Monoclonal extramedullary plasmacytoma (EMP) is a rare plasma cell tumor. The diagnosis is based on a mass of clonal plasma cells separate from bone or bone marrow without evidence of occult disease elsewhere. It occurs in the upper aerodigestive tract in more than 80% of patients, most often in the nasal cavity, paranasal sinuses, nasopharynx, oropharynx and larynx. Regional nodes are invaded in less than 10% of patients. The disease is more common in males with a peak incidence in the sixth decade. Primary EMP often presents with a mass and produces local compressive symptoms. The differential diagnosis includes benign reactive processes, carcinoma and lymphoma. Radiotherapy (RT) is an effective modality of treatment for EMP with high local control rates (85% to 100%). Currently moderate dose RT (40-50 Gy) using involved fields is recommended.

**CASE**

A 76-year-old man presented with a 5-month history of painful swallowing. He was a farmer and his past medical history included hypertension and a coronary bypass. He was a non-smoker. At the time of presentation he was experiencing partial airway obstruction. Endoscopically, a tumoral mass approximately 4 cm in diameter reaching to the left tonsillar region and lingual epiglottis from the tongue base was detected. Physical examination revealed a mobile, single 3-cm asymptomatic left cervical midjugular lymph node. MR imaging demonstrated a solid submucosal mass, measuring 4×4.5×7 cm, in the tongue base and left tonsil which partially obstructed the oropharyngeal airway (Figure 1). Additionally, post Gd-DTPA T1-weighted coronal MR image showed deep cervical bilateral lymph nodes. The mass and nodes showed a strong contrast enhancement. Clinically, this lesion suggested squamous cell carcinoma or malignant lymphoma. Histopathological analysis of the biopsy revealed a diffuse infiltration of atypical plasma cells beneath the surface epithelium. Plasma cells had a prominent eccentric nucleus with a 'spoke wheel' chromatin and abundant basophilic cytoplasm (Figure 2). Immunohistochemical study showed diffuse cytoplasmic and focal membranous CD138 (Syndecan-1, Clone 5F7, LabVision, Fremont, CA) and cytoplasmic CD79a (DAKO, Copenhagen, Denmark) immunoreactivity (Figure 3a and 3b). Focal membra-
Figure 2. Plasma cells with eccentric nucleus and abundant cytoplasm (hematoxylin eosin ×400).

Figure 3. a) Diffuse cytoplasmic, focal membranous (arrows) CD138 staining on the plasma cells (streptavidine-biotin peroxidase ×400). b) CD79a positivity on the majority of the neoplastic plasma cells (streptavidine-biotin peroxidase ×400). c) λ-light chain positivity with lack of κ-staining. d) Note the scattered reactive plasma cells (arrows) on the anti κ-immunostaining (streptavidine-biotin peroxidase ×100, ×200).
nous EMA (DAKO, Copenhagen, Denmark) positivity with lack of CD20 (Clone L26, LabVision, Fremont, CA) staining were detected on the neoplastic plasma cells. Diffuse strong γ-light chain (clone HP6054, LabVision, Fremont, CA), expression was detected whereas only scattered plasma cells were positive with anti κ-antibody (Clone L1C1, LabVision, Fremont, CA) (Figure 3c and 3d). Based on these findings, the tumor was diagnosed as a plasmacytoma.

He was referred to the hematologists. Further clinical examinations were performed to rule out multiple myeloma (MM). Quantitative immunoglobulins, full blood count, urea, calcium, creatinine, and β-2-microglobulin were all within normal ranges. No histological evidence of bone marrow involvement and distant bone lesions on radiological skeletal survey were detected. In serum protein electrophoresis, a high level of α-2 globuline and in urine analysis, proteinuria and high level of lambda light chain (6.24 mg/dL) were detected. After ruling out MM, the patient was diagnosed as having EMP of the oropharynx, which is of unknown origin.

Because of the morbidity of the surgery, the patient was subsequently treated with steroids and external beam radiotherapy at a dose of 50 Gy in 25 fractions with cobalt-60 gamma rays to involved sites (oropharynx and bilateral level Ib-V cervical nodes) with a three-field technique (one anterior and two lateral opposing fields). At the end of the treatment, there was tumor response and the patient was symptom free. Three months after the treatment, a partial response (a 75% reduction in size of tumor) and a complete response in the nodes were detected on MR image (Figure 4). On the left tonsillar site a remnant tumoral mass (2×1.5 cm) remained. All blood and urine tests were normal. The patient died of an intercurrent disease at 15 months from the diagnosis with no evidence of disease.

**DISCUSSION**

EMP is a plasma cell neoplasm of the soft tissue. It is usually well localized, with 80% of them occurring in the submucosa of the upper aerodigestive tract. The most common locations for an EMP to occur are the nasal cavity, paranasal sinuses, nasopharynx and oropharynx. The predisposition of this pathology for the submucosa of the upper respiratory tract has led to the hypothesis that chronic stimulation by inhaled irritants or viruses may promote the development of plasmacytoma. In our patient, we had worked as a farmer for 55 years and might have been exposed to agricultural inhaled irritants for a long time since EMP appears as a slowly growing mass and the diagnosis is commonly delayed. Huge tumoral masses preclude the origin of the tumor; therefore, it may not be defined until the treatment is completed. At the beginning, the origin of the tumor in the presented case was reported as the left tonsillar site or base of the tongue. However, 3 months after treatment a remnant tumoral mass was detected on the left tonsil on MR image. The base of the tongue and the left tonsil were considered as one tumor.

EMP involving the tonsillar site is rare. Alexiou et al reported that 82.2% of 869 cases of EMP described in the literature were found in the upper aerodigestive tract, and 17.8% of EMPs arising in the upper aerodigestive tract were in the oropharynx. To date, there have been 11 reported cases of tonsillar plasmacytoma in the series of head and neck EMPs and as case reports in the English medical literature. They were treated predominantly with surgery and radiotherapy giving a median dose of 40 Gy to the tumor and regional nodes. Local control was achieved in all patients. In the present case, the patient was treated only with RT at the dose of 50 Gy and local control was achieved.

Histologically, plasmacytomas have the typical microscopic appearance of a monomorphic plasma cell infiltrate set in a sparse, delicate, and reticulum stroma.
The plasma cells themselves are characterized by round eccentric nuclei. One type of Ig light chain—either kappa or lambda—is detected by immunohistochemical staining. The differential diagnosis includes benign reactive inflammatory processes, squamous-cell carcinoma and lymphoma. In the presented case, the presence of an epithelial tumor was excluded easily by the morphological assessment of the biopsy. Diffuse plasma cell infiltrate and monoclonality detected by the immunohistochemical staining directed us to rule out a benign reactive process in the differential diagnosis. Another main entity that we considered in the differential diagnosis is the plasmacytic differentiation of non-Hodgkin lymphoma. Plasmacytic differentiation of a marginal zone lymphoma and lymphoplasmacytic lymphoma was excluded by negativity of CD20 immunostaining. Plasmacytic differentiation is less commonly seen in other B-cell lymphomas, including small lymphocytic lymphoma and diffuse large B-cell lymphoma. In the present case, the uniformity of plasma cells and the immunohistochemical findings strongly supported a plasmacytoma.

Although levels are lower than the ones in MM, one-third of cases of EMP show a monoclonal band of serum protein at diagnosis and Bence-Jones protein is rarely seen in the urine. The presence of monoclonality did not predict the development of MM. These markers usually return to normal ranges after successful treatment of the primary disease. The presence of paraprotein at diagnosis but not its persistence may be an important indicator of dissemination of EMP. It was not possible, however, to analyze this relationship in a rigorous way because of the small number of cases with paraprotein at diagnosis. In our case, there was a high level of lambda light chain in urinalysis. Three months after the treatment, the markers had returned to normal ranges.

Because of the proven radiosensitivity of the disease, RT plays a main role in the treatment of EMP. No conclusive data have been published on the optimal radiation dose for EMP. Many authors have reported a wide range of doses varying from 30 to 66 Gy. Although some studies reported no dose-response relationship in RT for plasmacytomas, the others suggested that 45-50 Gy is necessary for a high local control rate. Mendenhall et al reported that for the patients treated with ≥40 Gy of radiation, there was only 6% incidence of local failure, which was superior to 31% for those who received <40 Gy. A higher dose (up to 50 Gy in 25 fractions) was recommended for bulky disease (>5 cm). In our case, a dose of 50 Gy was given because of a bulky tumor. Regression could be slower than expected, with the complete response occurring within 12 months after completion of treatment. In the presented case, 3 months after the treatment, a partial response was detected on tumor and a year after treatment a complete response was detected on MR image.

The other important issue related to RT is the necessity of elective regional lymph node irradiation (ENI). Cervical node metastases varies from 7% to 30% for EMP at the time of diagnosis. Some authors reported a relatively high rate of out-field nodal relapse, up to 18% and do recommend ENI. Others present a negligible risk for nodal relapse of up to a maximum 4% so do not recommend ENI. However, a third group of authors recommend a selective approach, with regional node irradiation to be implemented only in the case of bulky local disease or primaries originating from sites with rich lymphatic network (i.e., the oral cavity, oropharynx, nasopharynx and supraglottic larynx). In our case, because of the localization of the tumor and the presence of nodal involvement, cervical node regions (level Ib-V) were irradiated.

In summary, the diagnosis of EMP depends on specific histologic and immunohistochemical examination of the lesion, as well as a thorough search of the body to exclude MM. MRI is a useful method in evaluating the response to treatment and during the follow-up period. The role of surgery should be limited to biopsy, small resectable tumors and locoregional recurrences. Radiotherapy is an effective modality of treatment for EMP with high local control rates. Moderate dose RT (40-50 Gy) using limited fields encompassing the primary tumor and first echelon lymph nodes with primaries originating from sites with a rich lymphatic network is recommended.
EXTRAMEDULLARY PLASMACYTOMA

REFERENCES