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Diffuse large B-cell non-Hodgkin lymphoma involving the unilateral carotid space in an elderly man: A case report

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Abstract. An 84-year-old man presented with a history of repeated syncope and decreased heart rate and blood pressure over the last month. On physical examination, a mass sized ~3x3 cm was palpable in the left submandibular area; the mass was hard, poorly mobile, without tenderness or local skin irritation. The computed tomography angiography examination revealed a soft tissue mass in the neck, at the level of the left carotid bifurcation and above. The left common carotid artery bifurcation and internal and external carotid artery segment were embedded in the mass, and there were multiple enlarged lymph nodes in the left neck. The diagnosis of diffuse large B-cell non-Hodgkin lymphoma was confirmed by a percutaneous biopsy of the left submandibular mass. To the best of our knowledge, this is the first reported case of non-Hodgkin lymphoma involvign the carotid space.

Introduction

Diffuse large B cell lymphoma (DLBCL) is an aggressive B-cell lymphoma, histologically characterized by diffuse proliferation of large neoplastic B lymphoid cells with a nuclear size equal to or exceeding normal histiocyte nuclei (1). DLBCL is the most common type of lymphoma, accounting for 30-40% of adult non-Hodgkin lymphomas (NHLs) worldwide, generally encountered in the 6th and 7th decades of life (2). Prognostic factors in DLBCL are age, performance score, stage, proliferation fraction and gene expression profiles (3,4). DLBCLs are clinically and pathologically diverse. Over the last decade, the standard of care for DLBCL patients has been the addition of the anti-CD20 antibody rituximab to classic cytotoxic chemotherapy. Generally, lymphoma is a malignant neoplasm commonly occurring in the head and neck that may occur in multiple locations with variable presentations. Approximately 23-30% of patients with NHL present with extranodal involvement of the head and neck, with involvement of the Waldeyer ring in ~50% of the cases. Other sites of extranodal involvement include the orbit, parotid gland, brain, nasopharynx, hypopharynx, larynx, paranasal sinuses and uvula (5,6).We herein report what is, to the best of our knowledge, the first case of a patient with DLBCL involving the carotid space unilaterally. As the disease manifested without previously reported signs or symptoms, this may pose a diagnostic challenge for clinicians and pathologists.

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Key words: diffuse large B-cell non-Hodgkin lymphoma, carotid space, recurrent syncope, chemotherapy, radiotherapy

Case report

An 84-year-old man presented with a history of repeated syncope and decreased heart rate and blood pressure over the last month. There was no apparent cause for the syncope and the decreased heart rate and blood pressure. The patient had been emergently admitted to the local community hospital with paleness and sweating nearly 1 month prior to admission. Following chest compressions and intravenous injection of atropine and dopamine, the symptoms were relieved. On physical examination, a mass sized ~3x3 cm was palpable in the left submandibular area. The mass was hard, poorly mobile, without tenderness but with local skin irritation. Following local application of cactus extract, the redness and swelling subsided, the symptoms were relieved and the patient was discharged. After ~1 month, the symptoms of syncope with decreased heart rate and decreased blood pressure recurred and on December 21, 2014, the patient was admitted to the Emergency Department of The First Affiliated Hospital of Nanjing Medical University (Nanjing, China). Following chest compressions and intravenous administration of atropine and dopamine, the symptoms improved. Physical examination revealed that the size of the left submandibular mass had increased significantly in size to 5x4.5 cm. The mass was hard, poorly mobile, without tenderness, with normal color of the overlying skin. As the heart rate and blood pressure were significantly decreased, it was hypothesized that the cause may be compression of the left common carotid artery, aortic body and carotid sinus by the mass. The use of use dopamine and norepinephrine was continued to restore the blood pressure, and a computed tomography angiography (CTA) examination of the head and neck was performed. During the course of

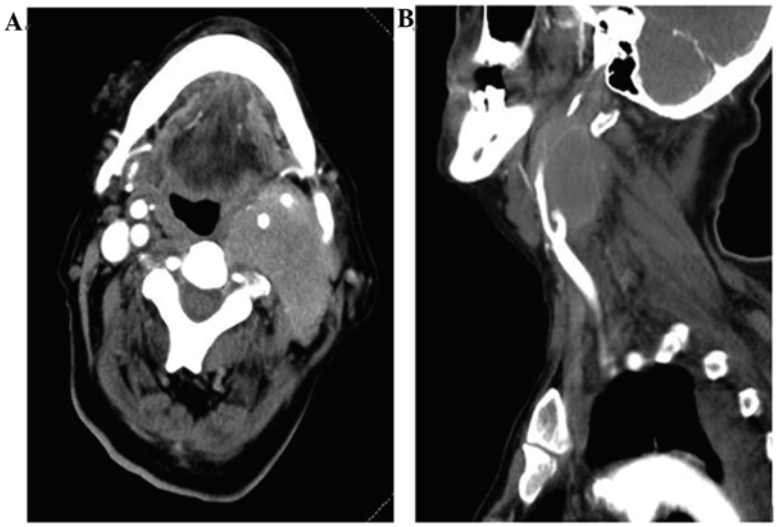

Figure 1. A computed tomography angiography scan of the head and neck revealed a soft tissue mass (A) in the left submandibular area and (B) in the neck, at the level of the left carotid bifurcation and above. The left common carotid artery bifurcation and internal and external carotid artery segments were embedded in the mass.

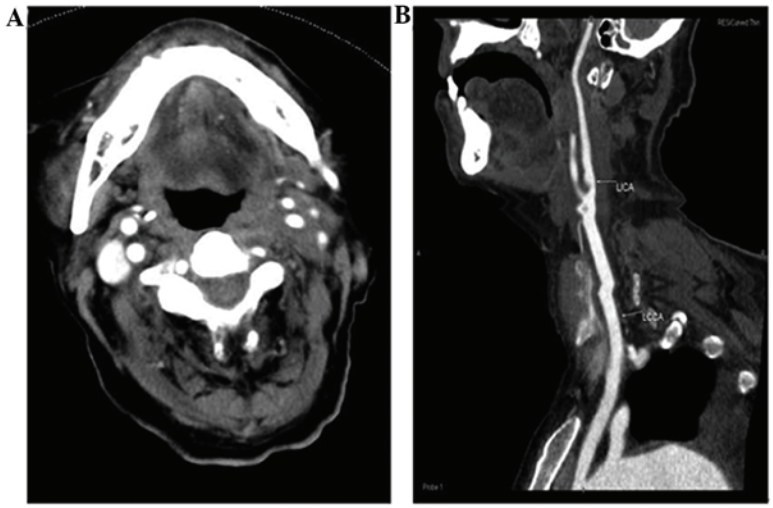

Figure 2. Computed tomography angiography scan of the head and neck following chemotherapy and radiotherapy. (A) The mass in the left submandibular area had almost disappeared; (B) the soft tissue mass at the level of the left carotid artery bifurcation and above had clearly decreased in size smaller compared with prior to treatment. The left common carotid artery bifurcation and internal and external carotid artery segments that were previously embedded in the mass were also clearly visualized.

the examination, the symptoms reappeared, but were relieved with active treatment. The CTA examination results (Fig. 1) revealed a soft tissue mass in the neck, at the level of the left carotid bifurcation and above, possibly representing fused lymph nodes. The left common carotid artery bifurcation and the internal and external carotid artery segments were embedded in the mass and there were multiple enlarged lymph nodes in the left neck. Percutaneous biopsy of the left submandibular mass was immediately performed. While waiting for the pathology results, the abovementioned symptoms recurred several times. The pathological and immunohistochemical results pointed towards the diagnosis of a malignant tumor of the lymphatic and hematopoietic system: The tumor cells were $CD3^-$, $CD20^{+++}$, $Pax\text{-}5^{+++}$, $CD10^-$, B-cell lymphoma (Bcl)-6^-, multiple myeloma oncogene 1 $(MUM1)^{+++}$ and $Bcl\text{-}2^{+++}$, $CD5^-$, $CD23^{+/-}$, pan-cytokeratin $(CK\text{-}pan)^-$, $vimentin^-$, $CD31^-$ and $CD34^-$; the Ki-67 index was >80%; combined with hematoxylin and eosin staining, the diagnosis of diffuse large B-cell lymphoma (DLBCL) with a non-germinal center origin was confirmed. A treatment plan was immediately designed, including systemic chemotherapy combined with local radiotherapy to the left submandibular mass. After five cycles of chemotherapy and seven sessions of radiotherapy, the symptoms were significantly alleviated and the left submandibular mass almost disappeared; thus, dopamine was withdrawn. A repeat head and neck CTA examination was performed (Fig. 2), and it revealed that the soft tissue mass at the level of left carotid artery bifurcation had clearly decreased in size compared with the previous CTA scan. Thereafter, the patient suddenly developed tenderness in the right upper abdominal quadrant, and his body temperature and leukocyte count (neutrophil fraction) increased significantly.

An abdominal ultrasound revealed choledocholithiasis and all the findings taken together indicated choledocholithiasis accompanied by infection. Therefore, chemotherapy and radiotherapy were discontinued. Following antibiotic treatment with cefoperazone-sulbactam, biliary drainage surgery and symptomatic supportive treatment for ~2 months, the patient's body temperature, leukocyte count and differential neutrophil count returned to normal; however, the size of left submandibular mass increased again. Local radiotherapy was administered for a total of eight sessions, but the growth of the mass could not be effectively inhibited. Due to the poor general condition of the patient, treatment was discontinued.

Antitumor traditional Chinese Medicine preparations, such as Kanglaite and Aidi injections, were used as palliative treatment, supplemented by immunomodulating agents, such as lentinan and thymosin. However, the mass progressively increased in size, and pulmonary infections occurred repeatedly. The patient's family requested treatment discontinuation and the patient was discharged from the hospital. Shortly thereafter, the patient succumbed to the disease.

Discussion

DLBCL is the most common malignant lymphoma subtype in adults, accounting for ~40% of all cases (1). DLBCL is characterized by significant heterogeneity and several morphologically diverse variants may be distinguished. The distinction between these variants potentially reflects differences in biology and may also be clinically relevant (2). In addition to these pathological differences, the clinical presentation may also vary. Furthermore, there is heterogeneity regarding the molecular events that drive DLBCL lymphomagenesis. This heterogeneity may be at least partially be explained by the presence of molecularly defined subtypes identified in large gene expression profiling studies over the last several years (3-8). Through applying a classification according to the cell of origin, in which the DLBCL tumor profiles are compared to the profiles of normal B cells, several molecular subtypes may be distinguished. The germinal center B-cell-like (GCB) DLBCLs are derived from germinal center B cells and, accordingly, express a variety of genes that are expressed in normal germinal center B cells. By contrast, activated B-cell-like (ABC) DLBCLs appear to originate from activated B cells that are undergoing transition to plasma cells (3,6,9). Primary mediastinal B-cell lymphomas appear to originate from a B-cell subpopulation in the thymus and are characterized by a specific gene expression profile (4,5,10). Finally, ~15% of DLBCLs cannot be assigned to a specific molecular subtype and are referred to as unclassifiable DLBCL (11). In particular, the distinction between ABC and GCB DLBCLs is not only relevant from a scientific standpoint, but also has significant clinical implications, as these subtypes are characterized by differences in overall survival when treated with the current standard treatment of rituximab and CHOP chemotherapy (R-CHOP). The vast majority of patients diagnosed with GCB DLBCL respond favorably to R-CHOP, whereas this regimen is less effective in ABC DLBCL patients (11).

Lymphoma is a malignant neoplasm commonly occurring in the head and neck that may occur in multiple locations with variable presentations. Approximately 4-5% of patients with Hodgkin's lymphoma present with extranodal involvement of the head and neck compared with 23-30% in those with NHL. The Waldeyer ring is the most common site of extranodal involvement in the head and neck, accounting for ~50% of the cases. Other sites of extranodal involvement include the orbit, parotid gland, brain, nasopharynx, hypopharynx, larynx, paranasal sinuses and uvula (12,13). Our patient presented with recurrent syncope accompanied by decreased blood pressure and heart rate as the main symptoms; a head and neck CTA examination indicated compression of the left carotid artery and carotid sinus by the mass. The diagnosis of diffuse large B-cell NHL was confirmed by percutaneous biopsy of the left submandibular mass. Immunohistochemical staining was positive for CD20, Pax-5, MUM1 and Bcl-2, and negative for CD3, CD5, CD10, CD31, CD34, Bcl-6, CK-pan and vimentin. In contrast with lymphomas presenting as nodal disease along the jugulodigastric chain, in this case the lymphoma presented in the extranodal carotid space. To the best of our knowledge, primary extranodal lymphomas of the carotid space have not been previously described in the literature.

The disease in this case was sensitive to chemotherapy and radiotherapy, but due to the development of late concurrent choledocholithiasis and infection, this treatment was discontinued. Although radiotherapy was re-initiated following antibiotic treatment and bile drainage, its efficacy was poor, and the mass increased significantly in size. Therefore, the treatment for DLBCL must have continuity as, following suspension, disease control may not be feasible.

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