

A Case of Huntington's Chorea With Unilateral Ectopic Gray Matter

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SUMMARY: *The authors report a single case of Huntington's chorea associated with a unilateral focus of ectopic gray matter. The patient's symptoms began at age 45 and included typical involuntary jerking movements of all extremities and face. Mental deterioration may have preceded the choreiform movements. The family history was positive for Huntington's chorea. Pneumoencephalogram showed atrophy of the caudate nuclei bilaterally early in the disease. The patient improved transiently with haloperidol therapy.*

The major pathologic features included

mild generalized cerebral atrophy with marked atrophy of the caudate nuclei and putamen. Within the white matter of the left frontal lobe, there were irregular nodules of ectopic gray matter with an overall diameter of 2 cm.

The rarity of either unilateral ectopia or Huntington's chorea alone, makes it impossible to judge if the two lesions might be linked by a common pathologic mechanism. The significance such a linkage might hold is discussed in light of several currently postulate pathologic mechanisms.

RÉSUMÉ: *Les auteurs rapportent un cas unique de chorée de Huntington associé à un foyer unilatéral de matière grise ectopique. Les symptômes du patient commencent à l'âge de 45 ans et incluent des mouvements brusques involontaires typiques de toutes les extrémités et du visage. Il est possible que la détérioration mentale ait précédé les mouvements choréiformes. L'histoire familiale était positive en faveur de la chorée de Huntington. Un pneumoencéphalogramme a montré une atrophie bilatérale du noyau caudé très tôt dans l'évolution. Il y eut une*

amélioration passagère avec l'emploi de l'halopéridol.

La pathologie montra une faible atrophie cérébrale généralisée avec une atrophie plus marquée des noyaux caudés et des putamen. Dans la matière blanche du lobe frontal gauche, on note des nodules irréguliers composés de matière grise ectopique d'un diamètre total de 2 cm.

Les deux entités d'ectopies unilatérales et de chorée de Huntington sont si rares qu'il est impossible d'évaluer s'il existe un mécanisme pathologique commun. Nous en discutons la signification éventuelle.

INTRODUCTION

It is extremely difficult to shed light on the pathogenesis of Huntington's chorea by routine pathological studies. While an appreciation of the full spectrum of associated defects might provide some insights, the rarity of this disorder can sometimes make it impossible to decide which changes are truly associated by a common pathogenesis, and which are coincidental. With these reservations in mind, we offer the following case; a single example of Huntington's chorea associated with an obvious developmental cortical defect.

CASE REPORT

This man had worked as a machinist and previously enjoyed excellent health with good co-ordination. In 1972, at age 45, he began to notice involuntary jerking movements which brought him to a neurologist. They affected all four limbs, but especially his legs and gait. He related that his mother had died of Huntington's chorea in her early forties.

On examination all major muscle groups were involved in the irregular and unpredictable jerking movements. There was no evidence of atrophy, weakness, or change in deep tendon reflexes and tone. Plantar responses were downgoing and suck, grasp and palmomental reflexes were absent. The sensory and cranial nerve examinations were normal. His composite I.Q. measured 84 on formal testing with low scores noted especially in abstraction and memory functions. His general physical examination was unremarkable and no Kaiser-Fleisher ring or other stigma of a metabolic disorder could be demonstrated.

Further workup included CBC, sedimentation rate, liver function tests, and serum electrolytes including cal-

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cium which all were normal. At lumbar puncture, the CSF pressure, sugar, protein, and cell counts were also normal. Serology of both blood and CSF was negative. Skull radiography was normal but a pneumoencephalogram (1972) showed bilateral atrophy of the caudate nuclei and mild cerebral atrophy. An EEG demonstrated only minimal slow wave changes with a minor left predominance. An EMG examination failed to show any changes in peripheral nerve or muscle.

A diagnosis of Huntington's chorea was made and haloperidol begun. This initially produced a modest improvement in the movements, but over the next 6 years he became worse. Re-investigation of possible metabolic causes proved fruitless. Towards the end, he vacillated between profound bradykinesia and poorly controlled movements depending on the level of haloperidol given. Intellect deteriorated further and although deep tendon reflexes became brisk with a few beats of clonus, the plantar responses were never upgoing. There was never any evidence of sensory change. He died in 1978, six years after the first symptoms were recognized.

PATHOLOGICAL FINDINGS

The brain, fixed in formalin, weighed 1180 grams. The gyri were moderately

atrophic, especially in the frontal regions. Serial coronal sections revealed marked atrophy of the striatum contributing to the appearance of enlarged lateral ventricles (fig. 1). The globus pallidus bilaterally also appeared atrophic and were slightly brown in color. Within the white matter of the left frontal lobe, there were irregular nodules of ectopic gray matter with an overall diameter of approximately two centimeters (fig. 2). Small subependymal nodules of similar tissue were seen to bulge into the left frontal horn (fig. 2). In one area, the ectopic gray matter blended with the overlying cortex. The cerebellar cortex appeared to be moderately atrophic as well.

With routine histological techniques, the cortical ribbon appeared moderately narrowed especially in the frontal regions, but no other abnormalities were noted. In the caudate nucleus and putamen bilaterally, there was a marked loss of smaller neurons with relative preservation of the larger ones (fig. 3). Wilson's pencil bundles were markedly reduced in both diameter and intensity of myelin staining (fig. 4). In the globus pallidus, the neurons contained increased amounts of lipofuscin within their cytoplasm and there were small amounts of iron in macrophages around blood vessels and in the cytoplasm of glial cells. This accounted for the brown discoloration

in this area seen in the gross. The cortex, striatum, and pallidum showed a loss of background neuropil with a mild degree of reactive gliosis. Within the ectopic gray matter, many of the neurons were pyramidal in type and an occasional neurofibrillary tangle was noted. The neuronal dendrites in this area had no predominant orientation (fig. 4). Within the molecular layer of the cerebellum an occasional focus of ectopic granular neurons was seen.

DISCUSSION

Huntington's chorea is currently considered to be a hereditary degenerative disorder affecting many parts of the brain (Hallervorden, 1957; Bruyn et al., 1979), but especially the cerebral cortex and neostriatum (Jelgersma, 1908; Alzheimer, 1911; Stone and Falstein, 1938; Earle, 1973). Despite its hereditary nature, developmental changes in the brain are not usually a recognized feature: the defect appears to be latent clinically and the brains of individuals to be afflicted are often tacitly presumed "normal" until the degenerative changes manifest usually in the fourth or fifth decades. This view is supported by CT scan studies of persons at risk for the disorder since neither ventricular, caudatal, nor cortical changes are evident which would allow the recognition of carriers (Neophytides, et al 1979).



Figure 1 — Coronal section of the forebrain showing apparent ventricular enlargement with shrinkage of the neostriatum and moderate cortical atrophy.



Figure 2 — Coronal section through the left frontal lobe showing the complex of ectopic gray matter.

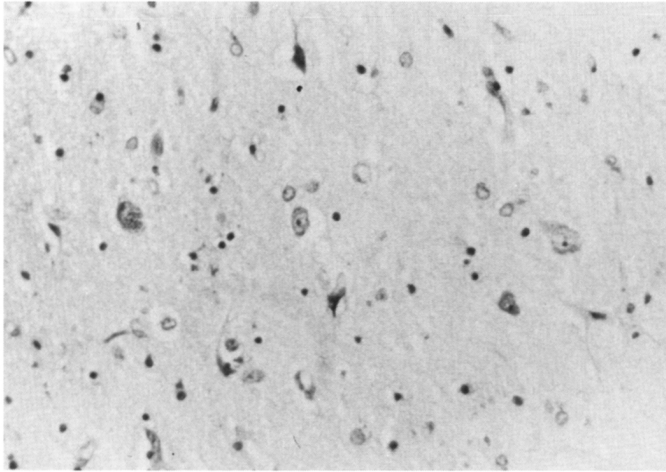


Figure 3 — Microscopic appearance of the caudate nucleus. Note the relative preservation of larger caudate neurons. Original Magnification 250 x.

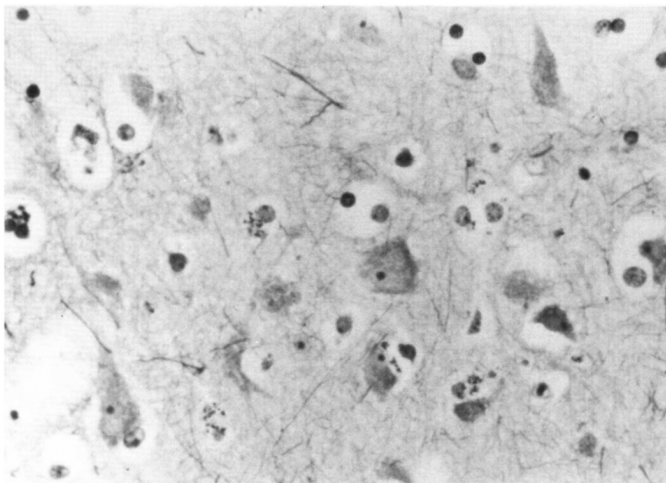


Figure 5 — Microscopic appearance of the ectopic gray matter. Original Magnification 400 x.

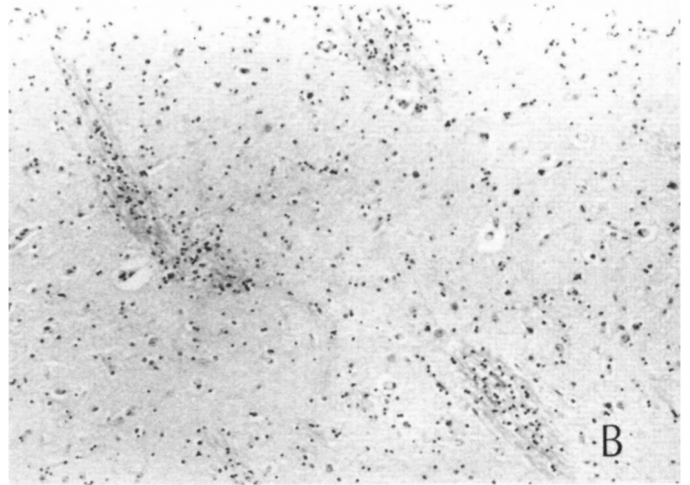
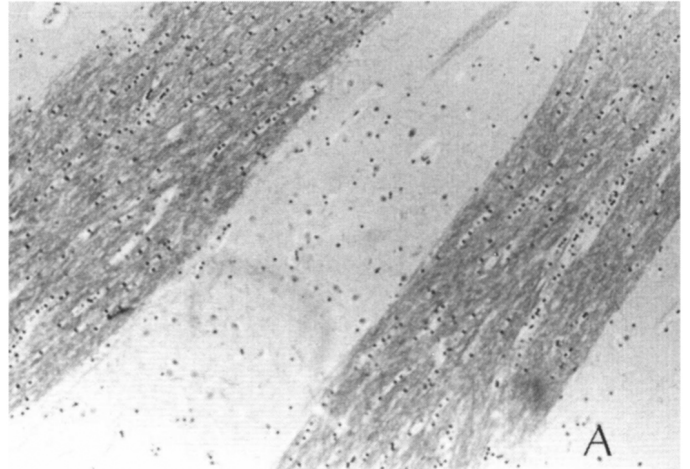


Figure 4 — Shrunken Wilson's pencil bundles (B) compared with normal (A). Original Magnification 100 x.

Detailed psychometric tests (Wilson and Garron, 1979; Lyle & Gottesman, 1979) however, question the assumption of a premorbidly "normal" brain, pointing out the gradual erosion of intellect long before the choreic movements begin. In addition, certain pathological changes noted by others in the cortex are difficult to ascribe purely to degenerative events and could conceivably have a developmental basis. The "architectural disarrangement of neurons . . . misaligned with respect to the columnar axis perpendicular to the cortical surface" noted by Bruyn et al., (1979) and a disturbed "alignment of nerve cells" mentioned by Tellez-Nagel et al.,

(1973) may be pertinent to this question.

The view that the brain may be abnormal from early on is also more in keeping with pathogenetic mechanisms postulating a chronic release of some toxic excitatory substance (Olney, 1979; McGeer et al., 1979) or a widespread abnormality of cell membranes (Noronha et al., 1979).

In the light of the above, the case reported here is doubly interesting. First, the brain of this Huntington's chorea patient clearly was not normal at the outset and declared so structurally. While the likelihood remains that the defect is coincidental, it could

conceivably represent an extreme example of the "misaligned" cortical neurons already noted by others (Bruyn et al., 1979; Tellez-Nagel et al., 1973). Second, the developmental defect occurred in the very cell population most under suspicion as a source of putative "excitotoxins", namely, the cortex (Olney, 1979). Although at present it would be impossible to accept the ectopic gray matter as a clue to pathogenesis in Huntington's chorea, the case reported here suggests that a careful search for developmental changes, perhaps obscured by degenerative events, might be worthwhile in both past and future cases.

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