Acute Neurological presentation of Hodgkin's lymphoma

JEYARAMAN RAJENDRAN
Department of Neurology,
MADRAS MEDICAL COLLEGE AND GOVERNMENT GENERAL HOSPITAL

Abstract:
The causes of ischemic stroke in young adults are many and diverse. It is important that a comprehensive search is made since many of the underlying disorders are treatable. Principal causes are extracranial arterial dissection, cardio embolism, premature atherosclerosis, hematological and immunological disorders and migraine. One of the causes for stroke in young are hematological malignancies. Among them non hodgkin's lymphoma has increased predilection for CNS manifestations. CNS manifestations of Hodgkin's lymphoma are rare. We present here a case of acute ischemic stroke in a young lady with Hodgkin's lymphoma.

Keyword: Hodgkin's lymphoma, stroke, neurological manifestations of Hodgkin's lymphoma

Introduction:
Stroke is the third most common cause of mortality. Approximately, 12% of first strokes occur in patients under 45 years of age of which 50% are ischemic. When evaluating strokes in young, it is important to enquire specifically about previous deep vein or pulmonary thrombosis (coagulopathies), arthralgia (systemic lupus), skin rash (vasculitis, anti phospholipid syndrome, Fabry's disease), miscarriages (anti phospholipid syndrome), a family history of thrombosis (inherited thrombophilias) or drug abuse. Vasculitis can affect the central nervous system as an isolated phenomenon (isolated angitis of the CNS) or as part of a systemic necrotizing vasculitis (Wegener's, Polyarteritis nodosa). Isolated angitis of the CNS presents a diagnostic challenge as there are usually no symptoms or peripheral markers. (such as abnormal ESR, positive auto antibody screens) outside the CNS. Cerebral angiography shows multiple segmental narrowing of medium and small vessels in approximately 50%. Hodgkin's lymphoma is a
hematolymphoid neoplasm, primarily of B cell lineage that has unique histologic, immunophenotypic, and clinical features. Neurorlogic complications of Hodgkin’s Lymphoma can be either directly from the disease, indirectly from the disease, or from its treatment. Direct neurologic dysfunction from Hodgkin’s Lymphoma results from metastatic intracranial disease. Indirect neurologic dysfunction may be caused by paraneoplastic disorders (such as paraneoplastic cerebellar degeneration or limbic encephalitis) and primary angitis of the central nervous system.

Case vignette:
A 24 yr old young lady, with a 4 year history of atypical episodic holocranial headache, presented with the complaints of sudden onset weakness of all 4 limbs. This was preceded by a sudden severe holocranial headache, throbbing in nature, continuous, without vomiting or visual symptoms lasted for 1 hour. Following this headache she had abnormal tonic posturing of both upper and lower limbs with loss of consciousness without tongue bite, injuries or urinary incontinence which lasted for 1 hr. she had post ictal confusion lasting for 1-2 hrs. On regaining consciousness she noticed stiff weakness of all 4 limbs left more than right, along with trunk and neck muscle weakness. She did not have thinning, twitchings or muscle pain. She did not have sensory disturbances, cranial nerve palsies, behaviour abnormalities, mood changes or abnormal movements. There were no autonomic function disturbances, fever, loss of appetite/weight, ear discharge, recent vaccinations, joint pain, skin ulcers, hyperpigmentation, photosensitivity, dryness of eyes or mouth. There were no similar illnesses in the past. She has been having episodic atypical holocranial headache for the past 4 years, lasting for 30 min to 1 hr occurring at 1-2 episodes per month which subsides with NSAIDs. There was no family history of headache or strokes. Examination revealed a single, non tender, firm, mobile, left supraclavicular lymphnode. Carotids were normal and there was no organomegaly. Higher mental functions, optic fundus, Ocular movements were normal. She had quadripareseis with bi pyramidal signs (left more than right) with left UMN facial palsy. Sensations were normal. There were no cerebellar or extra pyramidal signs.

CT Brain and MRI brain showed bilateral internal cortical watershed infarcts. MR angiogram of brain showed narrowing of Vertebral, carotid, middle and anterior cerebral arteries.

EEG – Normal, Nerve conduction studies – Normal CMAPs and SNAPs.

Fig 3. CT brain plain showing ill defined hypo densities in bilateral high frontoparietal regions

Fig 4. MRI Brain T2W showing bilateral cortical internal watershed infarcts.

Fig 5. MRI DWI showing diffusion restriction in the bilateral cortical internal watershed regions

Fig 6. MR angiogram showing narrowing of vertebral, internal carotid, MCA and ACA arteries.

Fig 1. X ray Chest PA view showing superior Mediastinal widening

Fig 2. CT thorax showing enlarged superior mediastinal LN

Vasculitis work up: ANA, LAC, C-ANCA, P-ANCA – NEGATIVE, Cardiolipin ab – Negative, serum C3,C4 - Normal CSF – proteins 60, sugar – 65, acellular, AFB & gram’s stain – Negative, No malignant cells.
FIG 7. CT cerebral angiogram showing normal vertebral and carotid arteries and their branches (CTA taken 7 days after MR imaging)

FNAC of the left supraclavicular lymph node showed reactive lymphocytosis. Patient underwent excision biopsy of the lymphnode. Excision Biopsy revealed Hodgkin's lymphoma of mixed cellularity type and she is on chemotherapy now. Weakness improved with anti-platelets and physiotherapy.

Fig 8. H&E stain of excision biopsy of left supraclavicular lymphnode Section shows effacement of architecture which is replaced by sheets of lymphocytes and plasma cells admixed with mononuclear and binuclear Reed-Sternberg cells.

**Discussion:**

The neurologic disorders related to Hodgkin’s Lymphoma (HL) can be classified into those that result directly from HL (metastatic complications), indirectly from HL, or from HL-directed treatment.

<table>
<thead>
<tr>
<th>Direct (metastatic)</th>
<th>Intraparenchymal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dural</td>
</tr>
<tr>
<td></td>
<td>Lymphomeningeal</td>
</tr>
<tr>
<td></td>
<td>Epidural spiral cord</td>
</tr>
</tbody>
</table>

**Indirect**

Paraneoplastic
Cerebellar degeneration
Lymphocytic encephalitis
CNS angiitis

**Treatment-related**
The majority of paraneoplastic disorders are thought to be immune-mediated. Several paraneoplastic syndromes have been reported in patients with HL of which cerebellar degeneration is the best characterized. There is a strong association between the circulating anti-neuronal antibody anti-Tr with paraneoplastic cerebellar degeneration and HL. The typical presentation is pan-cerebellar dysfunction (dysarthria, nystagmus, truncal ataxia, and appendicular ataxia) developing over months. Other possible paraneoplastic complications of HL include chorea and ataxia, subacute sensory neuropathy, motor neuron disease, myasthenia gravis, stiff person syndrome, brachial neuropathy, GBS and anti NMDA receptor encephalitis. Our patient didn’t fit in with any of the above.

An initiative of The Tamil Nadu Dr M.G.R Medical University
University Journal of Medicine and Medical Specialities
Other conditions that have been associated with PACNS include herpes zoster, non-Hodgkin’s lymphoma, human immunodeficiency virus, and Sjogren’s syndrome. \(^{18}\) Since herpes zoster infections are common in patients with HL, the relationship between zoster vasculitis and PACNS associated with HL is unclear. \(^{19}\) Our patient’s CT & MRI brain showed an internal watershed infarct and an initial MR angiogram showed a significant constriction of all major vessels. But the CT angiogram taken a week after showed normal vascular anatomy. This suggested the possibility of a reversible cerebro vasoconstriction syndrome (RCVS). Call–Fleming syndrome or RCVS describes a rare, reversible segmental vasoconstriction of cerebral arteries that symptomatically presents with a thunderclap headache followed by focal neurologic deficits most commonly in women aged 20 to 50 years. \(^{20}\) Our patient also presented with similar picture and hence RCVS is also highly likely even though there are no case reports for HL causing RCVS, so far in literature. The syndrome is generally self-limited and has a low incidence of recurrence.

**Conclusion:**

We present this case of stroke in young associated with primary angitis of the CNS or a reversible cerebro vascular constriction syndrome secondary to hodgkin’s lymphoma. Hodgkin’s lymphoma presenting as an acute stroke in young is very rare. Stroke as a first presentation of primary angitis of the CNS is also very rare. \(^{21}\) Our patient is improving well with chemotherapy. A high index of suspicion is needed in evaluating patients with strokes in young as early diagnosis can reduce the morbidity and mortality and can improve the quality of life.

**References:**


3. Shriver ME, Prockop LD. The economic approach to the stroke work up. Current opinion in neurology & neurosurgery 1993; 6; 74-7


19. Timothy L. Vollmer, MD; Joseph Guarnaccia, MD; William Harrington, MD; Steven V. Pacia, MD; Ognen A. C. Petroff, MD , Idiopathic Granulomatous Angiitis of the Central Nervous System -Diagnostic Challenges Arch Neurol. 1993;50(9):925-930.