

Limited Painful Mouth Opening

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Case Presentation

A 45-year-old woman was referred with a complaint of limited mouth opening. The restriction had progressively increased after the removal of the right lower third molar 2 months earlier. After tooth removal, the treatment for trismus consisted of analgesic, muscle relaxants, and mechanotherapy. Past medical history revealed a left nephrectomy 21 years ago and the loss of 15 kg during the past 4 months. There were no known drug allergies.

On extraoral examination, a slight asymmetry was seen on the left side of the face. The tenderness on the body of the masticatory muscles was recorded on palpation. The parotid glands were nontender and there were no masses. When the patient was referred to our clinic, maximal mouth opening was to 14 mm with right and left lateral excursions of 7 and 3 mm, respectively. There was no temporomandibular joint tenderness, but a deviation was noted with mouth opening. There was a submandibular lymphadenopathy. No sensory disturbance was noted.

On intraoral examination, oral hygiene was poor and she had periodontal problems. A mass was noted in the soft tissues posterior and lateral to the right maxillary tuberosity and retromolar region. Palatinal mucosa was inflamed and fragile on the right upper third molar, and the tooth was mobile (Fig 1).

Panoramic radiography showed that there was no bone irregularity in the extraction socket of the right lower third

molar tooth, but marked resorption of alveolar bone surrounding the right upper third molar and tuber maxilla was seen. The maintenance of bone extending from the ascending ramus of mandible to the coronoid process with a marked change into trabecular structures of the bone was not observed (Fig 2). Contrast-enhanced axial computed tomography (CT) scan demonstrated a heterogeneous enhancement with a large mass extending from the right posterior wall of the nasopharynx that blocked the piriform sinus opening and obliterated the parapharyngeal fatty tissue on the oropharynx and inferiorly angulus mandible to superiorly infratemporal fossa (ITF). There was no bone destruction (Fig 3).

Differential Diagnosis

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A preliminary differential diagnosis can be made from the history, physical examination, and radiographs provided. I will make an orderly assessment of some possibilities and discuss why each should be high or low on that list.

The infectious-inflammatory causes for this clinical and radiographic picture should produce more pain and erythema than is related. Also, no fluctuance is described on palpation and no drainage is reported clinically. Deep infectious problems such as actinomycosis or tuberculosis might produce this picture, but there is no history of lung problems or fever. As such, these items must be placed low on the differential diagnosis.

Odontogenic lesions such as ameloblastoma can be practically ruled out because the lesion appears to be resorbing bone from outside the bone cortex rather than originating within the bone. A more aggressive odontogenic tumor, such as an ameloblastic carcinoma, is similarly ruled out for this reason.

Benign mesenchymal tumors can grow to a large size in this area, such as a schwannoma or neurofibroma, or salivary gland tumors such as a pleomorphic adenoma of the deep lobe of the parotid gland. The lymphadenopathy mentioned does not favor these possibilities but could be caused by the previ-

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FIGURE 1. Intraoral view of the lesion.

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ous extraction of the carious and mobile upper right third molar.

Malignant tumors are the most likely group of lesions to be considered in this case because of the size of the lesion, the homogeneous consistency on the CT scan, the presence of lymphadenopathy, and weight loss. We are not informed whether the reason for the nephrectomy was for malignant or benign disease. The most common malignant kidney tumor in adults is hypernephroma. If this were the reason for the nephrectomy, this would be the top choice on the differential diagnosis. Because of the size and amount of trismus involved, a rhabdomyosarcoma or fibrosarcoma would also have a high degree of suspicion. Lymphoma should also be considered as this is in the area of Waldeyer's ring and could be the presenting sign of the disease. A



FIGURE 2. The maintenance of bone extending from the ascending ramus of mandible to the coronoid process with a marked change into trabecular structures of the bone was not observed.

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FIGURE 3. Axial computed tomography scan shows right soft tissue mass as seen in pterygopalatine fossa (PPF) and ITF; it displaces mandibular ramus laterally. Posterior wall of maxillary sinus was intact and pterygoid process is obliterated.

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metastatic tumor from an unknown primary is also a possibility. The most likely primary location would be breast, lung, or colon. We are given no indication of symptoms from those other systems. Another rare consideration would be a synovial sarcoma, although there should be some mixed radiopaque areas within the radiolucent lesion on the radiographs. Another rare malignancy that might be considered is the undifferentiated nasopharyngeal carcinoma (lymphoepithelioma). We are not informed of any pharyngeal ulceration, but with the trismus involved, it may not be able to be seen.

An incisional biopsy should be performed to determine the diagnosis. Other laboratory tests such as a sedimentation rate and SMA12 might aid in the differential but would not make the diagnosis. Hypernephromas are characteristically very vascular tumors. Care should be taken with the biopsy technique. My working differential diagnosis would be as follows:

1. Metastatic kidney tumor
2. Rhabdomyosarcoma, fibrosarcoma, synovial sarcoma
3. Lymphoma
4. Metastatic tumor from unknown primary
5. Pleomorphic adenoma from deep lobe of parotid gland or carcinoma ex-pleomorphic adenoma
6. Deep infection: actinomycosis, tuberculosis
7. Undifferentiated nasopharyngeal carcinoma

Subsequent Course

Under local anesthesia, incisional biopsy was made from the deeper retromolar area. Immunohistochemical staining was focal positive for cytokeratin 8-18, cytokeratin A-E:1-3, and neuron-specific enolase (NSE) and negative for leukocyte common antigen, CD 20, CD 3, CA 15-3, vimentin, and S-100 (Figs 4A, B, 5A, B). The laboratory values of liver and kidney function tests, complete blood counts, and other biochemical investigations were within normal limits. Thoracic and abdominal CT scans were within normal limits.

Pathologic Diagnosis

Histopathologic examination of the lesion demonstrated the infiltration of *undifferentiated small cell carcinoma*.

The patient was referred to Marmara University Medical School Hospital, Department of Medical Oncology, and hospitalized immediately. The patient was given 4 courses of systemic chemotherapy with cisplatin (80 mg/m²/day, on day 1) and etoposide

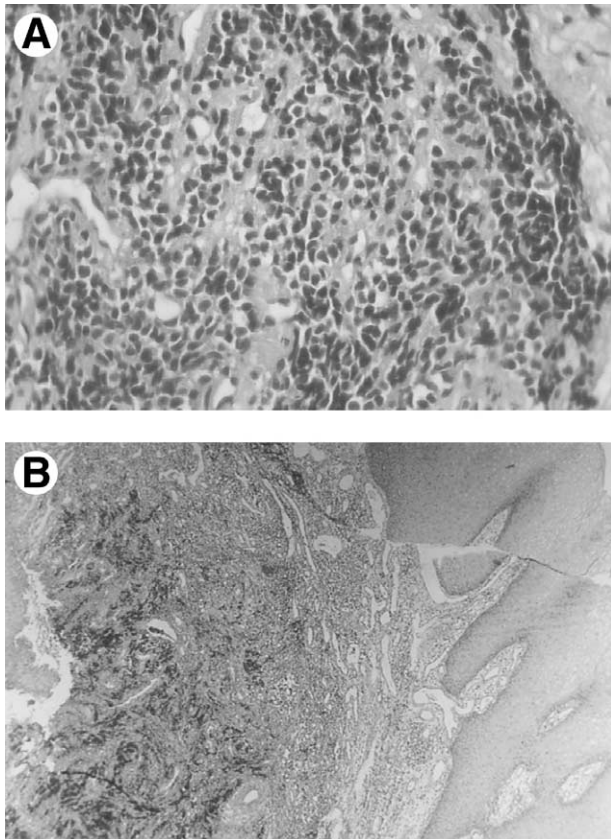


FIGURE 4. A, Tumor cells with narrow cytoplasm and hyperchromatic nucleus (hematoxylin and eosin stain, original magnification $\times 400$). B, Undifferentiated tumor cells under the surface epithelium (hematoxylin and eosin stain, original magnification $\times 40$).

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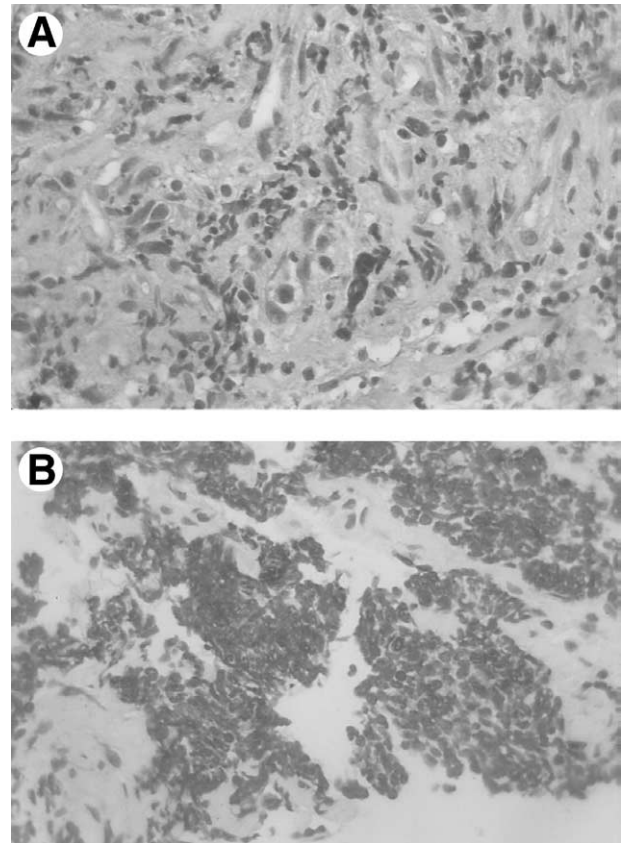


FIGURE 5. A, Cytokeratin 8-18 showed focal positive in tumor cells (anti-cytokeratin 8-18 primary antibody, original magnification $\times 400$). B, Neuron-specific enolase (NSE) showed focal positive in tumor cells (anti-NSE primary antibody, original magnification $\times 400$).

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(100 mg/m²/day, on 1 to 3 days), which was repeated every 21 days. During the third course of chemotherapy, she was also started on concomitant local radiotherapy to the oral cavity and the upper and lower neck including the supraclavicular area. She received a total of 45 Gy of radiation in 1.8-Gy daily fractions for 25 days. She had complete response to chemoradiotherapy and is free of disease during the last 13 months.

Discussion

Trismus, a tonic contraction of the jaw-closing muscles, has now received broader application in use, including all conditions characterized by the inability to open the mouth adequately. Normal maximal mouth opening, measured as the distance between the maxillary and mandibular incisors in healthy adults, is reported to be 46 ± 7 mm. When a mea-

sured interincisal opening is less than 35 mm, one must keep in mind a situation affecting the structure of the mouth opening. In head and neck carcinoma patients, it is very difficult to discriminate the true cause of trismus. It has been reported as the mechanical obstruction of the mandibular coronoid process and/or condylar process, secondary to local tumor extension into the pterygoid musculature, buccal mucosa, retromolar area, as well as ITF and PPF or pterygoid muscle fibrosis in the postirradiation period.¹⁻⁴ A number of studies have reported trismus in patients with malignant tumors in the head and neck.^{1,3,5,6} Inchimura and Tanaka¹ reported that trismus developed in 21 of 212 patients, of whom 4 showed the symptom at the first presentation and the remaining cases showed the symptom during or after treatment. Trismus after irradiation is found in between 27% and 30% of patients with nasopharyngeal carcinoma.^{7,8} In our case, maximal mouth opening was to 14 mm and trismus was detected at the first consultation.

The PPF and ITF are 2 deeper spaces of the oral and maxillofacial region that contain important structures, including the internal maxillary artery, pterygoid plexus, branches of trigeminal nerve (maxillary and mandibular nerves), and Meckel's ganglion. The anatomic structures adjacent to these 2 spaces are the posterolateral wall of maxilla anteriorly, the nasal cavity medially, the mandibular ramus laterally, the base of the skull superiorly, and the inferior level of the lateral pterygoid muscle and pterygopalatine canal inferiorly. Structures adjacent to the nasopharynx, such as nerves and vessels, facilitate the infiltration of NPC through foramina and fissures, from extracranial to intracranial spaces. Tumors of the nasopharynx and nasal cavity can often infiltrate the PPF through erosion of the medial wall of this fossa; that is, through the vertical plate of the palatine bone or through the medial pterygoid plate. Ruprecht and Dolan³ mentioned that the anterior spread of nasopharyngeal malignant lesions corresponded to this situation. Yu et al² stated that NPC might also spread lateroanteriorly into the ITF through the parapharyngeal space and lateral pterygoid muscle. The presentation may include nasal obstruction, frank epistaxis or purulent, bloody rhinorrhea, hearing loss, tinnitus, or headache. Patients may report facial hyperesthesia, paresthesia, or dysesthesia in the distribution of the second and third divisions of the trigeminal nerve.⁴ CT examination of our patient showed that a large mass without bone destruction extending from the right posterior wall of the nasopharynx blocked the piriform sinus and obliterated parapharyngeal fat tissue on the oropharynx and angulus mandible inferiorly to the infratemporal fossa superiorly. As

there was no sensory disturbance in our patient, the possible cause of trismus might be spreading of the tumor into the ITF through the pterygomaxillary space and fissure and pterygoid muscles.

Extrapulmonary small cell carcinomas (EPSCC) are recognized as a clinicopathologic entity distinct from small-cell lung cancer. Such carcinomas as primary tumors have been described in several locations in the head and neck, although most cases of metastatic tumor in the neck originate from a pulmonary primary tumor.⁹⁻¹¹ Because histologic criteria are the same, a pulmonary neoplasm has to be excluded in every case. The differentiation between a primary head and neck tumor and metastatic disease, as well as the location and staging, are essential criteria for therapy and prognosis. Prolonged survival is not infrequent, which is in contrast to the experience for small-cell lung cancer. Treatment consists of chemotherapy with cisplatin and etoposide, as for small-cell lung cancer, but local therapy such as radiotherapy is also considered for patients with nonmetastatic disease.⁹ They reported that patients having complete and partial remissions with chemoradiotherapy have median times to progression of 13+ and 24 months, respectively. Daoud et al¹¹ also reported a median of 14 months of overall survival in a mixed population of EPSCC with an overall survival of 25 months for patients with limited-stage disease. Our patient is still free of disease 13 months after the completion of her concurrent chemoradiotherapy.

In conclusion, restriction of mandibular motions may result from many causes. Although this seems to be a simple clinical presentation, the dentist must keep in mind that this might be one of the clinical findings of patients with malignant tumors of the head and neck region. In the unsuccessful treatment of patients with limited mouth opening, biopsy and advanced imaging techniques must be performed for diagnosis in order to prevent the appropriate treatment delay. To the best of our knowledge, this is the first case of EPSCC of the head and neck region presenting with trismus in the literature.

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