# Topical application of platelet supernatant gel in the management of radiotherapy-induced mucositis: a case report

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## Introduction

Radiotherapy is the treatment of cancer and other diseases with ionising radiation. Oral cancer is the sixth most common cancer in the world[1-2]. Surgery and radiotherapy have been the standard loco-regional treatment modalities employed in oral cancer with a high cure rate[1]. Radiotherapy, principally used with curative intent[3], is indicated for the majority of patients with head and neck cancers[1]. Oral mucositis, inflammation and ulceration that occurs in the oral cavity, is a major complication associated with radiotherapy administered to the head and neck area. It is associated with significant morbidity characterised by pain, odynodysphagia, dysgeusia, malnutrition, dehydration, and also increases the risk of systemic infections in immunocompromised patients[4,5]. Its severity is dependent on the type of ionising radiation, the volume of irradiated tissue, the dose per day, and cumulative dose. Patients undergoing radiotherapy for head and neck cancer receive approximately 200 cGy of radiation per day, 5 days a week, for 5 to 7 consecutive weeks[4,5]. Often the mucositis is of such severity that it requires parental analgesia, interruption of radiotherapy, and hospitalisation. This is of marked concern because there is strong clinical and radiobiological evidence that protraction of overall time of radiotherapy has an adverse influence on the curability of certain human tumours, particularly squamous cell carcinoma of the head and neck region[6]. Interventions are an area of interest and are constantly evolving in order to identify new therapeutic solution able to improve the quality of life of patients[7].

Platelet supernatant gel is a product derived from blood and is intended for non-transfusional therapeutic purposes. It increases and enhances natural haemostasis as well as processes of tissue repair and regeneration. It is produced by collecting the supernatant obtained after the activation of coagulation of platelet concentrate. The ensuing supernatant is rich in platelet growth factors that stimulate tissues growth and regeneration[8-10]. Platelet supernatant gel acts in synergy with plasma-derived factors to activate a complex network of autocrine functions that modulate healing[11-13]. The properties of platelet supernatant have been exploited in several medical and surgical specialties[14-18], and new uses for platelet gel are currently under investigation. Taking into account this background, we used platelet supernatant gel in the management of a patient with a severe radiation-induced oral mucositis.

## Case report

In September 2012 a 78-year old female was admitted to our Institution with a history of a painless right pre-auricular nodule that had gradually increased in size. Computed tomographic scans revealed a 1.9×2.5 cm solid lesion in the right parotid gland without evidence of positive lymph nodes. Magnetic resonance imaging showed enlargement of the right parotid gland with evidence of multiple cystic masses involving both the superficial and deep portions of the gland. Fine-needle aspiration biopsy was used for the diagnosis. Cytopathological examination suggested giant pleomorphic adenoma of the parotid gland with malignant transformation. Total parotidectomy with preservation of the facial nerve was performed in November 2012; the parotid gland and overlying skin were removed and lateral jugular lymph nodes were dissected out. Histologically, the lesion was classified as an undifferentiated carcinoma of the parotid gland. Of 74 lymph nodes removed, 28 were positive for the presence of cancer cells or micrometastases. Residual cancer cells were present at the surgical margins. Finally the disease stage was pT(3), pN(2b), M(x), R (+). Six weeks after surgery, the patient was irradiated with 2 Gy fractions; radiotherapy was delivered using opposed lateral fields with 6-mV photons to the right parotid lodge and right lateral cervical lympho nodes for the initial 50 Gy. An additional boost of 16 Gy was delivered to the right parotid space. Three-dimensional computed tomography

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planning was used to optimise dosimetry. The radiation fields are shown in Figure 1.

The patient was instructed to rinse her mouth with bicarbonate of soda solution at least four times a day. We ensured that she received adequate hydration and maintained or improved her overall nutritional status by suggesting non-irritating, nutrient-dense foods and fluids in accordance with the nutritional guidelines for the management of symptoms of mucositis[19]. Her body weight at the beginning of treatment was 62.8 kg. Complete oral examinations were done every day.

Mucositis was recorded at the end of every week and graded as recommended by the World Health Organisation (WHO)[20] (Figures 2 and 3). The grading criteria are as follows: grade 0 - no changes; grade I - soreness/(+) erythema; grade II - erythema (++), ulcer, can eat food (erythema with ulcers less than 1 cm$^2$); grade III - ulcer (+++), (erythema with ulcers more than 1 cm$^2$), requires liquid food; and grade IV - ulcer with haemorrhage and necrosis, alimentation not possible. Pain was recorded 3 times a week: at the start, in the middle and at the end of the treatment week. Pain was graded as recommended by the Lindquist/Hickey scale[20] (Figures 4 and 5): 0 (none) - no pain; 1 (mild) - slight burning; 2 (moderate) - oral pain but able to eat; and 3 (severe) - severe pain and unable to eat. In the first week there were no alterations in the oral mucosa and the patient did not report any pain (Figures 2 and 4). Starting from the second week, during which 10 Gy of radiotherapy were delivered, the patient reported worsening dysphagia and slight burning: there was erythema of the oral cavity (grade I mucositis) (Figure 2), but no pain was present (Figure 4). At 16 Gy of radiotherapy, a diffuse mycosis appeared in association with erythema with ulcers less than 1 cm$^2$ (grade II mucositis) (Figure 2**)**: oral pain was present but the patient was able to eat (Figure 4). Miconazole 2% oral gel was added to the therapy. The mycosis regressed and the patient's condition remained stable up to 24 Gy of radiotherapy when a confluent mucositis appeared, characterised by erythema with ulcers larger than 1 cm$^2$ (grade III mucositis) (Figures 3 and 4). Prednisone 12.5 mg/die, lidocaine unguentum 7.5% and lansoprazole 30 mg/die were prescribed to restrain the progression of the mucositis. At 28 Gy of radiotherapy, the mucositis remained stable while the patient reported worsening pain that limited her oral intake to liquid food (Figure 4). Spray

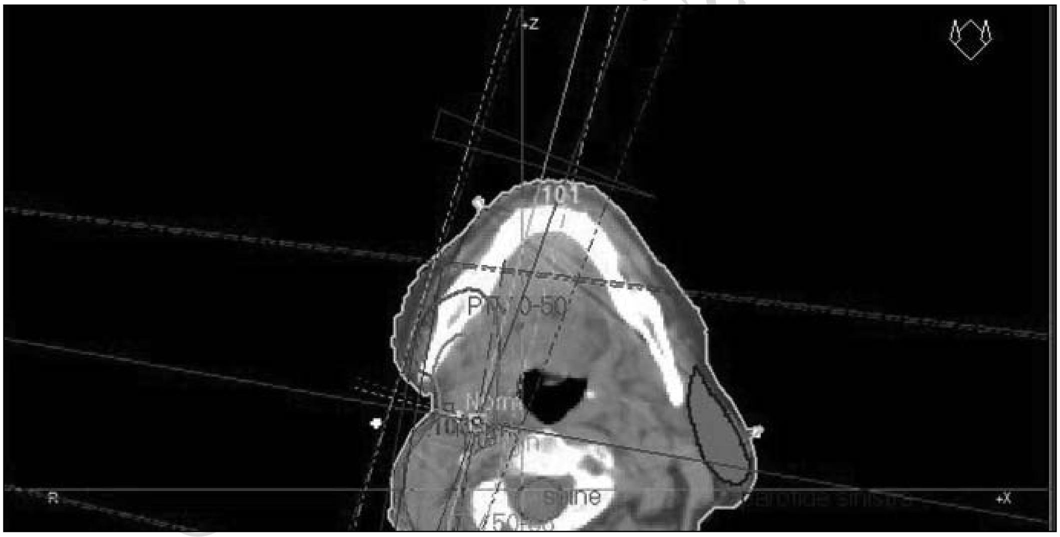


**Figure 1** - Planes of radiotherapy.

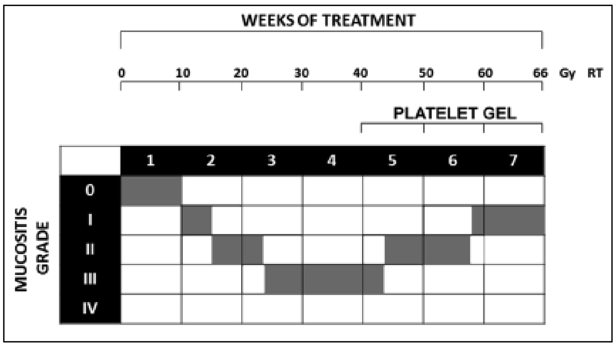


**Figure 2** - Grade of mucositis.

**Figure 3** - Grade III mucositis.



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treatment with hyaluronic acid and amino acids was added to the therapy. At 40 Gy of radiotherapy severe pain and confluent, grade III mucositis persisted (Figure 2 and 4). No clinical improvement was noted. Furthermore we recorded a weight loss of 5.5 kg (Figure 5).

Considering the rapid progression of the mucositis and the lack of clinical improvement, we decided to suspend the ongoing treatments and to start treatment with platelet suspension gel promptly. Since platelet supernatant has already been used in several medical and surgical specialties, such as oral surgery[14-18], without side effects and that the patient's clinical condition was seriously compromised, we proceeded without requesting the opinion of the ethics committee. The patient was fully informed about the procedure and the risks and gave her informed consent to the treatment. Platelet suspension gel was prepared as already described[11-13].

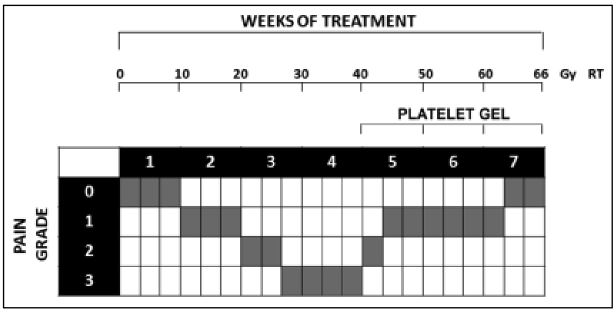


**Figure 4** - Grade of pain.

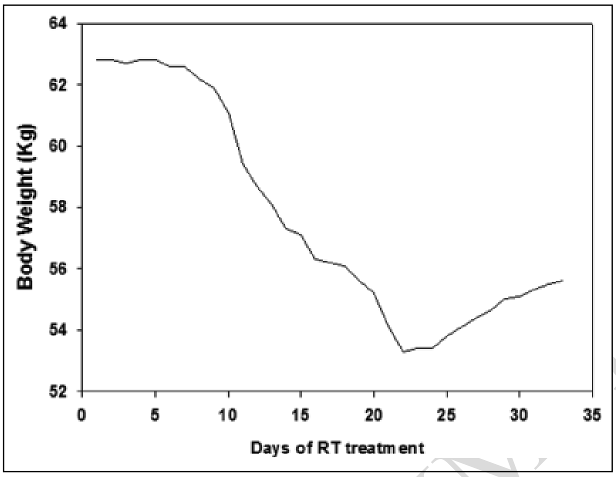


**Figure 5** - Patient's body weight during radiotherapy. RT: radiotherapy.

**Figure 6** - Mucositis at the end of radiotherapy after treatment with platelet supernatant gel.

Briefly, plasma rich in platelets (PRP) ($3\times10^6$ µL)[11-13] was prepared from buffy coat derived from a blood donor. The PRP was subjected to 40 Gy of radiation and coagulated by activation in a sterile room with calcium gluconate (1:10). Supernatant, rich in platelet growth factors, was recovered and stocked at −18°C for a maximum of 30 days. Before use, each single aliquot was mixed (1:1, total volume 20 mL) with miconazole 2% oral gel, which was the pharmacological vehicle. The patient was instructed to apply the platelet/miconazole gel four times/day, to keep it in the mouth as long as possible and not to swallow food or liquids for the next hour. As shown in Figure 4, the patient reported a marked decrease in pain symptoms already after 2 days of platelet/miconazole gel treatment. Starting from the fourth day of platelet/miconazole gel treatment, a progressive improvement of the mucositis was described. At 44 Gy of radiotherapy, the second day of platelet gel treatment, the patient had little pain in her mouth and this did not limit her oral intake of solid food (Figure 4). Clinically, the mucositis was classified as grade II (Figure 2). At 58 Gy of radiation delivered, the oral cavity evaluation showed erythema with just one ulcer; the patient could eat and drink and did not report pain (Figures 4 and 6). Furthermore a gradual recovery of body weight was evident (Figure 5).

## Discussion

Oral mucositis is a common and important side effect of radiotherapy of head and neck cancer. It is essential to prevent and control the development and progression of this side effect. Here we have described the case of a patient with parotid carcinoma and severe oral mucositis induced by radiotherapy, who was treated with platelet gel. Platelet gel rapidly repaired damage to the mucosa, blocked the progression of mucositis, reduced the intensity of pain and restored the patient's ability to eat. Based on our experience, we suggest that the use of platelet gel helps not just in delaying the progression of mucositis and its recovery, but also reduces the intensity of pain and is, therefore, more efficient in the management of radiation-induced mucositis. Furthermore this treatment enables



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radiotherapy to be continued without interruptions. Studies involving larger numbers of people would help to evaluate the significance of platelet gel in the treatment of radiation-induced oral mucositis.

## Authorship contribution

Mario Di Staso, Anna Rughetti, Luigi Dell'Orso contributed equally to this article.

*The Authors declare no conflicts of interest.*

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