

Case report

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Peripheral T-cell lymphoma presenting as an ischemic stroke in a 23-year-old woman: a case report and review of the literature

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Abstract

Introduction: Peripheral T-cell lymphoma of the unspecified variant is a highly aggressive subtype of T-cell non-Hodgkin's lymphoma. This is the first reported case of this type of lymphoma presenting as an ischemic stroke in a woman.

Case presentation: A previously healthy 23-year-old woman presented with fever and hemiplegia. She was subsequently intubated after scoring 7 out of 15 at the Glasgow Coma Scale. Brain computed tomography scans of the patient depicted a massive sylvian infarction while an abdominal computed tomography scan revealed multiple enlarged abdominal lymph nodes and a retroperitoneal mass adjacent to the left psoas muscle. A diagnostic work up for inherited thrombophilia yielded negative results. Blood and cerebrospinal fluid cultures for infectious agents also gave negative results. A biopsy of the retroperitoneal mass guided by computed tomography was inconclusive. A biopsy of an enlarged inguinal lymph node of the patient, combined with an immunophenotypic analysis, revealed an unspecified variant of peripheral T-cell lymphoma. The patient underwent chemotherapy but developed multiple organ failure. She died 26 days after she was admitted to our intensive care unit.

Conclusion: Peripheral T-cell lymphoma of the unspecified variant is a highly aggressive subtype of peripheral T-cell lymphomas. The latter exhibit no consistent immunophenotypic, genetic, or clinical features. Clinicians should be aware of atypical clinical presentations of the above lymphomas such as ischemic stroke.

Introduction

Peripheral T-cell lymphoma of the unspecified variant (PTCL-U) is a highly aggressive subtype of T-cell non-Hodgkin's lymphoma. The Revised European American Lymphoma (REAL) classification cites PTCL-U as comprising a mere 6% of all surveyed cases of lymphoma, thus

reflecting its rarity among the American and European populations [1,2]. Its clinical course is aggressive and may be characterized by the presence of diffuse adenopathy, extranodal disease, B-symptoms and a propensity for relapse [1-3]. We present the case of a woman who was admitted to our intensive care unit (ICU) due to cerebral

infarction. Further diagnostic investigations revealed that she had PTCL-U. While a brain tumor is a main differential diagnosis in patients with ischemia, PTCL-U presenting as a cerebral infarction has not been previously described in the literature. Furthermore, we also discuss in this case report some diagnostic issues related to the causes of stroke in patients with hematological malignancies.

Case presentation

A previously healthy 23-year-old Caucasian woman presented to our emergency department with left-sided hemiplegia and a fever (39°C). She was later intubated and admitted to the ICU when she scored 7 out of 15 at the Glasgow Coma Scale. Upon admission, the patient underwent a brain computed tomography (CT) scan, which depicted a massive sylvian infarction associated with severe cerebral edema (Figure 1A); hence, she underwent a decompressive craniectomy.

Physical examination was unremarkable except for the presence of multiple palpable left-sided inguinal lymph nodes. Laboratory tests revealed leukocytosis (WBC: 17,900 cells/mm³, 91% neutrophils), hemoglobin level at 10 gr/dL, elevated lactate dehydrogenase at 356 IU/L and C-reactive protein at 197 and 8 mg/L.

Consequently, the patient underwent an abdominal CT scan that demonstrated multiple enlarged lymph nodes and a retroperitoneal mass adjacent to the left psoas mus-

cle (Figure 1B). Finally, she underwent a transesophageal echocardiography that showed normal results.

Blood cultures taken from the patient were negative for bacterial, fungal and mycobacterial pathogens. Serologic tests for cytomegalovirus, herpes simplex virus, Epstein-Barr virus, Human Immunodeficiency Virus (HIV), tularaemia, *Yersinia pestis*, brucellosis, leptospirosis, Lyme disease, syphilis and *Toxoplasma gondii* were inconclusive. An examination of the patient's cerebrospinal fluid was negative. Results of the peripheral blood smear and bone marrow aspiration were not diagnostic.

Further laboratory tests for autoimmune disorders were also inconclusive. A diagnostic work up for inherited causes of thrombophilia such as protein C and S deficiency, antithrombin III deficiency, factor V Leiden gene mutation (associated with activated protein C resistance), prothrombin gene mutation, hyperhomocysteinemia, elevated lipoprotein (a) and polycythemia vera revealed no pathology. Furthermore, acquired prothrombotic states such as paroxysmal nocturnal hemoglobinuria, nephrotic syndrome, hyperviscosity disorders (Waldenstrom's macroglobulinemia, multiple myeloma) and sickle cell anemia were excluded conditions.

The patient underwent a CT-guided biopsy of her retroperitoneal mass, but no specific infection and/or malignancy was identified. Finally, a biopsy of an inguinal lymph node (Figure 2A) revealed the presence of PTCL-U.

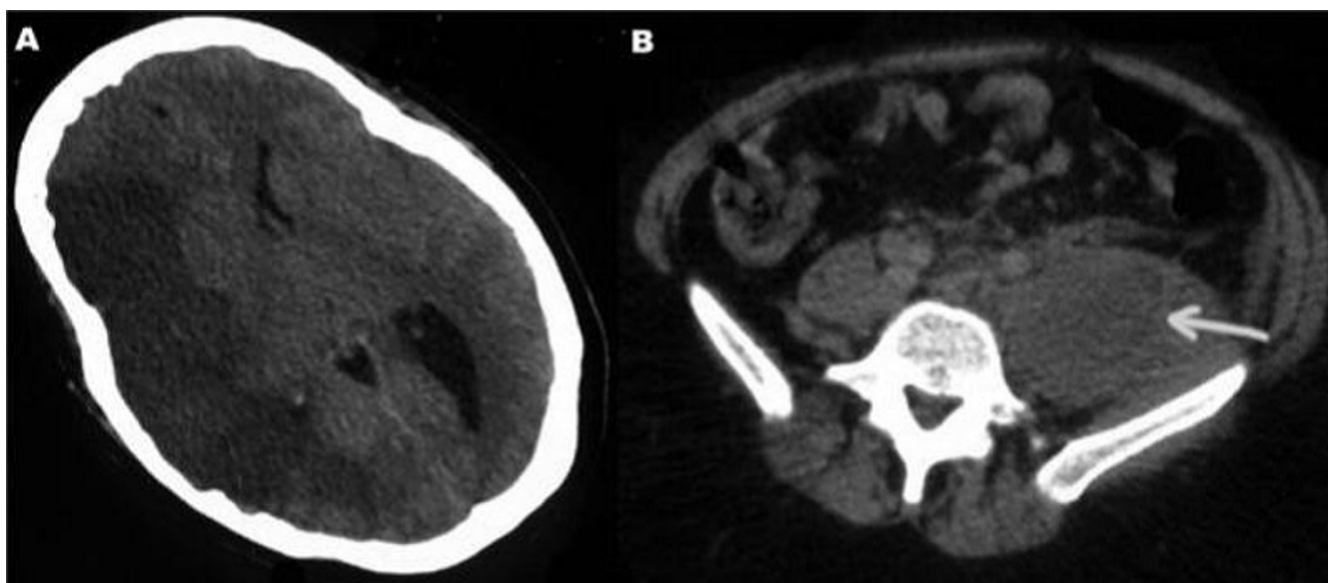


Figure 1

A) Brain computed tomography scan depicting a large right-sided ischemic region and cerebral edema. B) Abdominal computed tomography scans revealing multiple enlarged lymph nodes and a retroperitoneal mass adjacent to the left psoas muscle.

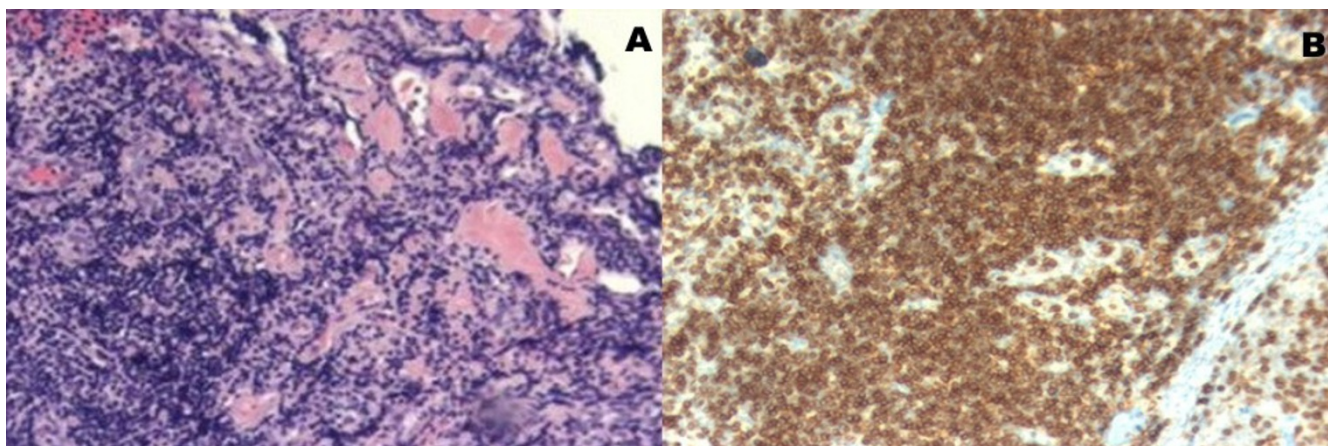


Figure 2

A) Histological section showing multiple lymphocytes and zones of fibrosis consistent with an inguinal lymph node. A hematoxylin and eosin stain magnified 100 times was used. **B) Histological section of the inguinal lymph node demonstrating positive antibodies against CD3 and verifying the T-cell origin of the lymphoma.**

An immunochemistry analysis of the patient showed positive antibodies against CD3 (Figure 2B) and CD5, thus verifying the T-cell origin of her lymphoma. Meanwhile, she showed negative antibodies against CD10, CD30, CD57 and B-cell lymphoma 6. Her CD4-to-CD8 ratio was 4:1 for T-lymphocytes. Her Ki-67 was positive for 8% to 10% of the nuclei population.

The patient underwent chemotherapy consisting of cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP), but she developed multiple organ failure and died 26 days after her admission to the ICU. An autopsy revealed small periventricular and intraparenchymal mass infiltrations that caused multifocal occlusion of the small blood vessels.

Discussion

Peripheral T-cell lymphomas comprise a heterogeneous group of tumors, which originate from mature T-cells and constitute less than 15% of all non-Hodgkin's lymphomas occurring in adults. The current World Health Organization (WHO) classification recognizes nine distinct clinicopathologic features of peripheral T-cell non-Hodgkin's lymphomas [3-5]. Viral infections such as the human T-cell leukemia virus and the Epstein-Barr virus as well as specific chromosomal translocations are implicated in the pathogenesis of PTCL-U [3]. These lymphomas, which usually affect adults at a median age of 61 years, are often associated with a poor outcome [5,6].

PTCL-U usually presents together with a generalized adenopathy and/or an extranodal disease, B-symptoms, mild anemia or thrombocytopenia, hypereosinophilia, pruritus, and hemophagocytosis [3,6-8]. However, this type of

lymphoma exhibits no consistent immunophenotypic, genetic or clinical features which makes diagnosis on a purely morphologic ground difficult. The diagnosis of PTCL-U requires careful immunophenotypic studies and can only be accurately made through exclusion [3,4]. T-cell-associated antigens such as CD3, CD5 and CD7 are variably expressed on immunohistochemistry, although one of the mature T-cell antigens (CD5 or CD7) is usually lost [9,10]. Furthermore, CD4 is more commonly expressed than CD8. This phenotypic diversity, however, does not have any obvious clinical correlation [3,4,6].

Because PTCL-U exhibits an aggressive behavior and usually presents at an advanced stage, its optimal therapy is contentious [3,4,6,11,12]. In this case, our patient presented with cerebral infarction. The differential diagnosis of stroke in young patients usually includes cardiac and hematologic diseases, inherited and acquired thrombophilias, malignancies, autoimmune disorders, inflammatory and noninflammatory vascular disorders, metabolic syndromes, and cocaine ingestion.

Meanwhile, the diagnosis of cancer leads to other possible causes of stroke such as disorders of coagulation, direct central nervous system metastases, nonbacterial thrombotic endocarditis, venous sinus occlusion, and tumor embolization [13]. Specifically, hematologic malignancies can have direct neurological effects caused by the interaction of the tumor with adjacent tissues, such as mass lesions, leptomeningeal infiltration or direct vascular occlusion. Indirect neurological effects, on the other hand, can be paraneoplastic syndromes, venous sinus occlusions and disorders of coagulation [14].

An autopsy of the patient revealed small periventricular and intraparenchymal mass infiltrations that caused small blood vessel occlusion. However, a brain CT scan upon her admission revealed a massive sylvian infarction. It should be noted that that no follow-up brain Magnetic Resonance Imaging (MRI) was performed; hence no definite pathophysiologic mechanism could be suggested to explain the autopsy results. The vessel obstruction could be attributed either to a dissemination of the lymphoma cells or to other paraneoplastic phenomena.

Conclusion

This case illustrates that peripheral T-cell lymphomas of the unspecified variant exhibit an aggressive clinical course and are usually associated with a poor outcome. Their clinical and pathologic characteristics are not consistent, which make diagnosis difficult. Clinicians should thus be conscious of ischemic stroke and other atypical clinical presentations of this type of lymphoma.

Abbreviations

REAL classification: Revised European American Lymphoma classification; WBC: white blood cells; WHO: World Health Organization; ICU: Intensive Care Unit; CNS: central nervous system; PTCL-U: peripheral T-cell lymphoma of the unspecified variant; CHOP: cyclophosphamide, doxorubicin, vincristine, prednisone; CT: computed tomography; HIV: Human Immunodeficiency Virus; MRI: Magnetic Resonance Imaging.

Consent

Written informed consent was obtained from the patient's next-of-kin for the publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

MF collected the data and drafted the manuscript. DK, AK, GS and KA participated in all medical interventions and drafted the final version of this manuscript. All authors read and approved the final manuscript.

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