

EDİTÖRE MEKTUP / LETTER TO THE EDITOR

Rare presentation as paraneoplastic syndrome for laryngeal cancer: immune thrombocytopenic purpura

Larenks kanseri ile nadir presente olan paraneoplastik sendrom: immun trombositopenik purpura

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To the Editor,

Various symptoms and signs can be observed in many cancer patients without direct invasion or compression of tumor and its metastasis. These symptoms and signs described as paraneoplastic syndromes, and usually developed through peptides produced by the tumor or antibodies against tumor-associated antigens. Endocrinologic problems and dermatological manifestations are the most common entities for paraneoplastic syndromes. Hematologic manifestations such as autoimmune thrombocytopenia are rarely seen.

A fifty-four-year-old, male patient diagnosed with laryngeal cancer and referred to our tertiary care department, has been suffering from hoarseness for 8 months. He was a heavy smoker of 80 packages per year, and he was consuming alcohol regularly. Six months ago, a biopsy of his left vocal cord was reported to be well differentiated squamous cell carcinoma. During the last 6 months, the patient underwent attempts of endolaryngeal surgery. However, they could not be completed because of severe bleeding from the larynx. A tracheostomy was performed to secure the airway. The laryngoscopic examination showed a tumor originating from the left vocal fold and extending to the subglottic area about 2 cms (Image 1). The tumor was reaching the anterior commissure and extending to the anterior part of the right vocal cord. Neck MRI showed invasion of the

thyroid and left arytenoid cartilages. There wasn't any lymph node involvement. Thoracic CT scan was normal.

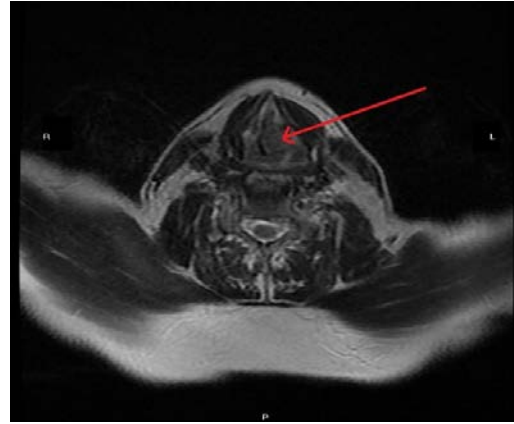


Image 1. Preoperative axial MRI section of the larynx at the glottic level

Complete blood count (CBC) showed a hemoglobin level of 12,7 g/dL, white blood cell (WBC) count of 11.000/ μ L and platelet (PLT) number of 20.000/ μ L (normal range 150.000-450.000/ μ L in adults). The patient's screening for hepatitis B, hepatitis C, and human immunodeficiency virus was negative. Hematologic consultation and peripheral blood microscopy revealed 2-3 platelets/area and no sign of

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myelodysplasia. Hematology department investigated the patient for *Helicobacter pylori* infection, viral vaccination story, medication that causes thrombocytopenia, and autoimmune disorders like Lupus. All tests was negative for the mentioned factors. The hematologist's also didn't find splenomegaly during abdominal examination. Bone marrow biopsy showed normal hematopoiesis, an increased number of megakaryocytes and no neoplastic infiltration. Stainable iron was reduced in marrow particles. (Image 2). The hematologist's diagnosis was immune thrombocytopenic purpura (ITP) and he suggested intravenous immunoglobulin (IVIG) 0,5 gr/kg per day for two days. After IVIG treatment, platelets increased to 85.000/ μ L in CBC, hematology department gave approval for surgery. They also suggested to make ready 3 units of platelet concentrate obtained by apheresis in case they will be necessary during or after the surgery.

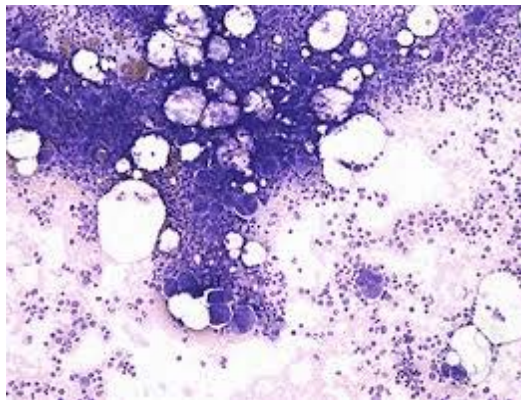


Image 2. Bone marrow biopsy showing increased number of megakaryocytes

The patient underwent total laryngectomy because of subglottic extension and thyroid cartilage invasion and left lateral neck dissection (levels 2,3,4). No bothersome bleeding was seen during the operation, so any blood products weren't used. The patient recovered uneventfully and was discharged from the hospital on the 7th day following the operation and no thrombocytopenia was seen in daily CBCs in the postoperative period. Low dose steroid therapy for 2 weeks was recommended after hospital discharge.

Histopathologic examination of total laryngectomy specimen showed well differentiated squamous cell carcinoma of the larynx, with 3.5 cm tumor diameter and invasion of inner cortex of thyroid cartilage, without perineural or lymphovascular invasion (Image 3). Surgical margins were clear and there were

lymph node metastases. No adjuvant chemotherapy or radiotherapy were recommended.

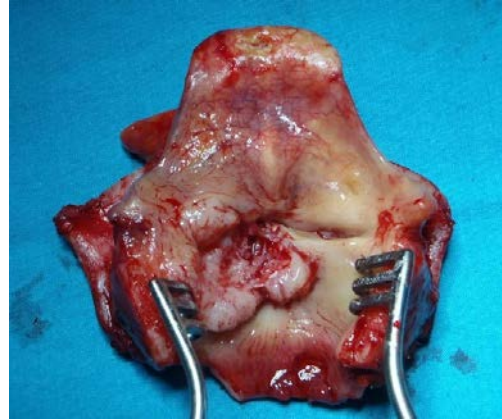


Image 3. Total laryngectomy specimen (front view)

During the postoperative follow up, the patient recovered from ITP and no recurrence of laryngeal cancer or thrombocytopenia within 36 months of follow-up. The patient's ITP condition was concluded to be a paraneoplastic syndrome.

More than a century, cancers cause various symptoms not ascribable to tumor invasion or compression is known¹. These symptoms described as paraneoplastic syndromes in the 1940s². The causes of paraneoplastic syndromes are not fully understood until recently. Nowadays, it has been understood that paraneoplastic syndromes occur in two mechanisms. The first mechanism is the functional peptide or hormones secreted by the tumor (as in endocrine paraneoplastic syndromes). The second is the immune cross-reactivity between the tumor and normal body tissues (as in rheumatologic paraneoplastic syndromes). It is predicted that paraneoplastic syndromes affect up to 2-20% of all cancer patients³. Increase in overall survival and improvement in diagnostic methods in cancer patients are possible reasons for this increment.

In recent years, medical advances have not only enabled us to understand pathogenesis but also increased the chances of diagnosis and treatment of paraneoplastic disorders. In some cases, early diagnosis of paraneoplastic disorders may lead to found an occult tumor at treatable stage. Since paraneoplastic syndromes can cause serious morbidity in patients effective treatment can lengthen survival, improve patient quality of life, boost the

delivery of oncological therapy. Treatments of paraneoplastic syndromes include identifying the underlying malignancy, immunomodulation (for neurologic, dermatologic, and rheumatologic paraneoplastic syndromes), and correction of electrolyte and hormonal imbalances (for endocrine paraneoplastic syndromes)⁴.

Lung cancer, especially small cell type, breast cancer, gynecological tumors and hematological malignancies have been shown as the most frequently associated cancers with paraneoplastic syndromes⁵. Head and neck tumors, regardless of histology, have rarely been associated with paraneoplastic syndromes. Ferlito et al reported that paraneoplastic syndromes of laryngeal and hypopharyngeal cancer were divided in six groups: dermatologic or cutaneous, endocrine, hematologic, neurologic, osteoarticular or rheumatologic, and ocular⁶. Rinaldo et al published 59 paraneoplastic syndrome with laryngeal cancer cases from 1963 to 2019⁷. Twenty-two of the paraneoplastic syndromes involved the endocrine system, 21 were dermatologic or cutaneous, 8 neurologic, 5 osteoarticular or rheumatologic, 1 ocular, 1 muscular, and 1 hematologic.

Ferlito and Rinaldo reported that the same case for hematologic paraneoplastic syndrome was *Trousseau's syndrome* (thrombophlebitis migrans, migratory thrombophlebitis, disseminated intravascular coagulation, or thromboembolism)⁸. Shutt et al reported an oesophageal carcinoma patient died because of refractory ITP⁹. Patient's couldn't operate due to local extension of tumor and also didn't take definitive chemotherapy because of poor performance score. Local radiotherapy was given for palliative treatment. Patient's thrombocytopenia got better with high dose IVIG initially. Then, thrombocytopenia became resistant to all treatment modalities. The patient died from severe gastrointestinal and pulmonary bleeding. Yang et al reported two nasopharyngeal carcinoma patients with ITP as a paraneoplastic syndrome¹⁰. They treated the patients with steroids before definitive radiotherapy.

Krauth et al published a critical analysis of paraneoplastic ITP cases in 68 patients with solid tumors, in which only one patient was diagnosed with laryngeal cancer¹¹. This patient's ITP was observed following recurrence of the laryngeal cancer and steroid treatment provided increased levels of platelets¹².

Regarding the fact that autoimmune thrombocytopenia was observed in patients with recurrent laryngeal cancer, it may not represent only a paraneoplastic syndrome, but also a sign of cancer recurrence. However, this is not a definite conclusion, since there are only few numbers of case reports in the literature.

ITP as a paraneoplastic syndrome in laryngeal cancer is rare, but it should be kept in mind that thrombocytopenia can be the finding of a paraneoplastic syndrome. Patients should undergo a thorough hematologic workup for appropriate management of ITP, particularly before surgery.

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