Radiol Oncol 2002; 36(3): 225-9.

Extramedullary plasmacytoma of the larynx: a report of three cases

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Purpose. *To report three cases of extramedullary plasmacytoma of the larynx treated at the Institute of Oncology in Ljubljana between 1969-1999.*

Results. *All three patients were treated with radiotherapy only, which resulted in permanent local and regional control of 7.8, 4.7 and 3.5 years. The function of the larynx was preserved in all of them. Two patients died, both to the causes other than plasmacytoma. In none of the patients disease progressed to multiple myeloma.*

Conclusions. *Extramedullary plasmacytoma of the larynx is a rare disease, highly curable when radiotherapy is used. Moderate radiation doses and limited fields ensure excellent cosmetic and functional result.*

Key words: laryngeal neoplasms - radiotherapy; plasmacytoma

Introduction

Extramedullary plasmacytoma (EMP) is a rare tumor of the larynx. Whereas more than 80 % of all EMP arise in the upper aerodigestive tract, only about 10 % of them are laryngeal.[1] Since the first report on EMP of the larynx in 1913 by Wachter[1], less than 100 additional cases have been described in the world literature, the subglottis and epiglottis area being the most commonly involved subsites within the larynx.[2] It occurs approximately three times more often in men than in women, and is usually seen at the age of 50-70 years.[2]

In the present report, we describe three cases of EMP of the larynx, which were seen at the Institute of Oncology in Ljubljana between 1969-1999. The incidence and difficulties in diagnosing the disease, and treatment options currently available are discussed.

Received 10 September 2002
Accepted 20 September2002

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Case reports

Case 1.

A 65-year-old male was diagnosed with EMP after a two-year history of hoarseness. From the very beginning, a reddish thickening that extended downwards toward the anterior commisure, with yellowish cystic top was

seen on the anterior third of the left ventricular fold on indirect laryngoscopy. No clinically evident lymphadenopathy could be found on the neck. No further diagnostic procedures were carried out at that time. After 18 months, a directoscopy with biopsy was performed due to gradual deterioration of his voice. Histopathological examination of tissue sample revealed highly vascularized fibrous stroma with intense lympho-plasmacytic infiltration, partially covered with parakeratotic squamous epithelium with partially ulcerated surface. Because of inconclusive histological report, further enlargement of the lesion, and persistent hoarseness, a second biopsy was taken one month later. Nonspecific granulation tissue with multinucleated giant cells was found; after staining, extensive deposits of amyloid with numerous plasma cells were seen, and a differential diagnosis of amyloidosis was made. On the review, the patient was diagnosed as having plasmacytoma with kappa light chain restriction. Of diagnostic tests aimed to exclude multiple myeloma, only skeletal survey was performed, which showed no abnormality. The patient was treated with radiotherapy, using cobalt-60 unit and the technique of two opposing lateral fields covering larynx and nodal regions Ib-IV. A tumor dose of 40 Gy was delivered in 2 Gy daily fractions five times per week. Afterwards, a boost of additional 20 Gy, using the same fractionation regimen and technique, was applied to the larynx and level II-III neck nodes only. Partial response regarding the size of the lesion with mobile larynx was seen at the end of the therapy, and at all subsequent follow-up visits. The patient died 7.8 years after having diagnosed EMP due to cerebrovascular insult. There were no tumor recurrence or systemic dissemination observed, while the patient's voice improved considerably even if not completely compared to pre-diagnostic state.

Table 1. Incidence of extramedullary plasmacytoma of the larynx in relation to other laryngeal neoplasms: review of the literature

Author (Ref.)	Incidence (%)
Cady, 1968 (3)	0.04
Shaw, 1972 (4)	0.07
Gorestein, 1976 (5)	0.19
Kralj, 1988 (6)	0.16
Kost, 1990 (7)	0.45
Present report	0.10

Case 2.

A 72-year-old male presented with a three-week history of acutely evolved hoarseness. Indirect laryngoscopy revealed a corn grain size polyp on the middle third of the right vocal cord. The vocal cord mobility was intact, as was the airflow. No enlarged lymph nodes were detected on the neck. Ablation of the tumor was performed under local anesthesia. Histological diagnosis was EMP, immunoglobulin-negative, with lambda light chain restriction. To exclude dissemination of the disease, immunoelectrophoresis of the serum and urine, and skeletal survey were done. Bone marrow biopsy was, however, not performed. The patient was irradiated with Co-60 gamma rays and two opposed lateral fields of 7×7 cm^2 covering the glottis and nearby structures only; there was no intention to treat regional lymphatics. The tumor dose of 46 Gy was applied in 2 Gy-daily fractions five times per week. On regular follow-up examinations, there was no tumor recurrence or disease dissemination detected. The patient retained the functional larynx with normal voice preserved for the next 4.7 years when he died due to a new primary tumor, colorectal adenocarcinoma.

Case 3.

A 50-year-old healthy female had a seven-month history of increasing hoarseness. On microlaryngoscopy under general anesthesia,

a pinky lesion occupying the anterior part of the right sinus of Morgagni, the size of a pea, was described by the examiner, and declared clinically for adenoma. There was no restriction in vocal cord mobility or clinically evident regional lymphadenopathy. The diagnosis of extramedullary plasmacytoma with kappa light chain restriction and negative immunohistochemistry for immunoglobulins was made on histopathological examination of bioptic specimen. The results of both serum and urine immunoelectrophoresis were within normal ranges as were those of beta-2-microglobulin and bone marrow biopsy. No osteolytic lesions were detected on skeletal survey. She was treated by radiotherapy using cobalt-60 gamma rays. First, the whole larynx and neck lymphatics of regions Ib-V were irradiated. A three-field technique of two opposing lateral fields and low anterior field was used to a tumor dose of 40 Gy delivered in 2 Gy-daily fractions five times per week. A booster dose of 10 Gy (2 Gy/fraction) was than added through two opposing fields to the tumor bed only. At the end of the therapy, no tumor was visible on indirect laryngoscopy with vocal cord mobility preserved. At the moment - 3.5 years after the diagnosis - the patient complains of mild xerostomia and caries; there is no sign of local recurrence or systemic dissemination, with serum beta-2-microglobulin being within the normal range. Her voice is preserved and its quality satisfactory.

Discussion

Even in specialized oncology centers, the probability of coming across with patient with EMP of the larynx is extremely small. According to the literature, it represents only 0.04-0.45 % of malignant laryngeal tumors (Table 1).[3-7] In other words: EMPs originating in the larynx account for 11 % of the upper aerodigestive tract plasmacytomas,[2] whose incidence is estimated to be less than 1 % of all head and neck malignancies.[8] In Slovenia, there were 2895 new malignant tumors of the larynx and 31 EMPs registered by the Cancer Registry during the years 1969-1999.[9] Three cases reported here represent 0.10 % and 9.7 %, respectively, of tumors in these two groups.

Diagnosis of EMP of the larynx is often delayed. Presenting symptoms are usually limited on non-specific, slowly progressive hoarseness over the period of months to years. Acute presentations are rare. Dysphagia, stridor, and pain are late symptoms, associated with locally advanced disease.[10] Secondly, the gross appearance of the lesion is variable: from yellow gray to dark brown polypoid or sessile mass, or diffuse thickening of the involved organ. The surface is usually smooth and the consistency semi-firm and rubbery.[5,8]

In addition, there are also problems with tissue sampling and histological identification. The plasma cells are commonly found in abundance in a variety of benign conditions, including chronic inflammation, which is often present in the immediate proximity of malignant tumors. For example, Pahor[11] discussed a case with initial diagnosis of a plasma cell polyp that was, two years later, correctly identified as laryngeal plasmacytoma. Two of three cases presented by Maniglia and Xue [12] were initially misdiagnosed as chronic inflammation and »amyloid deposit«, respectively, while Kost [7] reported on difficulties in diagnosing EMP in two of four patients. In the present series, we share the same experience in case 1. In all of our cases, however, immunohistochemical assessment of monoclonality was performed to exclude benign polyclonal lesions, which was not the case in the majority of other reports.[13]

After defining the locoregional extent of the disease, all additional hematological, biochemical and radiological tests are focused to identify or exclude the presence of other plas-

macytomas, or of systemic dissemination to multiple myeloma.[2] So far, none of the tumor characteristics or laboratory parameters could have predicted reliably the dissemination of the disease, which occurs most often in the first two years following the diagnosis of EMP.[14] EMP, however, has a tendency of being localized disease. According to the results of extensive literature review reported by Alexiou *et al.* [2], regional nodes are invaded in less than 10 % of EMP patients, and in approximately 16 % of patients, the disease progresses to multiple myeloma. The same holds true also for laryngeal tumors and our experience supports the rule.

A number of treatment options are available for EMP of the larynx, including radiotherapy, laser surgery, several endoscopic or open conservation procedures, and chemotherapy. The advantage of radiotherapy is its effectiveness due to proven radiosensitivity of the disease, high probability of excellent voice preservation [15], and less restrictive treatment selection criteria as compared to surgery. The disadvantages include a course of radiotherapy extending over several weeks and troublesome acute radiation toxicity. Analyzing larger series of EMP patients from our institution, we came to the conclusion that EMP is a highly curable disease when radiotherapy is used with or without previous surgery. According to the bulk of disease, 40-50 Gy, conventionally fractionated, is recommended for macroscopic disease, while after radical surgery, close observation only is justified. No elective radiotherapy should be considered in node-negative patients, but neck dissection followed by radiotherapy (36-40 Gy) or only radiotherapy (40-50 Gy) is recommended for node-positive cases. Irradiated volume should include surgical bed or affected nodal region(s) on the neck only.[14]

Surgery is, however, usually employed as a salvage procedure after unsuccessful radiotherapy, even though some authors consider it for the first-line therapy to avoid long-term sequeale of radiotherapy.[2,13] The role of chemotherapy in the treatment of primary tumors, recurrent disease, or in preventing or delaying progression to MM is controversial. As a rule, it is reserved for inoperable recurrences or disseminated disease.[14] After radical therapy, tumor control rate is approaching 100 %, but overall survival rate, ranging widely, is critically dependent on the degree of conversion to multiple myeloma.[2,14]

In conclusion, EMP of the larynx is a rare tumor, representing only 0.1 % of laryngeal malignancies in Slovenia. Diagnosis is often delayed due to non-specific presenting symptoms and gross tumor appearance, and difficulties related to histological identification of the disease. Tests to search for systemic dissemination are mandatory. Radiotherapy is highly effective in EMP, ensuring larynx preservation with excellent voice in the majority of patients treated.

Acknowledgement

This work was supported by the Ministry of Edication, Science and Sport of the Republic of Slovenia, Grant J3-3010-0302-01.

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