Lymphoepithelial carcinomas are characterized by proliferation of undifferentiated malignant epithelial cells together with an infiltrate of mature lymphocytes. They mainly appear in the nasopharynx but can also be encountered in other upper and lower aerodigestive sites such as oropharynx, stomach, trachea, and others. When they occur in the larynx they usually do so in the laryngeal ventricle and are characterized by protrusion of the laryngeal band, visible in laryngoscopy. They mainly metastasize to cervical lymph nodes no matter what size the tumour is and distant non-nodal metastases are not infrequent. Cases of 2 synchronous lymphoepithelial tumours in ENT regions without nodal involvement, albeit theoretically possible, are very uncommonly encountered. The very scant reports of primary laryngeal lymphoepitheliomas or only-laryngeal metastatic tumours make 2 simultaneous ENT lymphoepitheliomas an exceedingly rare form of presentation that may lead to important controversies regarding their diagnosis, staging and treatment. A case of 2 synchronous neoplasms in the larynx and nasopharynx is reported and the most significant aspects of this uncommon feature are discussed.

**Key words:** Synchronous lymphoepitheliomas. Laryngeal lymphoepithelioma. Laryngeal metastases. Rare laryngeal tumours. ENT lymphoepitheliomas.

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**INTRODUCTION**

Lymphoepitheliomas or undifferentiated carcinomas are malignant tumours of epithelial origin with an infiltrate of reactive lymphocytes, that were first described in the
occulting the nasopharynx almost entirely and penetrating through the right nostril toward the nasal fossa where it prevented the fibroscope from passing. No significant cervical adenopathies or masses are observed. There were no pathological findings in the remaining ENT examination.

In the study and image-based staging of the patient by means of computerized tomography (CT), the presence of a tumour was demonstrated to originate in the nasopharynx and spread to the right nostril and nasal fossa, without spreading to the oropharynx or to the parapharyngeal space; nor was there invasion of bone structures or paranasal sinuses, together with inflammatory polyposis characteristics affecting frontal sinuses and anterior ethmoids. No cervical adenopathies were apparent (Figure 1).

Biopsy of the lesions informed us that the inflammatory polyps were undifferentiated carcinoma of the nasopharynx (Figure 2). Distant image-based staging was completed and no masses were seen that would indicate metastasis. With the diagnosis of undifferentiated carcinoma of the nasopharynx T2aN0M0 (stage II), the patient was referred to the services of medical oncology and oncological radiotherapy for treatment. In the simulation CT for radiotherapy field planning, a small elongated image was seen, apparently originating in the left ala of the thyroid cartilage, with signs of destruction, eccentric growth originating from it and presenting a hard consistency on palpation, without any other clinical symptoms (Figure 1). A mild protrusion of the left laryngeal band was revealed on a further laryngoscopy; the rest of the larynx appears to be normal and laryngeal mobility was conserved. Given the difficulties in access for endolaryngeal biopsy and with the intention of not delaying the start of radiation therapy, it

nasopharynx, and although this is where they are most common, they have also been reported in other ENT areas, albeit with an extremely low incidence. They correspond to WHO type 3 for nasopharyngeal tumours. Their undifferentiated nature makes them highly aggressive and they are capable of metastasizing diffusely throughout the cervical node basin and also cause distant metastasis with very small tumour sizes. The most common non-nodal metastases are in the skeleton, lung, and liver. To the best of our knowledge, there have been no cases reported of lymphoepitheliomas or synchronous undifferentiated carcinomas of the nasopharynx and larynx or of single laryngeal metastases of undifferentiated carcinomas of the nasopharynx, although it is theoretically possible. We report the case of a double lesion of the nasopharynx and larynx, both of which were reported following pathology study as lymphoepitheliomas. The controversies of these circumstances were derived from both the patient’s tumour staging, as well as his treatment.

CLINICAL CASE

Sixty-four-year old male patient with no history of interest who presented at the Emergency Room of our hospital due to significant, active, bilateral epistaxis. Likewise, the patient reports nasal respiratory failure, closed rhinolalia, hearing loss, tinnitus and progressive bilateral obstruction of the ear for the last five months. During the ENT examination of the patient, the presence of apparently inflammatory bilateral nasal polyposis was noted along with the presence of an exophytic mass behind and at the level of the nasopharynx, occupying the nasopharynx almost entirely and penetrating through the right nostril toward the nasal fossa where it prevented the fibroscope from passing. No significant cervical adenopathies or masses are observed. There were no pathological findings in the remaining ENT examination. In the study and image-based staging of the patient by means of computerized tomography (CT), the presence of a tumour was demonstrated to originate in the nasopharynx and spread to the right nostril and nasal fossa, without spreading to the oropharynx or to the parapharyngeal space; nor was there invasion of bone structures or paranasal sinuses, together with inflammatory polyposis characteristics affecting frontal sinuses and anterior ethmoids. No cervical adenopathies were apparent (Figure 1).

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was decided to biopsy the tumour by means of fine needle puncture-aspiration, with a subsequent report of lymphoepithelial carcinoma. On the basis of the patient’s history, this tumour is considered to represent metastasis of the undifferentiated carcinoma in the nasopharynx and the patient was re-staged as T2N0M1 (stage IV). The patient has been treated with chemotherapy and concomitant radiation therapy with a full clinical response. The protocol that was followed is based on 3 cycles. In an initial cycle, 100 µg/m² of cisplatin (CDDP) are administered and radiotherapy, beginning with a total dose of 50 Gy on both lesions, 50.4 Gy on laterocervical node basins, and 46 Gy on posterior cervical basins, at a rate of 2 Gy/day with 6 MeV photons (9 MeV on the posterior basins). Subsequently, these were overlapped by a booster with 18-MeV photons at a rate of 2 Gy/day on the nasopharynx until a total dose of 70 Gy is reached and with 6-MeV photons on the larynx up to 70 Gy. In a second cycle, 80 µg/m² of CDDP and 100 µg/m² of 5-FU were administered over 4 weeks. Treatment was completed with a fourth cycle of CDDP at a rate of 80 µg/m².

DISCUSSION

The low incidence of lymphoepitheliomas or undifferentiated carcinomas of the larynx hinder the establishment of clearly defined clinical patterns and treatment regimens. They generally originate in the lymphoid and epithelial tissues of the laryngeal ventricle, although the bibliographic references available are scant3,8-10. They comprise undifferentiated, non-keratinized epithelial cells, with the presence of numerous mitoses together with predominantly T reactive lymphoid infiltrate of non-neoplastic characteristics and the absence of significant connective stroma. The lymphocytic infiltrate is also present in the metastases4,9,10,11. Because they are undifferentiated, they are highly aggressive both locoregionally and distantly, and can metastasize early and diffusely along the cervical node basins, irrespective of tumour size as a first option, and to the lung and bone when they present distant metastases5,9,10. Other distant metastases are exceptional and metastatic ENT organ involvement is highly unusual when there is no prior involvement of the node basins.

When the nasopharynx is involved, its favourite place to spread to, it retains this name but it becomes known as lymphoepithelioma-like carcinoma11,12 when it involves different areas.

When located in the larynx, they originate mainly from the laryngeal ventricle constraining a protrusion or bulging of the laryngeal band, sparing the mucosa covering it, or ulceration in advanced cases6,10.

They respond well to radiation therapy, with or without prior induction chemotherapy depending on the stage of the lesion, although they very often present as advanced disease with cervical metastases6,13. This favourable response, together with the anatomical characteristics of the nasopharynx limiting access for the surgeon, has led to non-surgical treatment being the first option6,9,12,14. Likewise, tumours of identical histological lineage located in other areas of the body have been treated in exactly the same way as nasopharyngeal tumours3,10,14.

However, for more accessible locations, such as the larynx, other authors prefer surgery, with or without complementary radiation therapy depending on tumour stage, although the results must be evaluated with caution, given that the low incidence of tumours in these locations makes it difficult to extract definitive conclusions regarding the efficacy of one treatment strategy or another in these lesions5,8,9,12,13,17.

In our patient, the initially normal laryngoscopic and radiological images, the history of undifferentiated carcinoma of the nasopharynx diagnosed and confirmed by pathology study and the appearance of the laryngeal lesion in the months following the appearance of the nasopharyngeal lesion led us to consider the possibility of laryngeal metastases of undifferentiated carcinoma of the nasopharynx; hence, the tumour stage would have been T2N0M1 (stage IV). In contrast, the absence of other clinical or radiological evidence of cervical, pulmonary, hepatic or other node involvement; the extremely exceptional incidence of single metastases in ENT areas, and specifically the larynx, without there being any prior nodal metastases18,19; the laryngoscopic image revealing protrusion of the laryngeal band and de-structuring of the thyroid cartilage in the adjacent area, and the fact that some authors state that lymphoid infiltrate does not typically appear in the metastases20 would lead us to think of a synchronous undifferentiated laryngeal carcinoma; as a result, the nasopharynx tumour stage would have been T2N0M0 (stage II) and there would have been a laryngeal tumour T4N0M0 (stage IV), which would necessarily entail a change in therapeutic strategy, both treatment as well as the postoperative follow-up of the patient. It would also have a bearing on the prognosis for cure and survival6,7,19-27.

Having studied the case, we decided to classify the laryngeal lesion as metastasis of the nasopharyngeal tumour, albeit with some reservations. Bearing these considerations in mind and in light of all that has been previously stated, and given the good response that can be expected with non-surgical treatment due to the histological type of both tumours and respecting the patient’s decision, chemotherapy and concomitant radiotherapy was chosen to treat both lesions and other possible microscopic metastases, reserving laryngeal surgery as salvage treatment should there be signs of relapse and should there be no distant metastases or relapse at the level of the nasopharynx, a circumstance that has not arisen to date.

CONCLUSIONS

Laryngeal lymphoepitheliomas, either primary or synchronous, or a sole metastatic lesion, are uncommon neoplasms of which there are scarce series published in the literature, which makes it difficult to draw definitive conclusions with respect to optimal treatment approach and survival according to treatment and tumour stage, as seen in our patient.
REFERENCES