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# Intracranial Vascular Calcifications, Glioblastoma Multiforme, and Lead Poisoning

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**Summary:** A 72-year-man with previous lead poisoning presented with raised intracranial pressure and localizing neurologic signs. CT scans showed a high-grade glioma and extensive intracranial calcifications, which proved to be vascular in distribution on postmortem examination. The latter findings support the concept of dystrophic calcification following lead-induced cerebrovascular injury. Lead poisoning should be considered in the differential diagnosis of unexplained intracranial calcifications. There is also evidence from previous studies to suggest a causative relationship between lead poisoning and development of glioma.

**Index terms:** Glioblastoma multiforme; Brain, effect of toxic substances on; Brain, calcifications

The pathogenesis of intracranial calcifications is diverse, from normal aging to a variety of pathologic sources (1). The latter group includes familial, neoplastic, endocrinologic, inflammatory, ischemic, and traumatic agents (2). It has been reported that lead poisoning may also cause intracranial calcification (3–5). We describe the computed tomographic (CT) and pathologic findings in a patient with extensive intracranial vascular calcifications consequent to lead poisoning. A coexistent glioblastoma multiforme was also found.

## Case Report

A 72-year-old man was admitted with a 3-week history of headache, drowsiness, and two episodes of generalized convulsions. He had worked in a metal factory 30 years earlier, and lead poisoning had been diagnosed at that time. The exact duration of his lead exposure was not known, but it had spanned several years. There was no history of recent lead exposure. He had been in relatively good health until 5 years previously, when hypertension, diabetes mellitus, and chronic renal impairment were di-

agnosed. Three years later, he suffered a stroke with residual right-sided hemiplegia.

On admission, his Glasgow Coma Scale score was 10/15 (aphasia, ability to locate painful stimuli, spontaneous eye opening). Bilateral papilledema was present with equal and reactive pupils and dense right-sided hemiplegia. Sensory function could not be assessed. The rest of the examination was normal.

Laboratory investigations showed an elevated blood lead level of 2.3  $\mu\text{mol/L}$  (recommended level, below 0.48  $\mu\text{mol/L}$ ) (6). There was normochromic, normocytic anemia, with a red cell count of  $3.25 \times 10^{12}/\text{L}$  and a hemoglobin count of 10 g/dL (no basophilic stippling), and mild renal impairment with plasma urea 12.7 mmol/L and creatinine 238  $\mu\text{mol/L}$ . Calcium and phosphate levels were normal.

A noncontrast CT scan of the brain was obtained to exclude a left-sided supratentorial mass lesion. It showed a large, poorly defined hypodense lesion with central hyperdensity in the left frontoparietal region (Fig 1A), with left-to-right midline shift, compression of the left lateral ventricle, dilatation of the right ventricle, and transtentorial herniation. A more striking finding was extensive symmetrical curvilinear and specklike calcifications in the cerebellum (Fig 1B), cerebral cortex, white matter (with accentuation at the gray-white junction), thalamic regions (Fig 1A), and basal ganglia. The calcifications were most prominent in the cerebellum. The provisional diagnosis was high-grade glioma with hemorrhage and intracranial calcifications resulting from previous lead poisoning.

A biopsy was not performed because of the patient's age and poor clinical condition. He was treated conservatively with steroids and anticonvulsants. Bronchopneumonia developed, and the patient died 7 weeks after admission.

On postmortem examination, the brain weighed 1435 g and showed diffuse edema, more severe in the left cerebral hemisphere, with transtentorial herniation. Coronal sectioning of the brain revealed a large necrotic tumor with central hemorrhage in the left frontal and parietal lobes (Fig 1C), extending into the corpus callosum, basal gan-

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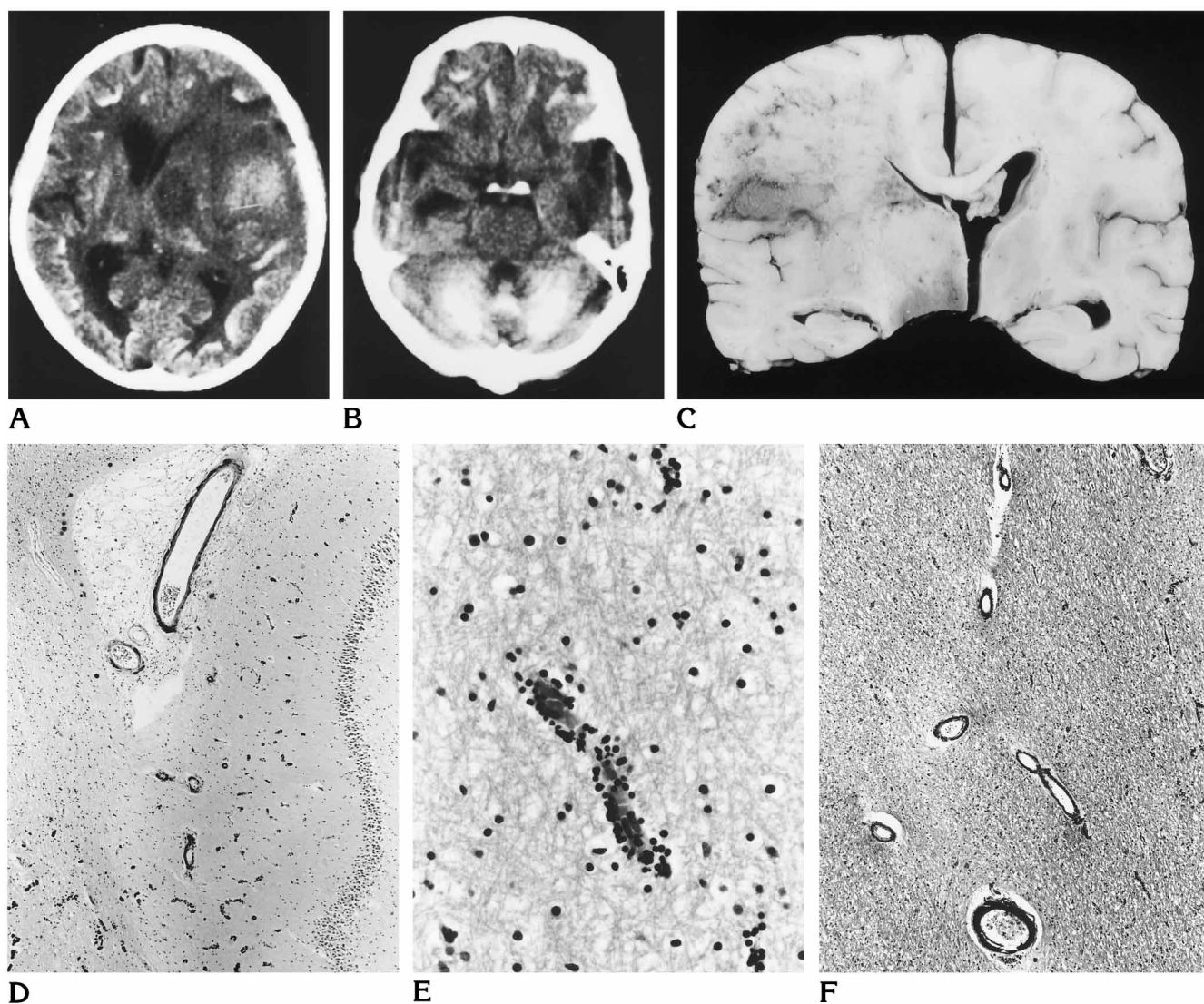


Fig 1. A 72-year-old man with lead poisoning.

A and B, Axial CT scans of the brain. At the level of the midventricular region (A), a tumor is seen in the left frontoparietal region, with hemorrhage, midline shift, and dilatation of the right ventricle. Multiple specklike and curvilinear calcifications are present in the cerebral cortex, white matter (with accentuation at the gray-white junction), and thalamic regions. At the level of the posterior fossa (B), calcifications are seen in the vermis and both cerebellar hemispheres.

C, Coronal section through the brain, viewed posteriorly, shows left frontoparietal tumor with hemorrhage.

D-F, Photomicrographs show white matter with calcification of capillaries and small- to medium-caliber vessels (hematoxylin-eosin,  $\times 100$ ) (D); calcospherites in the walls of the capillaries (hematoxylin-eosin,  $\times 250$ ) (E); and larger vessels with coalescence of calcospherites forming circumferential deposits (hematoxylin-eosin,  $\times 100$ ) (F).

glia, diencephalon, midbrain, and upper pons. Midline and lateral Duret hemorrhages were present in the pons. Microscopic examination confirmed a glioblastoma multiforme with marked cellular pleomorphism, endothelial proliferation, and necrosis.

Intracranial calcifications were not apparent macroscopically although there was mild gritty resistance on slicing the brain. Microscopic examination revealed calcifications in the cerebellum, cerebral cortex, gray-white junction, white matter (Fig 1D), basal ganglia, and thalamic regions. The density of calcifications was greatest in

the cerebellum, where the calcium deposits were concentrated within the granular layer, corpus medullare, and dentate nuclei. The pattern of calcification was striking, with deposits consisting of small calcospherites in the walls of the capillaries and in the tunica media of small- to medium-caliber vessels (Fig 1E). In larger vessels, there was coalescence of calcospherites to form larger concretions or circumferential deposits (Fig 1F). Calcospherites were also seen in the perivascular (Virchow-Robin) spaces. Calcification of brain parenchyma was not present. This pattern of vascular calcification in the ab-

sence of parenchymal calcification accounted for the curvilinear and specklike calcifications seen on CT scans.

Analysis of brain tissue by atomic absorption spectrophotometry showed an abnormally high lead content of 205  $\mu\text{g/g}$  ("normal" range after 30 years of environmental exposure, 5 to 40  $\mu\text{g/g}$ ) (7), indicative of a persistently elevated total body lead burden. As the left cerebrum was extensively destroyed by tumor, it was not possible to identify evidence of old infarct or hemorrhage.

## Discussion

Intracranial calcifications can occur both physiologically and pathologically (1). In elderly brains, mild calcification of vessels and parenchyma is a normal and common incidental finding in the basal ganglia, pineal gland, choroid plexus, dura, and habenula (3). Calcification in other brain regions or in patients under age 40 is abnormal. The pathogenesis may be familial (eg, tuberous sclerosis), neoplastic (eg, craniopharyngioma), endocrinologic (eg, abnormal calcium metabolism), inflammatory (eg, congenital toxoplasmosis), ischemic, or traumatic (2). Such factors as age, family history, previous infection, and the pattern and distribution of calcifications may assist in the differential diagnosis.

Several authors have suggested that lead poisoning may also cause intracranial calcification. In 1977, Tonge et al (5) showed a correlation between cerebellar vascular calcifications and raised bone lead levels in an autopsy series. In 1986, Reyes et al (3) reported extensive intracranial calcifications detected by CT in three adults with chronic lead poisoning. The radiologic distributions of the calcifications were similar to those in our case, but there was no pathologic description.

The pathogenesis of intracranial calcification in lead poisoning is uncertain. Overwhelming lead toxicity of the central nervous system is characterized by encephalopathy, with diffuse cerebral edema affecting mainly the cerebellum (8, 9). The primary lesion is thought to be vascular injury, a concept supported by demonstration of endothelial damage and abnormal cerebrovascular permeability in lead-poisoned suckling rats (10–12). Microscopically, a variety of vascular changes are seen, including edema, gliosis, neuronal loss, and a perivascular proteinaceous exudate (10). Tonge et al postulated that the proteinaceous exudate is incompletely cleared and undergoes dystrophic

calcification (5). He further demonstrated a proteinaceous matrix within the cerebellar vascular calcifications in his autopsy series. In our case, the confinement of the calcifications to within and around the walls of brain blood vessels strongly supports the mechanism of dystrophic calcification following primary lead-induced vascular injury. The predilection for maximal cerebellar involvement in lead toxicity of the central nervous system may account for the dense concentration of calcifications in this region.

The relationship between lead poisoning and gliomas is unclear. A variety of brain insults, including trauma, multiple sclerosis, and progressive multifocal leukoencephalopathy, have been associated with the development of glioma (13). One hypothesis is the dedifferentiation of reactive glia in the setting of local tumor-producing factors. Oyasu et al (14) found a 9% frequency of brain tumors, mostly poorly differentiated gliomas, in experimental rats fed high doses of lead subacetate. Two reports (15, 16) have described patients with chronic occupational lead exposure who died of complications of astrocytoma and glioblastoma. Schreier et al (17) also reported the findings in two children with delayed developmental milestones and elevated lead levels in whom grade II to III astrocytomas developed in the left frontal lobe and cerebellum. Diffuse astrocytic tumors in the cerebellum are relatively rare, in contrast to pilocytic astrocytomas. Since the cerebellum is the site of maximal involvement in lead encephalopathy, the association between lead poisoning and the development of high-grade gliomas may be more than incidental. Larger series in the future may provide more information.

In conclusion, we propose that the extensive intracranial vascular calcifications in this case represent dystrophic calcification following previous lead-induced cerebrovascular injury. Lead poisoning should be considered in the differential diagnosis of unexplained intracranial calcifications. Concentration of calcifications in the cerebellum and histologic findings of vascular calcification are more common in lead poisoning. In cases in which lead poisoning is a consideration, the clinician should inquire specifically about previous lead exposure (eg, occupational contact, consumption of illegal "moonshine" whiskey); measurement of blood and urine lead levels will confirm or exclude the diagnosis. The coexistence of glioblastoma and

lead poisoning in our patient is intriguing. There is ample evidence from previous animal studies and case reports to suggest a causative relationship between lead poisoning and glioma development. Perhaps these findings will provide the impetus for future epidemiological studies.

## References

1. Hayman LA, Bronen RA, Charletta DA. Adult cerebrum. In: Hayman LA, Hinck VC, eds. *Clinical Brain Imaging*. St Louis, Mo: Mosby-Year Book; 1992:117-153
2. Woodruff WW. *Fundamentals of Neuroimaging*. Philadelphia, Pa: Saunders; 1993:1-32
3. Reyes PF, Gonzalez CF, Zalewska MK, Besarab A. Intracranial calcification in adults with chronic lead exposure. *AJNR Am J Neuroradiol* 1985;6:905-908
4. Swartz JD, Faerber EN, Singh N, Polinsky MS. CT demonstration of cerebral cortical calcifications. *J Comput Assist Tomogr* 1983;7:476-479
5. Tonge JI, Burry AF, Saal JR. Cerebellar calcification: A possible marker of lead poisoning. *Pathology* 1977;9:289-300
6. Centers for Disease Control. *Preventing Lead Exposure in Young Children*. Atlanta, Ga: Centers for Disease Control; October 1991
7. Moore MR. Lead in humans. In: Lansdown R, Yule W, eds. *Lead Toxicity*. Baltimore, Md: Johns Hopkins University Press; 1986: 54-95
8. Whitfield CL, Ch'ien LT, Whitehead JD. Lead encephalopathy in adults. *Am J Med* 1972;52:289-298
9. Cullen MR, Robins JM, Eskenazi B. Adult inorganic lead intoxication: presentation of 31 new cases and a review of recent advances in the literature. *Medicine* 1983;62:221-247
10. Jacobs JM, Le Quesne PM. Toxic disorders. In: Adams JH, Duchen LW, eds. *Greenfield's Neuropathology*. 5th ed. London, England: Edward Arnold; 1992:881-987
11. Schochet SS Jr, Nelson J. Exogenous toxic: metabolic diseases including vitamin deficiency. In: Davis RL, Robertson DM, eds. *Textbook of Neuropathology*. 2nd ed. Baltimore, Md: Williams & Wilkins; 1991:428-460
12. Pentschew A, Garro F. Lead encephalopathy of the suckling rat and its implications on the porphyriopathic nervous diseases. *Acta Neuropathol* 1966;6:266-278
13. Hochberg FH, Gabbai AA. Risk factors in the development of glioblastoma and other brain tumors. In: Wilkins RH, Rengachary SS, eds. *Neurosurgery Update*. New York: McGraw-Hill; 1990: 233-244
14. Oyasu R, Battifora HA, Clason RA, McDonald JH, Hass GM. Induction of cerebral gliomas in rats with dietary lead subacetate and 2-acetyl-aminofluorene. *Cancer Res* 1977;30:1248-1261
15. Castleman B, McNeely BU. Case records of the Massachusetts General Hospital. *N Engl J Med* 1971;285:394-401
16. Portal RW. Cerebral tumor in a lead worker. *Br J Indus Med* 1961;18:153-156
17. Schreier HA, Sherry N, Shaughnessy E. Lead poisoning and brain tumors in children: a report of two cases. *Ann Neurol* 1977;1: 599-600