

CASE REPORT

A case of granulocytic sarcoma during complete remission of acute myeloid leukemia with multiple masses involving the larynx and nasopharynx

Akut miyeloid löseminin tam remisyon döneminde ortaya çıkan ve multipl kitleler ile birlikte larenks ve nazofarenksi eşzamanlı tutan granülositik sarkom olgusu

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A thirty-seven-year-old male patient presented with dysphagia and hoarseness six months after complete remission of acute myeloid leukemia (AML-M₀), which had been treated with chemotherapy. Physical examination revealed left vocal cord paralysis and involvement of the 9th, 10th, and 12th cranial nerves. Sagittal and axial magnetic resonance scans of the nasopharynx and neck showed a mass in the left retropharyngeal and perivertebral regions, 6x4 cm in size; another mass in the left vallecula, and infiltration of the right preepiglottic tissue by another mass of 2 cm. There was no bone marrow involvement. A diagnosis of granulocytic sarcoma without leukemia relapse was made and the FLAG-Ida regimen was administered, after which partial regression of the masses was observed. However, the patient died due to a pulmonary infection on the 17th day of chemotherapy.

Key Words: Antineoplastic combined chemotherapy protocols; laryngeal neoplasms; leukemia, myeloid; lymph nodes; nasopharyngeal neoplasms; sarcoma, granulocytic; thymus neoplasms.

Akut miyeloid lösemi (AML-M₀) tanısıyla uygulanan kemoterapiden sonra komplet remisyona giren 37 yaşındaki erkek hastada, remisyon sonrası altıncı ayda disfaji ve ses kısıklığı şikayetleri görüldü. Fizik muayenesinde sol vokal kord paralizisi ve 9, 10 ve 12. kranyal sinir tutulumu saptandı. Nazofarenks ve boynun sagittal ve aksiyal manyetik rezonans kesitlerinde, sol retrofarenjeal ve perivertebral bölgede yerleşim gösteren 6x4 cm boyutlarında bir kitle, sol vallekulada başka kitle ve sağ preepiglottik dokuda infiltrasyona yol açan 2 cm büyüklüğünde başka bir kitle belirlendi. Kemik iliği tutulumu saptanmadı. Lösemi nüksü olmaksızın granülositik sarkom tanısıyla FLAG-Ida rejimi uygulanmasından sonra kitlelerde kısmi gerileme görülmesine rağmen, kemoterapinin 17. gününde hasta pulmoner enfeksiyon nedeniyle yaşamını yitirdi.

Anahtar Sözcükler: Antineoplastik birleşik kemoterapi protokolü; larenks neoplazileri; lösemi, miyeloid; lenf nodu; nazofarenks neoplazileri; sarkom, granülositik; timus neoplazileri.

Granulocytic sarcoma (GS) is a rare localized proliferation of immature granulocytic cells infiltrating one or more extramedullary sites. Its incidence is

2.9% to 9% in patients with myeloid leukemia or myeloproliferative disorders.^[1-3] It tends to occur in young patients, with 60% below 15 years of age.^[3]

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Granulocytic sarcomas may occur in three patient groups, including those (i) with acute myeloid leukemia (AML), (ii) with myelodysplastic disorders undergoing leukemic transformation or chronic myelogenous leukemia with impending blast crisis, and (iii) in nonleukemic patients in the absence of AML, a myeloproliferative disorder, or a myelodysplastic syndrome.^[4-7] Usually GS and AML are diagnosed simultaneously. The most common presentation of GS is a mass lesion involving soft tissues, the periosteum, bones, lymph nodes, and the skin.^[5]

We report a case of minimally differentiated acute myeloid leukemia (AML-M₀) during first complete remission in which multiple GSs were found involving the larynx, nasopharynx, and mediastinal regions without evidence of AML.

CASE REPORT

A thirty-seven-year-old man presented with complaints of weakness and dizziness. On physical examination, there was no lymphadenopathy or organomegaly. Neurological examination was normal. A complete blood count on admission showed the following: hemoglobin 9.9 g/dl, white blood cells $1.2 \times 10^9/L$, platelets $15 \times 10^9/L$, and blasts on blood smear. Bone marrow aspirate was hypercellular with 99% of cell blasts. Flow cytometric analysis and cytochemical stains yielded a diagnosis of AML, type M₀. Cytogenetic analysis confirmed a normal XY male genotype. Treatment was instituted with intravenous idarubicin ($12 \text{ mg}/\text{m}^2$, 3 days) and cytosine arabinoside ($100 \text{ mg}/\text{m}^2$, 7 days). On Day 24, he was in complete remission and the first consolidation treatment was initiated with a combination of idarubicin

($10 \text{ mg}/\text{m}^2$, 3 days) and cytosine arabinoside ($1000 \text{ mg}/\text{m}^2$, 6 days). He was evaluated for allogeneic stem cell transplantation, but no HLA-matched donor was available.

Six months after the diagnosis, he presented with dysphagia and hoarseness. Physical examination showed left vocal cord paralysis, involvement of the 9th, 10th, and 12th cranial nerves, a left supraclavicular mass with a diameter of 2 cm, and right cervical anterior masses 0.5 cm in size. Endoscopic examination revealed a mass extending from the left wall of the nasopharynx to the left wall of the hypopharynx and the left vallecula, and left vocal cord paralysis. The uvula and the left palatine tonsils were displaced to the right by the mass effect. The tongue was deviated. No lymphadenomegaly or organomegaly was noted. A complete blood count showed white blood cells $8 \times 10^9/L$, hemoglobin 13 g/dl, platelets $264 \times 10^9/L$ with the following differential: neutrophils 67%, monocytes 9%, and lymphocytes 24%. The erythrocyte sedimentation rate was 70 mm/h; lactate dehydrogenase was 730 EU/L, and serum β_2 -microglobulin was 279 ng/ml. Bone marrow aspiration showed no evidence for leukemic infiltration. Although cranial magnetic resonance imaging (MRI) was normal, sagittal and axial MRI scans of the nasopharynx and the neck revealed a mass, 6x4 cm in size, in the left retropharyngeal and perivertebral regions, extending to the hypoglossal duct at the level of the first cervical vertebra and the foramen magnum (Fig. 1a, b). Both the premedullary and lateral cisternae were obliterated by the mass. The left vertebral artery was enwrapped. The medulla oblongata was dis-

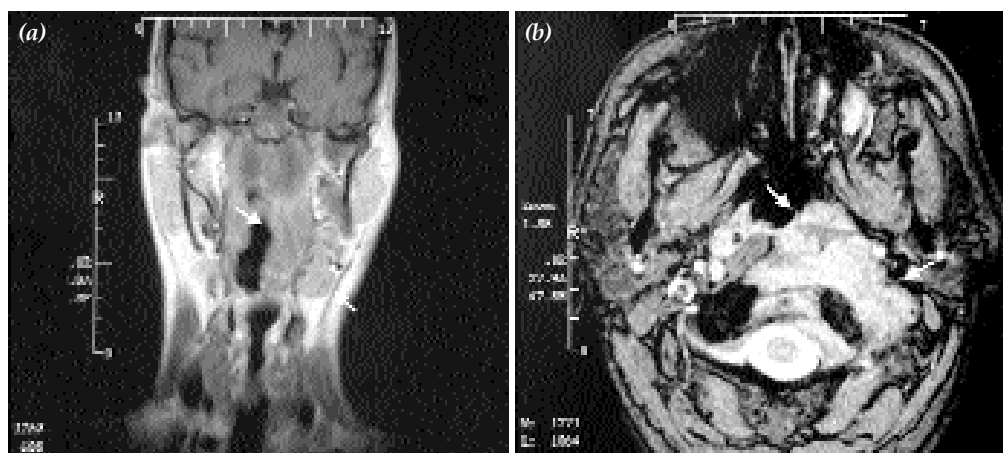


Fig. 1 - (a, b) Magnetic resonance imaging scans of the mass in the left nasopharyngeal area.



Fig. 2 - Magnetic resonance imaging scan of the mass in the right preepiglottic area.

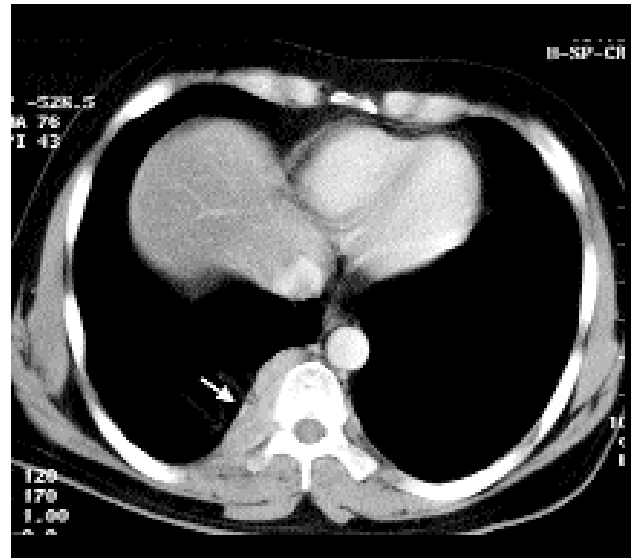


Fig. 3 - Computed tomography scan showing a right paravertebral mass at the diaphragm level.

placed to the right. The thickness of the left nasopharyngeal wall was increased and the constituents of this area were displaced anteriorly. Another mass was found in the left vallecula. The right preepiglottic tissue was infiltrated by another mass of 2 cm size (Fig. 2). Multiple lymph nodes with a diameter of 2 cm were present at levels II, III, and IV. Finally, axial MRI sections demonstrated another mass, 3x2 cm in size, on the left side of the first costochondral junction located paravertebrally.

Computed tomography of the thorax revealed multiple masses on both sides of the paravertebral regions, one of which was located on the right side of the diaphragm, measuring 4 cm in length and 2 cm in diameter (Fig. 3). There was another mass of thymic localization in the anterior mediastinum, that measured 1.5x2.5 cm. The patient underwent biopsy from the left supraclavicular mass. Microscopic examination disclosed diffuse infiltration of blast cells with round to oval nuclei and prominent nucleoli (Fig. 4) The cells were diffusely

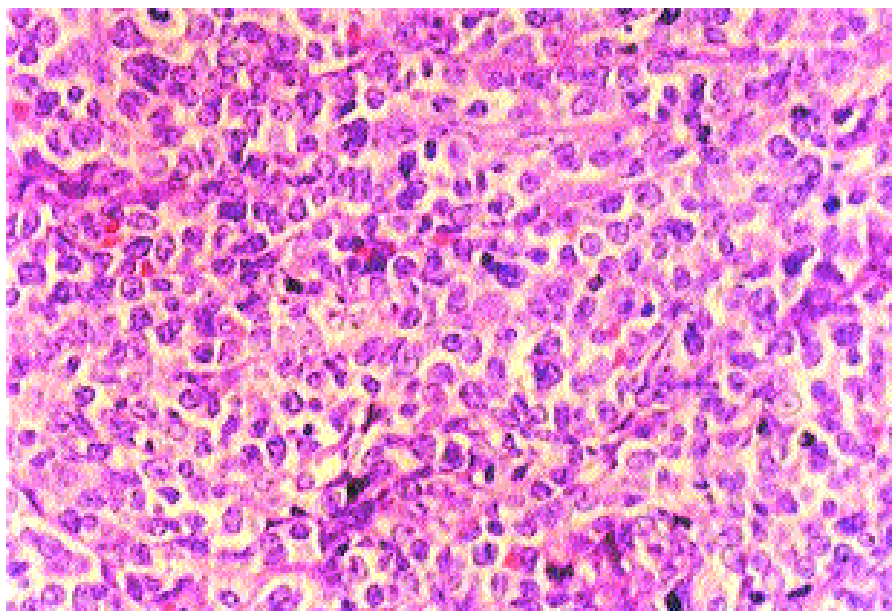


Fig. 4 - Histologic appearance of granulocytic sarcoma showing immature granulocytic cells (H-E x 200).

and strongly stained for CD34, but were negative for CD3, CD30, CD45, and CD79.

After clinical, radiologic, and histologic examinations, a diagnosis of "granulocytic sarcoma without leukemia relapse" was made and the FLAG-Ida regimen was administered (fludarabine 30 mg/m², 5 days; idarubicin 12 mg/m², 3 days; cytosine arabinoside 2 g/m², 5 days; granulocyte colony-stimulating factor 5 µg/kg/day). Due to the presence of dysphagia and aspiration associated with cranial nerve palsies, the patient received parenteral nutrition during and after chemotherapy. On Day 26 of his chemotherapy he was re-evaluated. Complete regression of the masses was noted in the cervical regions, but hoarseness and dysphagia still persisted. On endoscopic examination, the submucosal mass in the left hypopharyngeal lateral wall disappeared, the mass in the left wall of the nasopharynx largely regressed, but left vocal cord paralysis still persisted. There was no improvement in the involvement of the 9th, 10th, and 12th cranial nerves. Radiologically, all the enlarged lymph nodes regressed, and all the paravertebral masses of the mediastinum including that of thymic localization disappeared. However, cervical MRI scans showed that the nasopharyngeal mass did not completely regress, whereas the preepiglottic mass showed complete regression. To aid his eating and to prevent aspiration, a left vocal cord medialization was performed by injecting abdominal fat tissue to the left vocal cord area. This operation resulted in partial improvement in his hoarseness and he was able to drink without aspiration. Persisting lesions required another course of FLAG-Ida chemotherapy, on 17th day of which he died due to a pulmonary infection.

DISCUSSION

Granulocytic sarcomas usually occur during a leukemic episode in 80% of the cases, and they precede the onset of leukemia in only 20%.^[8] Although they may develop in almost every location,^[9-13] involvement of the larynx and nasopharynx is rare.^[14-17] Some factors have been described that predispose leukemia patients to the development of an extramedullary myeloid tumor, including certain chromosome abnormalities [t (8;21), inv (16)], morphologic subtype (FAB type M₂, M₄, M₅) and expression of surface markers such as CD56, CD2, CD4,

and CD7.^[10] Other chromosomal abnormalities have also been reported.^[18,19] The diagnosis of GS can be made histologically with the use of immunohistochemical staining. However, in the absence of systemic leukemia, the diagnosis may be challenging, because primitive granulocytes may lack visible granules under light microscopy and can easily be confused with lymphoma, anaplastic carcinoma, Ewing's sarcoma, eosinophilic granuloma, soft tissue sarcoma, and a poorly differentiated epithelial tumor.^[2,4,5,10,11,20]

Treatment strategies for GS may vary. The best results have been achieved with antileukemic therapy containing high-dose Ara-C (cytosine arabinoside).^[10] However, there is still no agreement about the kind or intensity of induction and post-induction chemotherapy. Surgery may be a choice of treatment for acute spinal cord compression.^[21] Apart from this, the role of surgery in GS is no more than a tool to obtain a tissue diagnosis.^[3,22] Since these tumors are radiosensitive, local radiotherapy may also be used alone or with chemotherapy.^[3,8,23,24]

In our case, GS developed six months after the diagnosis of leukemia, during which the patient showed hematological remission. He did not have special karyotypes or subtypes predisposing to GS, but he had very high CD7 levels. Granulocytic sarcoma involved multiple sites in our patient, including supraclavicular and cervical regions, the nasopharynx, preepiglottic area, vallecula, superior and inferior mediastinum, and the thymus. Histologic verification was obtained from only one lesion in the supraclavicular region. Attempts to obtain histologic verification from the nasopharynx failed because of insufficient material. Since the patient was suffering from dysphagia, aspiration, and hoarseness, we immediately started chemotherapy. Complete regression of the masses at thymic and mediastinal paravertebral locations, and partial regression of the nasopharyngeal mass after therapy served to corroborate the diagnosis of these masses as GS. Initially, we obtained a good response from the chemotherapy regimen containing high-dose Ara-C. Since it was suboptimal a second course was initiated. However, unanticipated death of the patient from a pulmonary infection prevented us from monitoring the eventual efficacy of chemotherapy.

Although radiotherapy was another treatment option for the nasopharyngeal mass in our patient, chemotherapy was thought to be more convenient to deal with multiple masses at different sites.

The pathogenesis of GS and even multiple GSs has yet to be elucidated. For spinal GS, embryonic hematopoietic nests in the spinal dura mater are thought to be the origin of tumor cells.^[4] Another explanation is that GS cells arise in the bone marrow, travel via the Haversian canals to reach the subperiosteal region of the bone, whence they spread to other parts of the body.^[22] For cutaneous GS, trauma-induced extravasation of myelodysplastic cells is thought to be responsible for the local replication of tumor cells within the skin.^[25] Chromosomal translocations have been demonstrated including t(8;21) and t(9;11) in some cases with multiple GSs.^[24,26]

In conclusion, GS involving the larynx and nasopharynx is a rare condition, and to our knowledge, involvement of the larynx and nasopharynx in association with other sites has not been reported, making our case interesting for the evaluation of multiple GSs. In case of GSs occurring after the onset of leukemia, aggressive antileukemic chemotherapy should be considered to improve prognosis because bone marrow relapse almost always follows GS. Further studies are required to elucidate the pathogenesis of multiple GSs.

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