

Contrast Enhancing Lesions in Progressive Multifocal Leukoencephalopathy: A Clinicopathological Correlation

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ABSTRACT: A 60 year old man with chronic lymphocytic leukemia (CLL) developed a subacute neurological illness associated with multiple contrast enhancing lesions on CT scan. At autopsy large demyelinating lesions characteristic of progressive multifocal leukoencephalopathy (PML) were found in the right cerebral hemisphere surrounded by a dense leukemic infiltrate. The areas of contrast enhancement, highly unusual for PML, coincided with the CLL infiltrate.

RÉSUMÉ: Lésions hypercontrastantes dans la leuco-encéphalopathie multifocale progressive. Un homme de 60 ans atteint d'une leucémie lymphoïde chronique (LLC) a développé un syndrome neurologique subaigu associé à des lésions multiples hypercontrastantes au CT scan. On a retrouvé à l'autopsie, de grandes lésions démyélinisantes caractéristiques d'une leuco-encéphalopathie multifocale progressive (LMP) entourées d'un infiltrat leucémique dense dans l'hémisphère droit. Les zones hypercontrastantes, phénomène inusité dans la LMP, coïncident avec les infiltrats de LLC.

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This report describes a patient with chronic lymphocytic leukemia (CLL) who developed two unusual complications of this illness, leukemic infiltration of the brain and progressive multifocal leukoencephalopathy (PML). The rarity of the former and the atypical CT scan appearance of the latter led to diagnostic difficulties.

CASE REPORT

A 60 year old man developed CLL in 1978, at age 54. Treatment included chronic low dose prednisone and intermittent chlorambucil. A splenectomy was performed in 1982. The CLL remained under control (WBC < 20,000) until his death in April 1984 with no evidence of blast crisis or Richter's syndrome. Dull vertex headaches and tinnitus began 8 months prior to death. He awoke on January 31, 1984, with severe vertex headache and was unable to dress himself. Left arm and hand weakness developed over the next four days. A CT scan revealed a low density lesion in the right frontal lobe (Figure 1a). There was a faint rim of contrast enhancement, but no mass effect (Figure 1b). He was thought to have had a stroke. The left arm weakness worsened steadily, he became tearful and forgetful and began to have difficulty with directions. When re-examined, poor recent memory, dressing apraxia, severe spastic weakness of the left arm and absent position sense in the

left hand were noted. A repeat CT scan disclosed low density lesions in the right frontal and parietal lobes with perimeter enhancement. The spinal fluid examination was normal. Brain biopsy revealed an extensive perivascular monoclonal (IgM, λ) lymphocytic infiltrate in the cerebral cortex consistent with CLL. The biopsy specimens contained very little white matter. He received whole brain radiotherapy (2500 rads/10 fractions) and did not improve. Eighteen days after completing treatment he had two generalized seizures, ventricular tachycardia and died.

PATHOLOGY

The general autopsy revealed extensive mediastinal and retroperitoneal lymphadenopathy and diffuse leukemic infiltration of the lungs, liver, kidneys and bone marrow. The meninges and external surface of the brain and spinal cord were normal in appearance. Coronal sections of the cerebral hemispheres revealed a large area of yellowish discoloration and softening in the white matter extending from the right frontal lobe at the level of the caudate to the right occipital pole. The overlying cortex appeared normal. Transverse sections of the brain stem, cerebellum and spinal cord were unremarkable. Microscopic exami-

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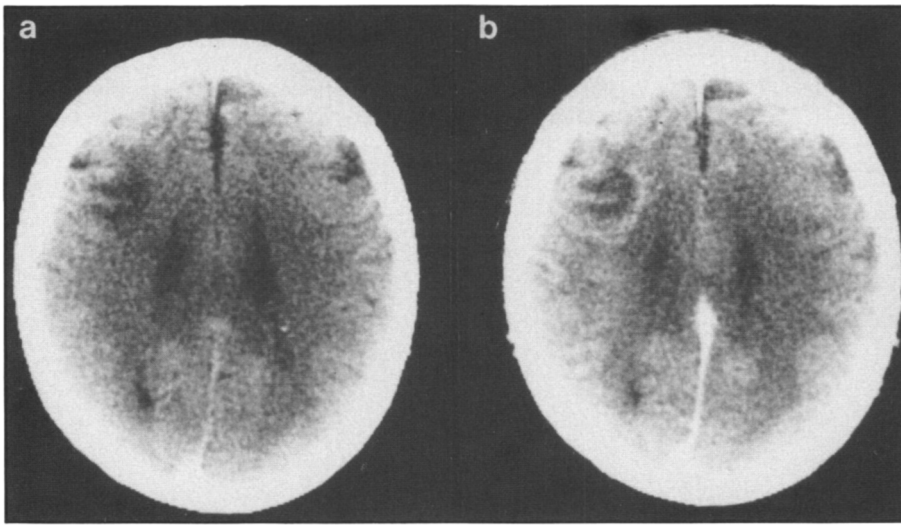


Figure 1 — The unenhanced CT scan (a) shows a right frontal low density lesion without mass effect. Following intravenous contrast (b) faint perimeter enhancement is seen.

nation of the brain revealed extensive demyelination, bizarre multinucleated astrocytes, microglial nodules and abnormal oligodendrocytes with hyperchromatic nuclei and basophilic intranuclear inclusions in the right frontal, parietal and occipital lobes, findings characteristic of PML. Perivascular and parenchymal leukemic infiltrates were scattered throughout the brain but were conspicuous in the white matter and cortex of the right cerebral hemisphere surrounding the PML lesions (Figure 2). There was no unusual glial or vascular reaction at the margins of the PML lesions and the adjacent brain was not oedematous, grossly or microscopically.

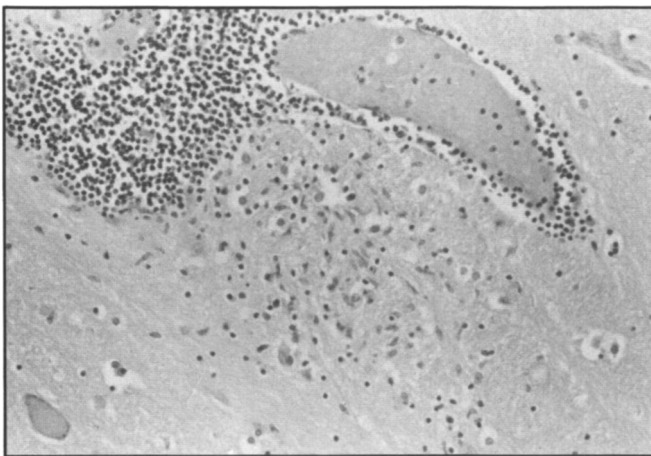


Figure 2 — A section from the right frontal cortex adjacent to a large PML plaque demonstrates a perivascular leukemic infiltrate with invasion of the surrounding brain parenchyma and a nearby microglial nodule (Haematoxylin + Eosin; 40X).

DISCUSSION

This case is unusual in two respects, the infiltration of brain parenchyma by chronic lymphocytic leukemia, and the CT scan appearance of the PML lesions. Invasion of the perivascular spaces and brain substance rarely occurs in chronic lymphocytic leukemia^{1,2} except in those instances in which CLL converts to an acute leukemia (i.e., blast crisis) or malignant lymphoma (i.e., Richter's syndrome). PML, a rare viral infection of the brain in the immunocompromised host, is a well

recognized complication of CLL.³ Enlarging low density lesions in the cerebral white matter which lack mass effect and do not enhance following intravenous contrast are the characteristic CT scan findings.^{4,5}

The dense lymphocytic infiltrate in the right cerebral hemisphere proved by immunohistochemical techniques to be neoplastic in nature and identical to the leukemic cells in the peripheral blood. Perivascular lymphocytes are occasionally observed near PML plaques but in most instances there is no discernible inflammatory reaction to the virus or diseased brain.⁶ The immunopathological findings in this case confirm Richardson's suspicion that sizeable collections of lymphocytes in PML lesions are neoplastic.⁶ The observation that the infiltrate was most pronounced in the brain adjacent to the PML lesions is unexplained.

The CT scan findings were atypical in as much as the PML lesions enhanced. Contrast enhancement along the edge of PML lesions has been described previously and attributed, in the absence of detailed neuropathological evaluation, to "inflammatory" changes at the site of active demyelination.⁷ In our patient the PML lesions were surrounded by a dense perivascular and parenchymal leukemic, as opposed to inflammatory, infiltrate with the contrast enhancement seemingly related to the invasion of brain by CLL. Contrast enhancing abnormalities on CT scan do not exclude the diagnosis of PML but suggest complex pathology.

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