CASE STUDY

Radiation-induced Leiomyosarcoma of the Posterior Neck Region

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KEYWORDS
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Abstract
Introduction: Leiomyosarcomas are mesenchymal malignant tumours that appear in smooth muscle cells. Their most frequent locations are the uterus and gastrointestinal tract. Their occurrence in head and neck is considered exceptional. We present a patient with a posterior neck region leiomyosarcoma who had received radiation for a nasopharyngeal carcinoma 20 years earlier. The incidence ratio of these tumours in radiated patients (therefore considered radiation-induced) ranges from 0.035 to 0.2%.
Radiation-induced sarcomas are difficult to diagnose due to the induration and fibrosis in the radiated area and the non-specific symptoms that they present. Their prognosis is very poor.
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PALABRAS CLAVE
Sarcoma; Leiomiosarcoma; Radioinducido; Cuello

Leiomiosarcoma radioinducido de la región posterior del cuello

Resumen Los leiomiosarcomas son tumores mesenquimales malignos, que se originan en las células del músculo liso. Las localizaciones de aparición más frecuentes son el miometrio y el tracto gastrointestinal. En la región de cabeza y cuello los leiomiosarcomas aparecen de forma excepcional. Presentamos el caso de un leiomiosarcoma en la región posterior del cuello, en un paciente radiado 20 años antes por un tumor de nasofaringe.
La incidencia de este tipo de tumores que cumplen los criterios de tumor radioinducido se sitúa entre el 0,035 y el 0,2%. Los sarcomas radioinducidos son difíciles de diagnosticar en estadios tempranos, debido a la induración y la fibrosis de la zona radiada y a la sintomatología inespecífica que presentan. Su pronóstico es malo.
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Introduction

Leiomyosarcomas are malignant tumours arising from smooth muscle cells or mesenchymal stem cells. They appear in middle-aged subjects without a clear gender predominance. Due to the absence of smooth muscle in the region, they account for less than 1% of neoplasms in the head and neck area. This type of tissue is only present in the hair erector muscles and blood vessels.

The most common locations of this tumour are the oral cavity, superficial soft tissues, paranasal sinuses and mandible. Virtually all types of cancer have been described in the head and neck region following radiotherapy treatment. The skin and thyroid are the most commonly affected tissues. Radiation-induced leiomyosarcomas are exceptional. They appear in between 0.035% and 0.2% of all irradiated patients, representing less than 5% of sarcomas and have a poor prognosis.

Case Report

We report the case of a 67-year-old male who, 20 years earlier, was treated for undifferentiated cavum (nasopharynx) carcinoma (T2N3MO) through neoadjuvant chemotherapy (3 cycles with CDDP [cisplatin] and 5-Fu), followed by radiotherapy (66 Gray [Gy] in the cavum and 60Gy in the lymph node chains, with overimpression of 10Gy in the lateral cervical region). Subsequently, 3 months after the end of the radiotherapy treatment, he required a rescue procedure: left, radical, cervical dissection, due to persistence of the necrotic lesion invading the sternocleidomastoid muscle and partially collapsing the jugular.

The examination revealed a 9 cm×5 cm mass at the left, posterior, cervicodorsal level, painless on palpation, infiltrating and non-rolling, with the remainder of the ENT examination being normal (Fig. 1). We performed fine needle puncture-aspiration (FNA) which revealed a non-typeable mesenchymal lesion. The imaging study (Fig. 2) showed a 8 cm×5.4 cm×4 cm mass, which caused erosion of the neighbouring bony structures, suggestive of sarcoma. There were no signs of local, regional or distant recurrence of the cavum neoplasm. Deep biopsy of the lesion revealed a malignant, pleomorphic, soft-tissue tumour, consistent with a pleomorphic leiomyosarcoma of grade 3 according to the histological malignancy scale. The immunophenotype was: vimentin+desmin+focal; h-caldesmon (h-CALD)+S-100 protein; neurofilament (NF); histiocytic marker CD 68+ high Ki-67 positive cell index (MB-1 index) (Fig. 3).

This diagnosis led to complete excision of the tumour. The final control of the surgical site required carrying out a latissimus dorsi muscle flap in a second surgical procedure. Treatment was completed with 1 cycle per month of 4-epiadriamycin for 4 months. The patient is currently free of disease, 35 months later.

Discussion

The carcinogenic potential of ionising radiation was recognised soon after the discovery of X-rays in 1985 by Roentgen. Radiation-induced malignancy is a long-term complication of radiotherapy with a scarcely-understood mechanism. The criteria for radiation-induced malignancy in sarcomas were established by Cahan et al. in 1948. These criteria rate cases from 1 to 4 according to the following guidelines: (1) no evidence of new tumour at the time of irradiation; (2) appearance in a previously irradiated field; (3) histological evidence of sarcoma; and (4) latency of 5 years from irradiation.

In 1999, Murray et al. established a latency period longer than 5 years after irradiation. Moreover, they proposed that the primary and secondary tumours should be of different histological entities. They can be classified according to size and location following the TNM scale and, according
to Broders and Angervall, there are 4 degrees of histological malignancy, with 1 and 2 being low-grade and 3 and 4 being high-grade. This is determined by the degree of cellularity, differentiation, mitosis, cellular atypia and necrosis identified.\(^6\)

The most common histological subtypes are malignant fibrous histiocytoma and osteosarcoma. Other variants are angio- and lymphangiosarcomas and spindle-cell sarcoma.\(^1,3,5,8,10\) Up to 25% of cases develop in patients with retinoblastomas.\(^3,11\) This association appears to be related with the hereditary retinoblastoma gene (RB1) as an additional, predisposing factor.\(^1\) In 1999, Patel et al. studied a series of 10 patients with these types of tumors located in the head and neck region and reported that 40% of them were a subtype of sarcoma known as malignant fibrous histiocytoma.\(^12,13\)

Numerous mechanisms through which radiation could induce genetic changes are currently being discussed, but the exact development of radiation-induced tumors is still not understood.\(^14-16\) Most of them have been shown to develop after receiving a total dose of 55 Gy, with a range between 16 and 112 Gy.\(^10,11,17\) The estimated incidence of sarcoma among patients who have received radiotherapy is of 0.035%–0.2%.\(^4,8,11\) However, this frequency is expected to increase due to the increase in life expectancy of the population, combined with improved survival of cancer patients.\(^10,11\) It is rare in the head and neck region. Demirkan et al. found only 23 cases of radiation-induced leiomyosarcoma in 2003.\(^1\) Lesions usually have a tendency towards metastatic spread, without causing nearby lymph node metastasis, and with surrounding satellite lesions.\(^1\) The differential diagnosis should include more common cases, such as spindle-cell and benign lesions.\(^14\) The definitive diagnosis is obtained through histological and immunohistochemical analysis (it is positive for alpha-actin specific to smooth muscle tissue).\(^12,14\)

Treatment should be complete excision and include the pseudocapsule and a 1 cm safety margin.\(^1,3,4,7-10\) A resection with conventional margins cannot be carried out in the head and neck region (due to adjacent neurovascular structures and spinal cord) and the absence of cervical compartments hinders the approach.\(^11,14\) Surgical resection–reconstruction must be properly planned to include the performance of regional or free flaps, if necessary. These tumors do not respond to re-irradiation.\(^1,3,8\) Except for osteosarcomas, which respond timidly to methotrexate, they are usually chemoresistant.\(^1\) The survival rate at 5 years is 10%–30%.\(^4,8,9\)

**Conclusion**

Radiation-induced leiomyosarcomas are very aggressive and have a poor prognosis. The only curative treatment is complete surgical excision.

**Conflict of Interests**

The authors have no conflict of interests to declare.

**References**


