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NEUROENDOCRINE CARCINOMA OF THE LARYNX WITH LAMBERT-EATON MYASTHENIC SYNDROME: A RARE CASE REPORT.

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Introduction

Neuroendocrine carcinomas (necs) of the larynx are varied and heterogeneous tumours of rare observation in clinical practice. The WHO classification of 2017 divides them into: (i) well differentiated neuroendocrine carcinomas (WD-NEC); (ii) moderately differentiated neuroendocrine carcinomas (MD-NEC); and (iii) poorly differentiated neuroendocrine carcinomas (PD-NEC), which includes (a) small cell neuroendocrine carcinoma (smcc) and (b) large cell neuroendocrine carcinoma (LCNEC).

Case report

A 68-year-old male patient presented with severe dysphonia and dysphagia during the previous 3 months. Fibrolaryngoscopic examination revealed the presence of a voluminous ulcer-vegetative neoformation that involved the epiglottis, the anterior commissure, the aryepiglottic folds and the tongue base, with a significant reduction in the respiratory space (Figure 1). Blood chemistry tests revealed positivity for carcinoembryonic antigen and tumour antigen 15-3. The patient's clinical history was characterized by poor personal care, marked asthenia, cachexia, xerostomia, constipation and urinary retention. The Karnofsky index was 50%. He lived in a retirement home and was suffering from dysphagia and chronic vascular disease. A total-body computed tomography examination revealed a voluminous expansive neoformation that presented enhancement after contrast, of the left lateral wall of the larynx. There were also multiple bilateral lymphadenopathies (Figure 2). The patient underwent a total laryngectomy with a radical modified neck dissection on the left side with sacrifice of the internal jugular vein and spinal nerve. Selective neck dissection of levels II, III and IV was performed contralaterally. The excised lesion was extremely voluminous (10 cm X 8 cm) (Figure 3). The histological examination showed a poorly differentiated carcinoma (G3) with aspects of neuroendocrine differentiation consisting of small cells with pale cytoplasm, nuclei with finely blotted chromatin and absence of nucleoli. The immunohistochemical study showed positivity of the neoplastic cells for CK7, synaptophysin and only focal mild positivity for CD56. The results were negative for p40 and p63. The Ki-67 proliferation index was approximately 85%. In the left neck dissection, there were seven lymph nodes infiltrated by carcinoma; and in in the right neck dissection, there were two infiltrated lymph nodes. The patient was treated with three cycles of neoadjuvant chemotherapy using the cisplatin–etoposide regimen (130 mg/m2 cisplatin intravenously per day for 3 days and 45 mg/m2 etoposide intravenously per day for 2 days every 3 weeks) and then radiotherapy with a total dose of 70 Gy using a linear accelerator. Approximately 1 month after surgery, a clear improvement in the patient's condition was recorded. After 3 months, the patient resumed walking without the aid of an orthopaedic walker in addition to there being an improvement in autonomic manifestations (constipation, xerostomia, urinary retention). Four years after surgery, the patient is still in follow-up at and is free from disease.

Fig. 1

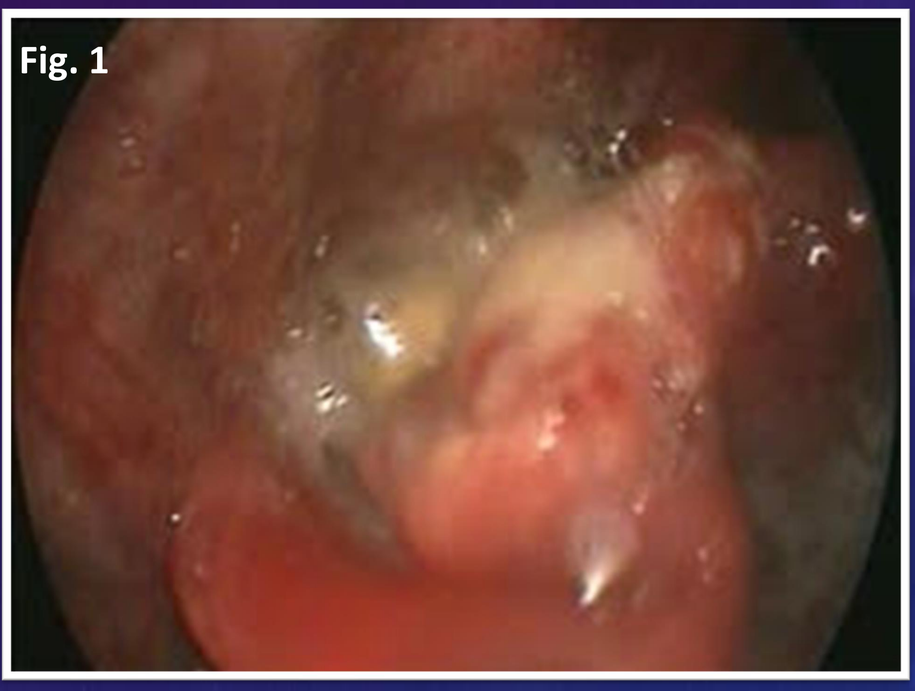

Fig. 2

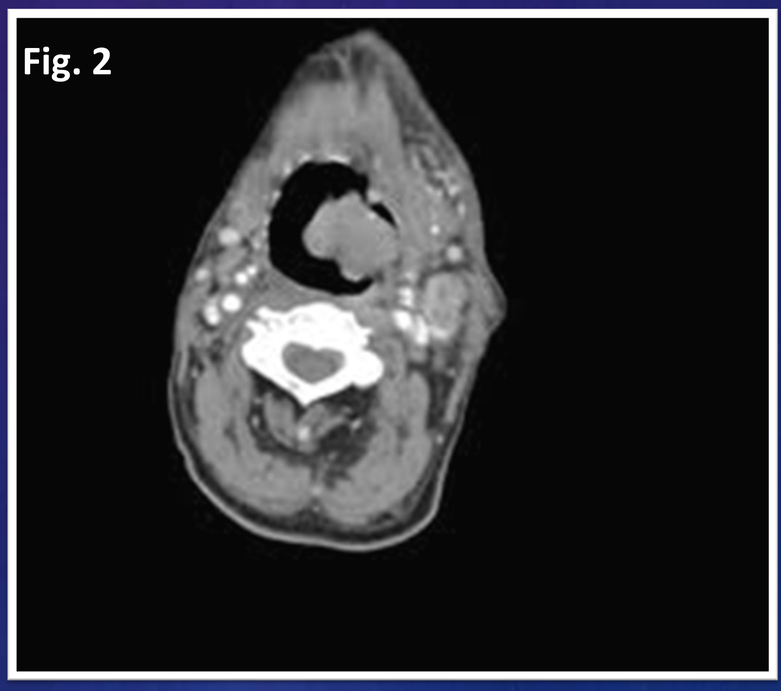

Fig. 3

Discussion

Nowadays there aren't significant differences for an optimal therapeutic management between the various types of NEC. A radical surgical approach is recommended in WD-NEC and MD-NEC; and in the latter this is accompanied by laterocervical neck dissection as it is possible to develop micrometastases in the early stages of this cancer. The most effective approach to the treatment of these lesions is yet to be determined: currently, it seems that only early and aggressive therapies with a multimodal approach can be considered. Paraneoplastic syndromes related to neuroendocrine carcinomas of the larynx are extremely rare but can cause severe symptoms and almost always correlate with poor prognosis. Of the 10 cases of PNS related to laryngeal neuroendocrine carcinoma reported in literature, nine of these syndromes were of an endocrine type. Only one case of PNS linked to laryngeal cancer (an SmCC) had a neurological manifestation, which was LEMS. **This current case report represents the second patient with a neurological manifestation in whom the laryngeal cancer was first treated with surgery.** For a large proportion of them, a precise mechanism underlying paraneoplastic syndromes' development has not yet been identified, but in some cases, PNS are the consequence of an ectopic synthesis of a hormone or a mediator by the tumour, while the structures affected by the symptomatology are not affected by the tumour. Neuroendocrine carcinomas of the larynx are rare lesions with different prognostic characteristics. PNS can rarely accompany the neoplasm and therefore be useful in monitoring its evolution. The diagnosis should be made using a multidisciplinary approach. An early diagnosis of a PNS and its treatment can have positive effects on the general clinical outcome, with more appropriate direct therapy on the tumour and an improvement in quality of life.