Angiosarcoma of the larynx. Case report and review of the literature

A proposito di un caso di angiosarcoma della laringe. Revisione della letteratura

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Parole chiave

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Summary

Angiosarcoma of the larynx is a rare malignant tumour of vascular origin, accounting for less than 1% of all malignant tumours of the larynx. Angiosarcoma involves, in particular, the head and neck in areas such as the scalp and face. The causes are unknown, even if, in some cases, it is believed to be radiation-induced. The case is described of a patient with hypopharyngolaryngeal angiosarcoma, which became manifest with dysphagia, dysphonia and a palpable right latero-cervical mass about 7 cm in length. The patient underwent total pharyngolaryngectomy, right hemithyroidectomy, and bilateral neck dissection. Histological examination of the surgical specimen revealed a large haemorrhagic lesion involving the right pyriform sinus and homolateral hemilarynx. Right radical neck dissection revealed 9 metastatic lymph nodes, 1 of which with capsular invasion. Upon complete recovery the patient, underwent adjuvant post-operative radiotherapy. Six months later she is still alive with no clinical or radiological signs of disease. A careful review of the literature produced very few reports of such cases, only 6 of which in the last 30 years. Survival rate is very low, even if feasible average can be advanced, in view of the paucity of the case reports. Histological diagnosis is not always straightforward, as this neoplasm may be misdiagnosed as other vascular tumours (Kaposi's sarcoma, haemangiopericytoma), as non-neoplastic lesions (granulomas secondary to intubation) and as poorly differentiated squamous cell carcinoma. Immunohistochemical evaluation by means of markers, such as vimentin and factor VIII, offers a significant contribution to the diagnosis of angiosarcoma. The treatment of choice for laryngeal angiosarcoma is surgical excision, ample and radical, whenever possible, followed by adjuvant post-operative radiotherapy.

Riassunto

L'angiosarcoma della laringe è un raro tumore maligno di origine vascolare, rappresentando meno dell'1% di tutti i tumori maligni della laringe. In particolare, l'angiosarcoma interessa il distretto della testa e del collo in sedi come lo scalpo e la faccia. Le cause sono sconosciute anche se in alcuni casi si suppone la sua secondarietà a trattamento radioterapico. Noi presentiamo il caso di una paziente affetta da angiosarcoma ipofaringo-laringeo, manifestatosi con disfagia, disfonia e una massa palpabile latero-cervicale destra di circa sette centimetri di diametro. La paziente è stata sottoposta a faringo-laringectomia totale, emitiroidectomia destra, svuotamento linfonodale del collo bilaterale. L'esame istologico del pezzo operatorio ha evidenziato una grossa lesione emorragica interessante il seno piriforme destro e l'emilaringe omolaterale. Lo svuotamento destro del collo di tipo radicale demolitivo, ha evidenziato ben 9 linfonodi metastatici, di cui uno con superamento capsulare. Dopo la completa guarigione si è proceduto con la radioterapia complementare post-operatoria. Da sei mesi la paziente è viva senza segni clinici e radiologici di malattia. Da un'attenta revisione della letteratura i casi riportati sono veramente pochi, di cui solo 6 negli ultimi 30 anni circa. La sopravvivenza è molto scarsa anche se per l'esiguità della casistica non si può effettuare una media ragionevole. La diagnosi istologica non è sempre univoca per la possibilità di confondere questa neoplasia con altri tumori vascolari (Sarcoma di Kaposi, emangiopericitoma), con lesioni non neoplastiche (granuloma laringeo da intubazione) e con un carcinoma squamoso scarsamente differenziato. La valutazione immunoistochimica dei markers come la vimentina e il fattore VIII, contribuisce in modo importante alla diagnosi di angiosarcoma. La terapia d'elezione per l'angiosarcoma laringeo è l'exeresi chirurgica, quando possibile, ampia e radicale, seguita da radioterapia complementare post-operatoria.

Introduction

Angiosarcoma, a malignant tumour of the vascular tissue, or, rather, of eminently vasoformative connective tissue, comprises irregular blood-filled spaces, with irregular contours; the bizarre vessel walls are unequivocal evidence of sarcomatous connective tissue.

Angiosarcoma of the larynx is an extremely rare tumour. An analysis of the Head and Neck Sarcoma Registry of the United States [1] shows that of a total of 214 cases of sarcoma, of every type, treated in an 8-year period only 31 are angiosarcomas, most of which localised in the scalp; a review of all of the cases shows only 5 originating in the larynx. Fur-

thermore, this tumour was, initially, be confused with other vascular tumours (Kaposi's sarcoma, haemangiopericytoma), with non-neoplastic lesions (granulomas secondary to intubation), and with poorly differentiated squamous cell carcinoma.
The anatomopathological feature of this tumour consists in the irregular spaces delineated by the pleomorphic endothelial cells; however, immunohistochemistry enables a definitive diagnosis to be made [2], with the expression of several factors (VIII and vimentin) and the absence of others (cytokeratin and epithelial membrane antigens).

Case report

A 74-year-old female came to our Outpatient Clinic complaining of increasing painful dysphagia over the last few months, and initial dysphonia. Objective examination revealed a large infiltrating neoplasm, involving the right pyriform sinus and the entire homolateral hemilarynx, which appeared fixed; a large right latero-cervical adenopathic protuberance, 7 cm in diameter, had appeared 3 months earlier.
The patient denied drinking and smoking, and did not present any significant occupational risk; the case history revealed arterial hypertension which was well controlled with drugs.
Routine blood tests showed a significant hypochromic anaemia, but the patient denied having had any bleeding.
Contrast-enhanced computed tomography (CT) of the head/neck/chest/abdomen revealed an extensive hypopharyngolaryngeal lesion, on the right, involving the paralaryngeal and pre-epiglottic spaces, with large liquid filled lymph nodes between levels I and IV of the neck, on the right, adhering to the thyroid and internal jugular vein. The other areas examined were negative for metastases.

Table I. Result of immunohistochemical evaluation.

Vimentin (V9)	+
Factor VIII (Z002)	+
CD 34 (TUK 3)	–
Actin (IA 4)	–
Desmin (ZC 18)	–
S 100	–
Cytokeratin (AE1)	–
Cytokeratin (AE3)	–
Pancytokeratin (LU-5)	–
EMA (E29)	–
Thyroglobulin	–
Ki-67	20%
P53 (DO-7)	40%

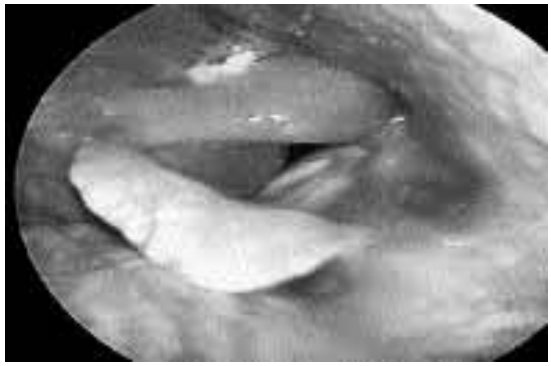

Fig. 1. Optic fibre laryngoscopy.

Microlaryngoscopy and oesophagoscopy confirmed the presence of a lesion arising in the superior part of the right pyriform sinus and extending to the aryepiglottic and arytenoid plicae, the infrahyoid part of the epiglottis, the false and true vocal folds, on the right; the hemilarynx was completely fixed. The mucosa covering the lesion was apparently intact and slightly more erythematous. The subglottic space and oesophagus were within normal limits (Fig. 1).
Multiple biopsies of the lesion were performed.
Histological examination of the purplish-red specimen revealed a haemorrhagic tumour with irregular vascular spaces surrounded by cells with a pleomorphic, hyperchromic nucleus; the percentage of necrosis detected was 20% and mitosis was 3-4 per high-power microscopic field under 40X magnification.
Results of the immunohistochemical evaluation, by means of prognostic markers, is shown in Table I.
The morphological and immunohistochemical findings, therefore, supported a diagnosis of angiosarcoma.
The patient underwent total pharyngolaryngectomy with "en bloc" lymph node removal by radical neck dissection, on the right and selective dissection, between levels II and IV, on the left; right hemithyroidectomy was also performed (Fig. 2).
The histological examination of the surgical specimen, 14x9x5 cm in size, revealed ulcerated mucosa in the right pyriform sinus (where previous biopsies had been performed); the mucosa sheathed a reddish-grey neoplasm, approximately 5x4x4 cm in size, which infiltrated the wall of the larynx and the adjacent soft tissue, in its medial portion.
A total of 21 lymph nodes were excised, on the left, all of which were negative for metastasis; on the right, of the 23 lymph nodes examined, nine were found to be metastatic, and one of these, measuring 2 cm, presented capsular invasion.
The patient then underwent a cycle of radiotherapy, as outlined below:

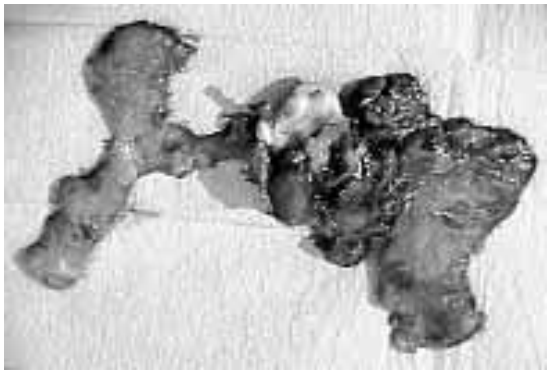

Fig. 2. Surgical specimen.

1. pharynx and neck: 41.8 Gy - 22 fractions - 2 fields;
2. barrage: Gy - 22 fractions - direct;
3. neck (right): 6 Gy - 3 fractions - direct;
4. boost: 21 Gy - l0 fractions - 2 fields.

At the next ORL check-up and at follow-up 6 months later, comprising CT scan of the neck and chest, the patient was free of disease; clinical check-ups continue on a monthly basis.

Discussion

Laryngeal sarcomas account for less than 1% of all malignant tumours of the larynx. Angiosarcoma, in fact, involves the head and neck mainly in sites such as the scalp and face, while it only rarely affects the larynx.
It should, however, be stressed that the true incidence might be even lower than that reported in the literature, since some of the earlier cases described may have been misdiagnosed as other vascular tumours of the larynx [3] (Kaposi's sarcoma, haemangiopericytoma) or as non-neoplastic lesions (granulomas secondary to intubation) [4].
A review of the literature [2 3 6-11] reveals a total of 16 cases (the first dating back to 1924 [6]).
As far as concerns the survival rate, this is one of the sarcomas with the grimmest prognosis. If all possible sites of origin of the tumour are evaluated, the mean survival is 20 months [5]. If only the larynx is considered, no conclusions may be drawn, due to the paucity of the case reports in the literature, even if the aggressiveness of this tumour is evident, with death usually occurring only a few months after diagnosis due to local recurrence or distant metastases (especially in the lung). In only one case, is the patient still alive with no signs of disease, after 6 years [3].
The risk factors in this neoplasm are unknown, even if it is believed to be secondary to radiation therapy [2 5 10].
The treatment of choice for laryngeal angiosarcoma is surgical excision (ample and radical), followed by adjuvant post-operative radiotherapy [11], as this tumour has shown variable radiosensitivity: some Authors have observed good palliative results [12 13], while others have reported total radioresistance [14 15].

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