoembryonic antigen and S100 protein.

The secondary outcomes were measured by a physical therapist and were the following: 1) EORTC QLQ-C30 questionnaire along with the complementary EORTC QLQ-OPT30 module specifically designed for patients with eye cancer. Both surveys assess various dimensions of quality of life during past week from each item on a scale of 1-4 (1: not at all, 2: a little, 3: quite a bit, 4: very much), whereas the OPT30 module has a particular focus on evaluating visual functioning limitations. Patient overall health and quality of life were assessed, ranging from 1 to 7 (1 for very poor to 7 for excellent). A total score

between 0 and 100 was calculated for each scale. For global and functional scales, a higher score is considered better, while for symptom scales a lower score is better (Aaronson et al., 1993); 2) The Hospital Anxiety and Depression Scale (HADS) was used to measure symptoms of anxiety (HADS Anxiety) and depression (HADS Depression), with optimal cut-off points as > 9 units for anxiety and > 7 units for depression among patients with cancer (Annunziata et al., 2020); 3) Levels of physical activity prior to hospitalization (minutes/week during last month); 4) Agility and coordination were evaluated with the timed-up-and-go-test (average value of two trials), which consisted of rising from a chair on command, walking a distance of 3 metres, turning around, and walking back to the chair as fast as possible; 5) Muscle strength of lower limbs (endurance strength) was assessed with the 30-s-sit-to-stand test, which was to stand up and sit down as many times as possible in 30 seconds; 6) Pain intensity before, during and after training was also assessed with the Visual Analogue Scale (VAS), by having respondents mark a point along a continuous linear scale anchored by two polar descriptors (e.g., 0 = 'no pain' to 100 mm = 'worst imaginable pain').

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