

Coincidence of Anaplastic Lymphoma of the Stomach with Kaposi 's Sarcoma: A Rare Presentation

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Abstract

Anaplastic large-cell lymphoma is an aggressive non-Hodgkin lymphoma of T cell/null cell origin. It rarely affects the gastrointestinal tract. We present the case of a 58-year-old patient diagnosed with anaplastic lymphoma of the stomach in association with Kaposi's sarcoma of the skin.

Keywords: Anaplastic lymphoma, Stomach, Kaposi's sarcoma

Introduction

Primary malignant lymphoma of the stomach comprises only a small percentage (approximately 10%) of all malignant tumors of this organ.¹ Anaplastic large cell lymphoma (ALCL) is a type of non-Hodgkin lymphoma (NHL) of T-cell origin. Anaplastic large-cell lymphoma comprises approximately 3% of all adult NHLs² and 10% to 20% of childhood lymphomas.³ Kaposi's sarcoma (KS) is a vascular tumor that typically presents with cutaneous lesions in the form of multiple patches, plaques or nodules, but may also involve mucosal sites, lymph nodes, and visceral organs.⁴ We report the case of a 58-year-old male who presented with KS of the skin

together with ALCL of the stomach.

Case report

A 58-year-old male presented to the Emergency Department with abdominal pain, melena of one month's duration, and significant weight loss of 12 kg. There was a history of night sweats and poor oral intake, but no fever. He reported a history of bilateral pigmented skin lesions on his lower limbs for 2 months. On examination, he was pale with no palpable lymphadenopathy and both lower limbs had multiple violaceous papular, pigmented lesions, plaque, and scale formation that extended from his feet up to the knees (Figure 1A). His complete blood count on presentation was as

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follows: hemoglobin (8.1g/dl), white blood count ($7.1 \times 10^3/\mu\text{L}$), platelets ($101 \times 10^3/\mu\text{L}$). Biochemistry was normal with a lactate dehydrogenase level of 304. Serology for hepatitis B, hepatitis C, and human immunodeficiency virus was negative. Ultrasound (USG) of his abdomen revealed pancreatic lesions, hepatic lesions, and multiple abdominal lymph nodes. Computerized tomographic (CT) scan of the whole body revealed an enlarged liver (20.8 cm) and spleen (15.1 cm), stomach wall that had diffuse circumferential thickening, and enlarged lymph nodes at the trachea, perisplenic, and para-aortic group. He underwent endoscopic examination which revealed a fungating mass in the cardia and body of the stomach. Biopsy results revealed gastric mucosal fragments infiltrated by large atypical lymphoid cells with prominent nucleoli

(Figure 2A-D). Immunohistochemistry results were positive for CD45 and CD30, and negative for CD3, CD5, CD19, CD20, ALK, and pancytokeratin (Figure 3). A diagnosis of ALCL was made. The skin biopsy showed endothelial proliferation and extravasated RBCs consistent with KS (Figure 1B,C). He received chemotherapy that consisted of cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP protocol) with improvement in his general condition and resolution of the skin lesions after 2 courses of chemotherapy. Written informed consent was taken from the patient.

Discussion

Kaposi's sarcoma is a locally aggressive endothelial tumor that typically presents with cutaneous lesions.⁵ There are 4 forms based

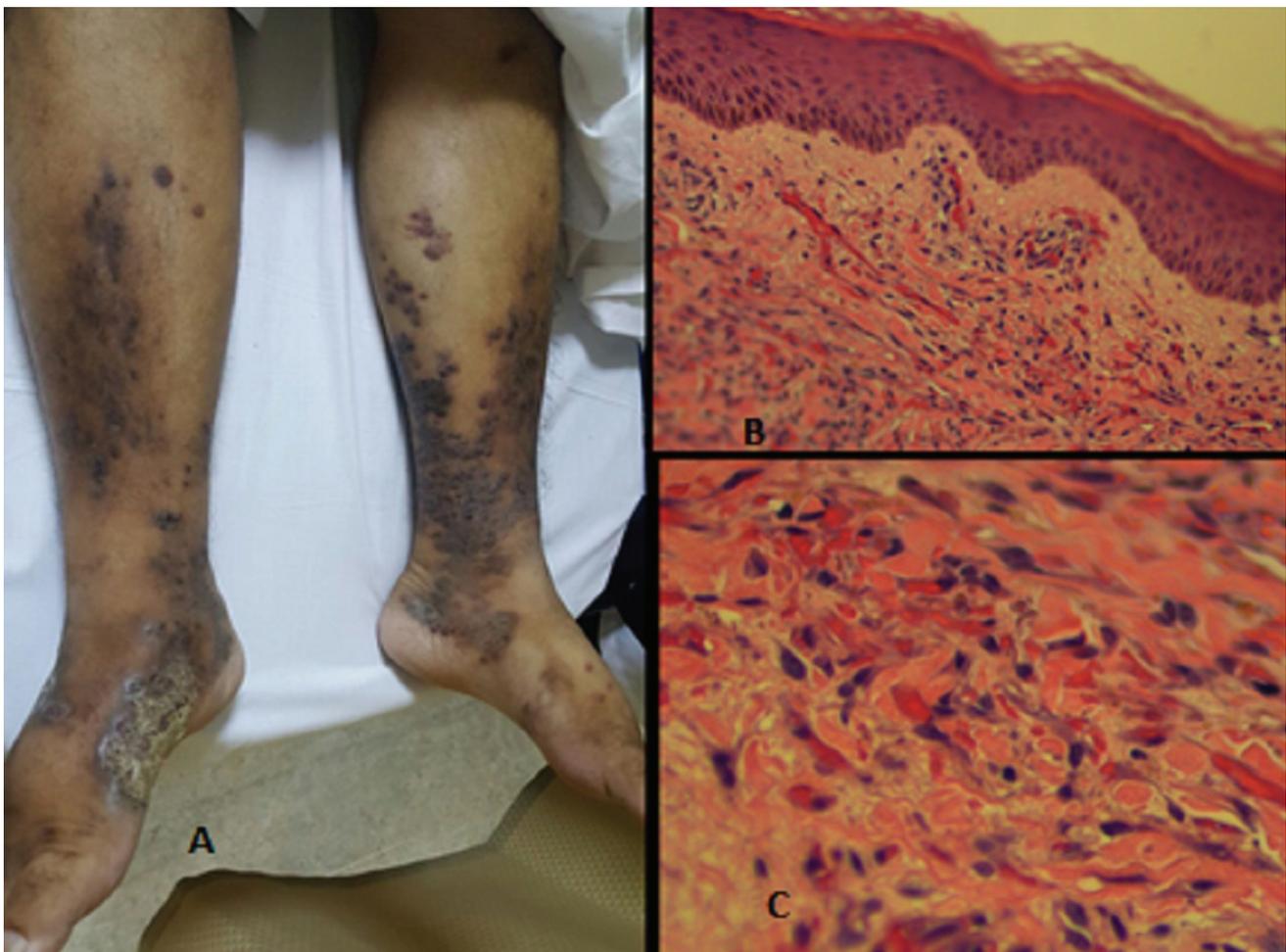


Figure 1. A) Multiple violaceous, papular, pigmented lesions, plaque, and scale formation that extended from the foot up to the knee in both lower limbs. B,C) Skin biopsy that shows endothelial proliferation and extravasated RBC's (hematoxylin and eosin; B: 20 \times , C: 40 \times).

primarily on population demographics and risks – classic, lymphadenopathic (endemic), transplant associated, and acquired immunodeficiency syndrome associated (epidemic). Classic KS can be associated with an underlying second malignancy or altered immunity. It presents with multiple red to purple skin plaques or nodules in the distal lower extremities and remains localized to the skin and subcutaneous tissue.⁴ In our case, KS was associated with ALCL of the stomach.

Primary gastrointestinal lymphoma (PGIL) comprises 4% to 18% of all NHL and 30-50% of all extranodal NHL, which makes the gastrointestinal tract the most common site of extranodal NHL. T-cell lymphomas are much less common than their B-cell counterparts in the gut. Primary T-cell lymphoma in the stomach is particularly associated with human T-lymphotropic virus type

1 (HTLV-1) infection.⁶ In 1985, Stein and colleagues identified a subset of NHL termed “Ki-1 lymphomas” characterized by large CD30 (Ki-1) anaplastic cells, which had a tendency to grow cohesively and a predilection to invade lymph node sinuses. Although most cases were T-cell or null-cell lineage, 15% had a B-cell phenotype.⁷ In the Revised European American Lymphoma classification, the name of this specific subset was updated to ALCL and confined to cases that were T-cell or null-cell type.⁸ In the 2001 WHO classification, the category ALCL referred to systemic neoplasms of T- or null-cell lineage and ALCL that arose in the skin were designated as cutaneous ALCL, a distinct entity.⁹ This group represented approximately 2% of all NHL and approximately 20% of all T-cell lymphomas in North America, and was less frequent in Europe

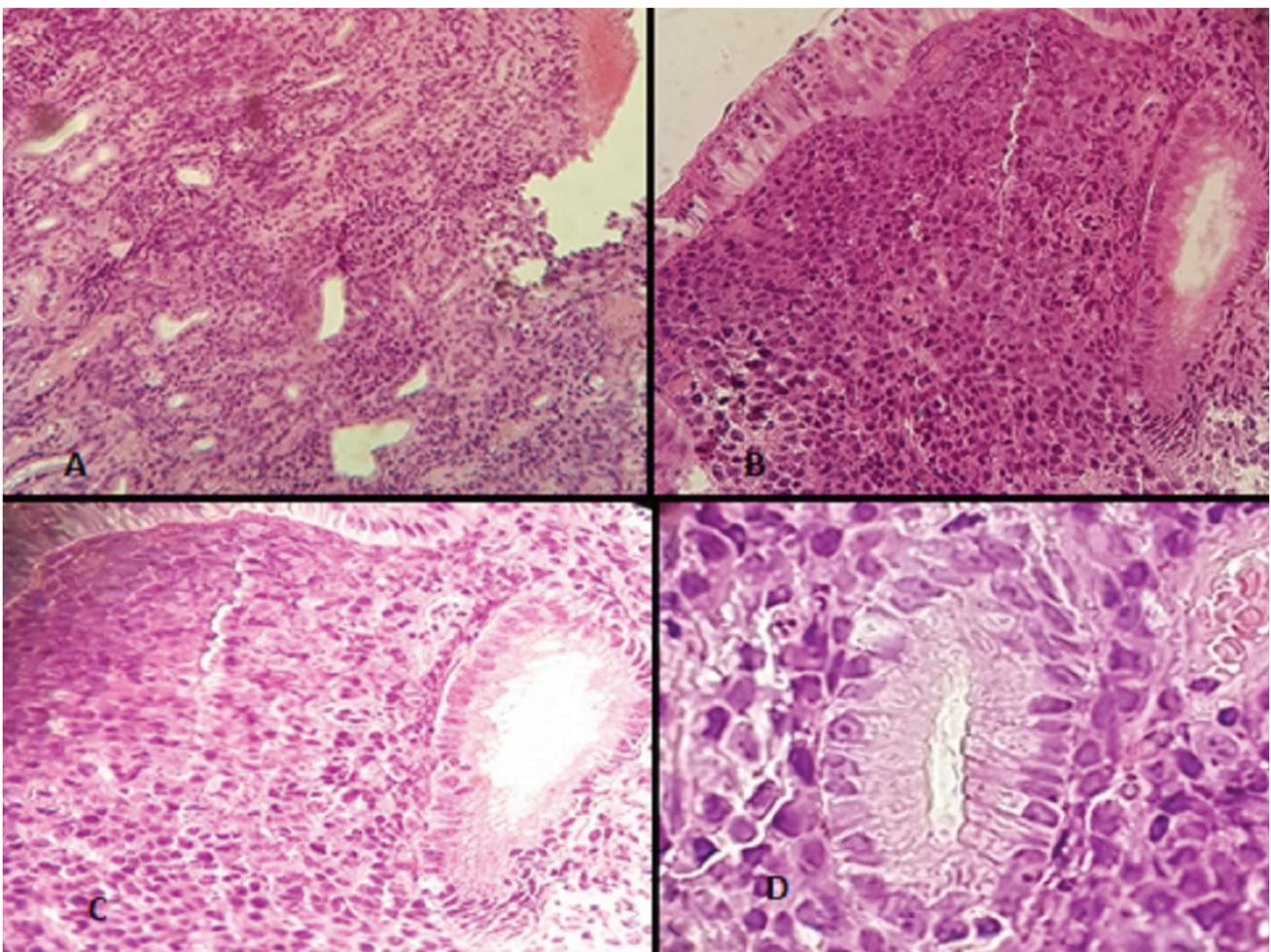


Figure 2. Sections that show gastric mucosal fragments infiltrated by large atypical lymphoid cells with prominent nucleoli (hematoxylin and eosin; A: 10×, B: 20×; C: 20×, and D: 40×).

and Asia.² Anaplastic lymphoma kinase (ALK) protein, an aberrant tyrosine kinase, serves as an additional diagnostic and subclassification tool for ALCL. Our patient was diagnosed as ALK-ALCL with KS.

A specific translocation t(2;5)(p23q35) that involves fusion of the nucleolar shuttling protein nucleophosmin (NPM1) to the receptor tyrosine kinase ALK is detected in more than 30% of ALCL cases. This translocation leads to the expression of the constitutively active NPM-ALK kinase, which is a potent trigger of multiple signaling pathways and is sufficient to drive cells toward malignant transformation. In ALK+ ALCL, it has been shown that most changes that lead to cell transformation are induced by transcription factors (TFs) such as STAT3/5, CEBPB, and AP1. In ALK- ALCL, recurrent driver mutations in JAK1 and STAT3 genes as well as chimeras that combine TFs with tyrosine kinases (ROS1 or TYK2) and overexpression of truncated ERBB4 transcripts have been described.¹⁰

Although ALCL is most common in children and young adults, it has a bimodal age distribution and can occur in older adults.¹¹ Extranodal site

involvement includes skin, soft tissue, bones, the lungs, liver, and bone marrow. Involvement of gastrointestinal tract is extremely rare.⁹ Morphologically, ALCL have cohesive clusters of pleomorphic large cells with a high mitotic rate. Cells can be large to small but the classic “hallmark cell” is always present and has an eosinophilic region near eccentric kidney or horseshoe shaped nuclei. The cytoplasm is abundant and often has denser focal staining in the perinuclear Golgi region of the cytoplasm. They have a CD4+, CD30+ phenotype with expression of epithelial membrane antigen and cytotoxic granule proteins.¹²

Anaplastic large cell lymphoma is sensitive to cytotoxic chemotherapy, both in the first line and relapsed settings; however, duration of response tends to be short-lived, particularly for ALK-ALCL with 5-year failure-free survival of only 36%. In a study, researchers have recommended administration of CHOP plus etoposide to younger patients with T-cell lymphoma as first-line therapy because this may help decrease the number of patients with early progression or relapse, and bring more patients to transplantation. For patients beyond 60 years of age, 6 courses of CHOP-21

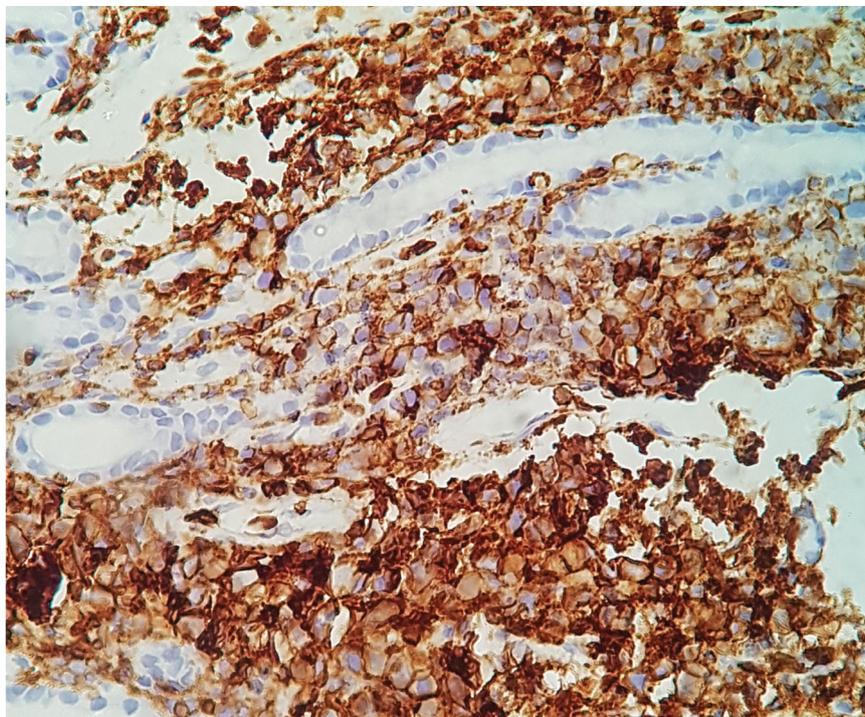


Figure 3. Immunohistochemical study that shows CD30 positivity in malignant cells. (40×).

should remain the standard first-line therapy. Anaplastic large cell lymphoma has a high relapse rate and approximately 20% to 50% of patients with systemic ALCL die from the disease.¹³ Our patient underwent chemotherapy (6 cycles of CHOP) with marked regression of disease and is currently on follow-up.

In conclusion, ALCL is an aggressive NHL with rare involvement of the stomach. In our case it coexisted with KS, which is another rare association. The patient had good response to chemotherapy and is currently on follow up.

Conflict of Interest

None declared.

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