PARENCHYMATOUS CORTICAL CEREBELLAR ATROPHY ASSOCIATED WITH PICK'S DISEASE

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Parker and Kernohan (1) reviewed the published cases of parenchymatous cortical cerebellar atrophy and found only 11 cases which they considered, on the basis of clinical and necropsy findings, to be true examples of this type of cerebellar atrophy. They described an additional case of their own and outlined the clinical course and pathologic anatomy of the condition. The same authors (2) reported a second case two years later.

Zülch (3) in reviewing the literature on primary cortical cerebellar atrophy, tabulated 32 cases which he considered to belong in this category and added two of his own. The cases of Holmes (4) and Thorpe (5), in which there was evidence of familial incidence, were included by Zülch, but Parker and Kernohan were of the opinion that no familial cerebellar atrophies were of this type. Two cases reported by Hassin (6) were not included in Zülch’s review. Hassin described his cases under the term of sclerotic atrophy of the cerebellum, which he considered more suitable for this pathologic entity and which Lichtenstein and Levinson (7) considered to be examples of parenchymatous cortical cerebellar atrophy. The subjects, both women, were 27 and 32 years of age respectively and neither had exhibited cerebellar symptoms during life.

Since the review by Zülch, several other cases have been reported. Akelaitis (7) described two cases of primary parenchymatous atrophy of the cerebellar cortex occurring in brothers and associated with mental deterioration. The first was 42 years of age at death and the second was 51; the duration of symptoms in each case was approximately two years. Courville and Friedman (8) reported a case in a female, age 33, discussing in great detail possible etiologic factors. Their patient following a slow recovery from epidemic meningitis manifested residual clumsiness all her life. Richter (9) described a case in which the symptoms of the disorder were similar to those existing in two siblings, a brother and sister, of the patient. The first symptoms in all three so affected appeared at 47, 47, and 55 years of age respectively. The duration of the disease in the brother who came to autopsy was 18 years. Weber and Greenfield (10) recorded clinical and pathologic findings in the case of a woman with familial cortical cerebellar atrophy who died at the age of 78 with symptoms of 18 years’ duration. Hall, Noad and Latham (11) reported a case of familial

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cortical cerebellar atrophy in which the symptoms first appeared at age 55 and progressed slowly until death which occurred at the age of 82 years. Minogue and Latham (12) found marked cortical cerebellar atrophy in a girl, age 18, who gave a 12-year history of epilepsy. Moyano (13) described an instance of senile atrophy of the cerebellum in which the pathologic findings included those ordinarily seen in parenchymatous cortical cerebellar atrophy; death occurred at age 78. A similar case in a subject 60 years of age, was reported by de Haene (14) as late cerebellar atrophy with cortical predominance. This name ("Atrophie cérélleuse tardive à prédominance corticale") was originally applied to this type of cerebellar atrophy by Marie, Foix and Alajouanine (15) who described these cerebellar alterations in three cases.

Primary degeneration of the granular layer of the cerebellar cortex was noted by Norman (16) in two cases. Lichtenstein and Levinson (17) recently described three cases of cortical cerebellar atrophy without ataxia and emphasized that the disorder may be asymptomatic and discovered accidentally at necropsy. Their first case was a colored man, age 36; the second a colored woman, age 52; while their third was a white female infant. They stated that atrophy of the cerebellar cortex may affect certain specific cellular elements predominantly, as for example the Purkinje cells or the granule cells (as described by Norman) or may affect all the parenchymatous elements indiscriminately; for the latter state they suggested the term panatrophy.

REPORT OF CASE

History. F. D., a married woman, aged 45, was admitted to the Colorado Psychopathic Hospital on July 2, 1944. Her speech was unintelligible although very voluble. The history of the case was obtained partly from her family and partly from the abstracts of previous hospitalization records.

The patient began having "dizzy spells" 14 years before this admission. They were characterized by vertigo, feelings of weakness and disturbances of vision lasting a few days. She never lost consciousness and would usually recover from the attacks. These episodes became more frequent and severe. On June 16, 1939, while doing her laundry, she suddenly became ill, complained of dizziness, and could not stand up. Her behavior and thinking at this time suggested a toxic psychosis and in July, 1939 she was admitted to Woodcroft Hospital, Pueblo, Colorado. She remained there one month, improved mentally and physically but still had some disturbance of vision and difficulty in walking when discharged. These symptoms progressed slowly and in December, 1939 she was taken to the Mayo Clinic. There she manifested ataxia of the lower extremities, a positive Romberg sign, horizontal nystagmus, intellectual impairment, and emotional instability. She was thought to have a diffuse central nervous system lesion either inflammatory or degenerative in character. Her symptoms continued to progress and in May, 1940, she was again examined at the Pueblo Clinic, where at this time, multiple sclerosis,—cerebellar type, was regarded as the diagnosis.

She was readmitted to Woodcroft Hospital on June 2, 1940. She was then unable to walk without being supported. The ataxia of her lower extremities had increased and the upper extremities were now showing early signs of incoordination; the patellar and Achilles reflexes were hyperactive; the superficial reflexes were diminished and sensation was reduced; there were no sphincteric difficulties; the vision was fairly good and the degree of nystagmus had lessened; her speech had become slow, scanning, and monotonous; her mental symptoms at this time were described as consisting of dullness, indifference, apparent happiness, absence of all intellectual activity, memory defects, and childish sentimentality. She was discharged on June 30, 1940, with the diagnosis of multiple sclerosis.
There followed a brief period of improvement, then a decline with her symptoms slowly progressing until 1943 when she lost control of her sphincters for a period of two weeks. Three months prior to her admission to the Colorado Psychopathic Hospital she began to complain of weakness and abdominal pain, accompanied by dysphagia and nocturia. She began to lose weight rapidly. Sphincter control was again completely lost and her speech became unintelligible. In May, 1944, an abdominal mass was detected; it increased approximately four times in size within a period of one month.

The past history revealed that the patient was born in Austria and that she received only a limited education. She had always spoken in her native tongue and had made little effort to learn English. The family history was uncertain but did suggest the existence of some familial traits relating to the patient’s condition: a younger brother in Austria who died in his early twenties—possibly from a malignancy—was reported to have been mentally ill and to have had difficulty in walking.

**Examination.** The patient at the time of admission to Colorado Psychopathic Hospital was a helpless, debilitated woman who was in some respiratory distress. She was cyanotic. Her stream of talk was monotonous, slurred, and unintelligible. She cooperated to the best of her ability by following simple instructions. She was completely paralyzed except for slow, ataxic movements of her upper extremities. The musculature of the lower extremities was flaccid and moderately atrophic. The patellar and Achilles reflexes were absent. A bilateral Babinski sign was present. Sensation could not be evaluated. She had lost control of bowels and bladder. The chest was dull to percussion with exaggerated breath sounds over the lower part of the right lung posteriorly. The heart was somewhat enlarged to percussion; there were no murmurs. The abdomen was rounded with a very large, moderately tender, firm mass, suggestive of enlargement of the liver, palpated on the right side. No fluid wave could be demonstrated. The blood pressure was 132 systolic and 92 diastolic.

The mental status could not be accurately evaluated because of her poor general condition.

The laboratory studies indicated the presence of a moderate anemia and some minor changes in the plasma proteins. The cerebro-spinal fluid showed no abnormalities; the Wassermann reaction was negative. X-ray examination of the long bones and of the skull showed no significant alterations and that of the chest disclosed considerable elevation of the right diaphragm and prominent hilar and bronchial markings bilaterally. The patient’s condition declined progressively and she died suddenly on July 9, 1944.

**Necropsy findings.** Autopsy was performed by one of us (K. T. N.) 134 hours after death. The anatomical diagnoses were: Carcinoma of the right bronchus, invading the adjacent lung tissue, with metastases to mediastinal and abdominal lymph nodes, liver, pancreas, kidneys, right adrenal, left ovary, posterior lobe of the pituitary gland (microscopic foci) and brain (microscopic foci); Parenchymatous cortical cerebellar atrophy mainly of the upper portion with degeneration of the inferior olivary nuclei; Pick’s disease with atrophy of the right island of Reil, hippocampi, temporal poles, and caudate nuclei; Small leptomeningeal hemorrhage in the left cerebellopontile angle; Aseptic; Edema and congestion of the lungs; Pleural adhesions, mainly on the right; and Arteriosclerosis of the descending aorta.

**PATHOLOGIC FINDINGS IN THE CEREBELLUM**

The cortical atrophy was marked and fairly uniform on the entire dorsal surface of the cerebellum but involved mainly the quadrangular lobules, the vermiculus, and other areas of the superior vermis. It shaded off very gradually toward less atrophic and apparently normal areas of the inferior surface.

In the more markedly involved convolutions (fig. 1) almost all Purkinje cells were gone. In areas still containing Purkinje cells some were fairly well preserved while others were markedly deformed with hyperchromatosis of nuclei and indistinct nucleoli. Occasionally Purkinje cells were displaced into the molecular layer. Some showed a round
homogenous cytoplasm with traces of pigment. The granular layer was much narrower than normal and the granule cells were sparsely distributed. Irregular particles of eosinophilic material were seen between the remaining granule cells. The molecular layer was also somewhat reduced in thickness but its cellular contents appeared approximately normal. There was no evidence of fibrillary gliosis but there was an increase in the number of Bergmann glia cells in several convolutions. Silver stains revealed good preservation of the pericellular baskets in the atrophic regions and of the transverse axons of the basket cells (fig. 2). Neurofibrils were indiscernible in the atrophic axons and dendrites of Purkinje cells. The climbing and mossy fibers were quite well preserved. The white matter of the folia was somewhat shrunken with a slight degree of demyelination but no gliosis. Under low magnification the individual folia were small and rounded. Very small meta-

![Image](http://jnen.oxfordjournals.org/)

**Fig. 1.** Atrophic cerebellar convolution. A small nodule of metastatic carcinoma appears at the left of the section.

static tumor nodules were found in some cortical areas. The process had the appearance of a degenerative atrophy of the cerebellar cortex of unknown origin.

In addition to the foregoing changes of a primary character there were secondary alterations such as complete loss of nerve cells in the rostral three-fourths of the inferior olivary nucleus on either side (fig. 3), large numbers of small astrocytes in the olives, a reduction in myelinated fibers in and around them, and a slight fibrillary gliosis. Only the caudal portions of the olivary nuclei contained a moderate number of fairly well preserved neurons but many of these showed some pigment atrophy. There was no appreciable atrophy of the pons. The dentate nuclei contained approximately the normal number of neurons; part of them were well preserved while others showed some pigment atrophy. The dentate nuclei were rich in glia cells with a fair number of large protoplasmic astrocytes with very light staining nuclei.

A very unusual feature was the association of the foregoing changes with those of Pick's disease, but there was no evidence of Friedreich's disease, olivo-pontocerebellar atrophy,
Fig. 2. A silver preparation showing empty baskets and well-preserved transverse fibers.

Fig. 3. Section through a portion of the olivary nucleus showing complete loss of nerve cells.
lateral sclerosis or optic atrophy. In the left cerebellopontile angle, there was a fresh insignificant leptomeningeal blood clot. Metastatic carcinomatous nodules in the cerebellum were not significant so far as the cortical atrophy was concerned.

In studying the pathologic features we followed the outline recently proposed by Lichtenstein (18) for the study of cerebellar atrophies and found it convenient and practical.

**Cerebral Alterations**

The leptomeninges over the cerebral convexity were glistening and somewhat edematous with occasional slight brownish discoloration. After fixation of the brain the right island of Reil showed considerable narrowing of the cortex which was of a peculiar leather-like consistency, somewhat brownish, fissured and indented. A similar condition was found bilaterally in the hippocampal gyri and in the convolutions of the temporal poles. The right side appeared to be more involved than the left.

![Fig. 4. Pick's Disease. Section through right insular cortex showing atrophy with loss of nerve cells and gliosis.](image)

Microscopic studies revealed severe changes in all the shrunken areas of the cortex. In most of the affected convolutions the majority of the nerve cells had disappeared (fig. 4); only scattered neurons were visible and many of them appeared to be atrophic with shrunken cytoplasm. In some fields the second and fifth cortical layers seemed slightly better preserved. Everywhere, pale, large glial nuclei with only traces of cytoplasm (sometimes in groups of two or three) were noted. Special stains showed that many of these glial cells were fibrillary astrocytes. The cortical nerve fibers had largely disappeared. The ground substance had a somewhat loose fibrillary and meshy appearance with small, irregular vacuoles; suggestive of status spongiosus. A very few rod cells were also present. The convolutional white matter showed some demyelination and sclerosis.

There was no sharp border between the diseased and normal areas. In the transition zones the number of nerve cells increased very gradually and many of them were dark and small. There was also marked gliosis in such areas.

The polymorphic layer and the dense portion of the hippocampus showed marked paucity of neurons and an equally marked increase in glia cells. Sommer's sector was fairly well preserved but the presubiculum region showed severe devastation and gliosis. This was also true of the hippocampal gyrus and less so of the fusiform gyrus.

The convolutions of the temporal poles exhibited great devastation,—mainly confined
to the middle layers,—but the number of glia cells was far less than in the island of Reil and hippocampal area; fibrillary gliosis was not clearly visible. The convolutional white matter was likewise less involved.

The head of the caudate nucleus was quite deficient in nerve cells and showed marked gliosis (mainly large protoplasmic astrocytes). The basal ganglia, otherwise, were much better preserved but did show occasional small areas of astrocytic proliferation. The substantia nigra was not involved.

In general, the atrophic areas of the cerebrum showed relatively increased vascularity. A considerable number of argentophile plaques was observed, mainly in the hippocampal region. While they were more numerous in the atrophic zones, they were fairly ubiquitous; scattered, small plaques were visible in the normal, non-atrophic frontal cortex. Alzheimer's fibrillary alterations were not seen.

Lesions in the brain other than those described above were of minor significance. There were occasional small groups of carcinomatous cells similar to those found in other metastatic foci.

**DISCUSSION**

The etiology of parenchymatous cortical cerebellar atrophy and that of Pick's disease have been, respectively, discussed by Courville and Friedman (9) and Malamud and Waggner (19). We shall try to evaluate the various concepts only as they apply to our case since we are aware of the possibility that in individual cases different etiologic factors may be operative.

Infectious diseases, including virus infections and syphilis, intoxications, malformations, and disturbances of the circulation did not come into question in our case. The malignancy to which the patient succumbed arose late in the course of the nervous ailment and cannot be considered of etiologic significance. We feel, therefore, that both parenchymatous cortical cerebellar atrophy and Pick's disease in our case are manifestations of an endogenous, probably heredofamilial, disposition.

A familial incidence of parenchymatous cortical cerebellar atrophy is suggested by the death in his early twenties of a brother of the patient who was described as having had difficulty in walking. Evidence that this type of cerebellar atrophy does show familial and hereditary tendencies is furnished by the cases of Akelaitis (8), Weber and Greenfield (11), Hall, Noad and Latham (12), Holmes (4), Thorpe (5), and Richter (10). Marie, Foix and Alajouanine (11) and Parker and Kernohan (1), however, were unwilling to concede the existence of such a predisposing factor.

Richter discounted the importance of the concept that previous infections, cerebral arteriosclerosis and alcoholism "exert a harmful influence upon the Purkinje cells such that these elements are conditioned to an early and selective degeneration at a later date" since these supposed predisposing causes are so diverse and of such common occurrence. The occurrence of a familial tendency in his case and in others previously reported and reviewed by him, seemed to him "to place the problem of the etiology (of parenchymatous cortical cerebellar atrophy) strictly in the realm of genetics."

It seems quite possible that there may be both familial and non-familial forms of parenchymatous cortical cerebellar atrophy as well as of Pick's disease.
If complete investigations of family trees were possible in all cases of either condition, however, it might be shown that heredity is a predisposing factor in all of them.

We are inclined to classify our case with the systemic atrophies as proposed by Spatz (20), who reviewed various combinations of heredofamilial diseases. In so doing we believe that we are dealing with atrophy in the strict sense, particularly so far as the cerebellar damage is concerned; the elements of the nervous tissue disappear in an exceedingly chronic way, often without leaving a trace; degenerative features are negligible and barely noticeable on microscopic examination; the loss of parenchyma leads to reduction in size and shrinkage of the tissue with little if any glial scar formation. With regard to Pick’s disease, the process leading to atrophy is perhaps somewhat less chronic; more activity in the supporting tissue is observed and fibrillary gliosis is evident. These forms of atrophy are systemic inasmuch as they are circumscribed and involve several more or less well-defined systems, usually in a symmetrical fashion. Again parenchymatous cortical cerebellar atrophy fits into this scheme better than does Pick’s disease; in the former we find the systems of the Purkinje and granule cells to be involved; in the latter the systemic character is not quite as evident although the temporal poles, the insulae and the hippocampi are fairly well defined units as pointed out by von Economo and Koskinas (21).

The systemic atrophies under discussion cannot be considered to be solely indicative of early senescence. We see regressive changes of an intensity which is not reached in normal senile involution; in addition there are in Pick’s disease proliferative reactions of the supporting tissue that are likewise unknown in normal senility. Therefore we can only state that these atrophies are definitely related to, but not entirely identical with, senile involution. This was justly emphasized by von Braumühl (22) who explained presenile and senile tissue lesions on the basis of the colloidal processes of hysteresis and syneresis.

The selectivity of the involvement is not readily understood. It would be erroneous to state that only neocerebral or neocerebellar areas become atrophic. Certainly parenchymatous cortical cerebellar atrophy affects paleocerebellar areas. Pick’s disease, which is so often said to establish itself only in neocerebral regions, may do so in phylogenetically old zones as well; this is shown in our case by the advanced atrophy of the insula and the gyrus hippocampi.

Only one definite statement can be made with regard to the location of the cerebellar atrophy: the diseased areas are more or less identical with those showing pronounced involution in normal senility. Attention has been called to this point by Gellerstedt (23).

The diagnosis of parenchymatous cortical cerebellar atrophy in the case described, as differentiated from olivo-pontoocerebellar atrophy, is based mainly upon the failure of the process to involve the basis pontis. Marie, Foix and Alajouanine (16) considered this to be the most important point in the differentiation of the two conditions. The same authors differentiated paren-
chyramatous cortical cerebellar atrophy (late cerebellar atrophy with cortical predominance) from cerebellar heredo-ataxia chiefly on the basis of associated degeneration in Gowers' tracts of the spinal cord in the latter condition coupled with more or less marked degeneration in the pyramidal tracts. Changes in the cord were absent in our case.

The cerebellar alterations in the case herein reported appear to conform to the usual picture as seen in parenchymatous cortical cerebellar atrophy. The distribution of the atrophic changes in our case was characteristic of parenchymatous cortical cerebellar atrophy as described by Parker and Kernohan (1). Thorpe (5), Arechambault (24), Marie, Foix and Alajouanine (16), Akelaitis (8), Courville and Friedman (9) also described the atrophy as localized to the superior vermis and the adjoining areas of the cerebellar hemispheres. Many of the cases that have been designated as parenchymatous cortical cerebellar atrophy, however, have had a much more extensive distribution; these include the cases of Weber and Greenfield (11), Hall, Noad and Latham (12), Richter (10), Holmes (4) and Minogue and Latham (13). In Hassin's cases (6) there was no involvement of the vermis.

The olivary degeneration in our case was perhaps somewhat more marked than has ordinarily been reported, but marked changes in the olivary nuclei were also seen by Akelaitis (8), Weber and Greenfield (11), Hall, Noad and Latham (12), Holmes (4), Thorpe (5), Lichtenstein and Levinson (7). Hall, Noad and Latham reported that there were "no healthy neurons in the olivary nuclei" in their case. The changes in the olivary nuclei in parenchymatous cortical cerebellar atrophy have been considered by all these investigators to be secondary to the cerebellar degeneration. Lichtenstein (25) defended the term "retrograde degeneration" for this phenomenon and reported its occurrence in two cases of maldevelopment of the cerebellum observed by him; he also reviewed the cases of Anton and Zingerle (26), Neuburger and Edinger (27) and Rubinstein and Freeman (28) who had previously reported retrograde degeneration of the olives in cases of cerebellar malformation and agenesis.

Parker and Kernohan (1) observed that parenchymatous cortical cerebellar atrophy usually begins before senile changes are manifest and that the preservation of the intellectual faculties distinguishes it from a general senile breakdown of the nervous system. Cases similar to ours where mental deterioration was associated with the cerebellar symptoms have been described, however, and this has been accounted for by associated cerebral cortical pathology (Akelaitis, Thorpe, Richter). While the cerebellar symptoms may exist without any other evidence of a general breakdown of the nervous system, these cases (including ours) seem to indicate that the combination of cerebellar and cerebral symptomatology is not particularly unusual.

Cerebral changes in association with cerebellar alterations. Cerebral atrophy has been observed not infrequently. In the alcoholic patient with parenchymatous cortical cerebellar atrophy reported by Stender and Lüthy (29) the entire brain was found to be grossly atrophied. The cerebrum revealed microscopic evidence of senile-degenerative and arteriosclerotic changes and softening of the putamen. Kirschbaum and Eichholz (30) reported a very similar case. Maas and Scherer (31) found recent paling in many areas of the cerebral cortex and
basal ganglia which were due to vascular lesions of unknown etiology and were associated with cortical atrophy of the cerebellum. Schröder and Kirschbaum (32) observed reduction in thickness of the cerebral cortex and acute degeneration of the cells of the striatum in their case. Sclerosing atrophy of cells in the third, fifth, and sixth layers of the cerebral cortex was present in a case of cerebellar atrophy reported by van Bogaert and Bertrand (33), which, however, was of the olivopontocerebellar type. The lesions were particularly marked in the "prefrontal" regions and less so in the temporal lobes.

Courville and Friedman (9), in their case of parenchymatous cortical cerebellar atrophy, observed thickening of the arachnoid over the upper dorso-lateral surfaces of the frontal and parietal lobes and mild atrophy of the regional convolutions. Weber and Greenfield (11) described the brain in their case as small with widening of the sulci. They found rarefaction of tissue and small lacunae in the basal ganglia with loss of nerve cells and neuroglial proliferation. Richter (10) described slight atrophy of the gyri at the frontal poles of the cerebrum and somewhat more involvement of the dentate nuclei of the cerebellum than is ordinarily seen in cases of parenchymatous cortical cerebellar atrophy. Akelaitis (8) found diffuse involvement of the nerve cells in the third and fifth layers of the frontal cortex and, to a lesser degree, of the parietal cortex in his first case and similar changes together with gross atrophy of the frontal and parietal areas in his second case. The essential changes in both cerebellar hemispheres, which were not grossly atrophied, were fairly typical of the disease entity under discussion. In his second case there was an excessive amount of lipochrome pigment in the cells of the dentate nuclei. Hassin (6) found scattered foci of softening in the cerebrum and an occasional area of rarefaction in his first case but stated that these had no relationship to the changes in the cerebellum; he attributed them to the patient's toxic state. No macroscopic or striking microscopic changes were present in the cerebrum of his second case. In view of the cerebral findings in the case reported herein, Hassin's comments regarding the similarities of cerebellar and cerebral atrophy are of interest. They were as follows: "The only morbid condition of the central nervous system which is fully analogous to cerebellar cortical atrophy macroscopically and microscopically is Pick's disease. In Pick's disease the lesion is in the cerebrum; it is also circumscribed and confined to one or more lobes, or to a portion of a lobe in which the ganglion cells and nerve fibers are degenerated and the glia is proliferated, causing shrinkage of the cortex; there is also excessive vascularization, sclerosis causing hardness of the tissues and absence of inflammatory phenomena." In both cerebellar atrophy and cerebral atrophy or Pick's disease the nerve changes are degenerative and are either of indefinite etiology or partial manifestations of such chronic conditions as arteriosclerosis or other degenerative vascular diseases. However, neither Pick's disease nor cerebellar cortical atrophy is directly due to such vascular disturbances as arterial thrombosis, an inflammatory vascular process, atresia of the blood vessels or nutritional disturbances, for on the basis of such vascular factors it would not be possible to explain the exclusive and irregular or scat-
tered involvement of the ganglion cells, aside from the fact that the blood vessels in the conditions under discussion are practically normal."

A possible relationship of cerebellar atrophy to Pick's disease was suggested by Rothschild in his discussion of the paper presented by Akelaitis (8). He cited a case of Pick's disease described by Löwenberg as an illustration of this relationship. Löwenberg's case (34) of Pick's disease had marked atrophy of the vermis, both quadrangular lobules, and of parts of the semilunar lobules of the cerebellum. The myelin of the atrophic convolutions was greatly affected but the supragranular plexus was well preserved. Demyelination was pronounced in the infragranular plexus. Nissl stains showed an uneven distribution of the atrophy; some convolutions were entirely atrophic while others showed only partial degeneration. The molecular layer, in the atrophic folia, was reduced to about one fourth of its normal width. Purkinje cells were reduced in number, and the granular layer was greatly rarefied. There was no glia cell activity in the cortex but glia fibers were abundant in the white matter of both cerebellar hemispheres. The neurons of the dentate nucleus were well preserved. Verhaart (35), in a publication which antedated that of Löwenberg, also described involvement of the cerebellum in a case of Pick's disease with severe shrinkage of the frontal lobes in a female, aged 53. The superior and inferior semilunar lobules of the cerebellum were markedly atrophied and showed, on microscopic examination, loss of Purkinje and granule cells with hypertrophy of Bergmann's glia cells. Verhaart did not emphasize the relationship of the two atrophic processes present in his case.

Argentophile plaques were present in our case of Pick's disease in association with parenchymatous cortical cerebellar atrophy. The significance of these plaques is open to question. They are not by any means a common finding in Pick's disease, except perhaps in patients whose death occurred at a very advanced age. We find it difficult, therefore, to regard these plaques merely as evidence of premature aging (Gerstmann, Straussler, and Scheinker (36)) or early senescence [Rothschild (37)]. We are rather inclined to consider them an incidental finding. One of us (38), in a former special study, has observed plaques in the brains of about 30 per cent of mentally normal patients who died from malignancy during the 5th or 6th decades of life; he believed that the plaques were indicative of a general metabolic disturbance linked with cancer. In our patient there was a bronchogenic carcinoma with metastasis. The plaques in the case under discussion were found in both atrophic and non-atrophic cerebral regions; most of them were small, faintly argentophilic, and had a felt or filigree pattern, thus resembling those seen in other instances of malignancy and being somewhat different from the types commonly encountered in senile brains. No plaques were seen in the atrophic cerebellar cortex. Considering all these facts, we feel that the plaques in our case are related to the fatal malignancy rather than to the cerebral and cerebellar atrophies.

The two cases of Akelaitis (8), the case reported by Löwenberg (34), and

*Rothschild also mentioned the association of Alzheimer's disease and cerebellar atrophy, but it is beyond the scope of this paper to consider this type of presenile dementia.
Verhaart's case (35) are most similar to that reported herein. The cerebral changes in Akelaitis' case were not, however, typically those of Pick's disease and were not so classified by him. Löwenberg apparently did not consider the changes in the cerebellum of his case to be typically those of parenchymatous cortical cerebellar atrophy. Verhaart's case was a true case of Pick's disease, and the cerebellar changes were, to a certain degree, characteristic of parenchymatous cortical cerebellar atrophy, although not so classified by the author. In our case the histologic findings in the cerebral cortex were definitely those of Pick's disease although the distribution of the atrophic process was somewhat unusual; the changes in the cerebellum were those of parenchymatous cortical cerebellar atrophy as described by Marie, Foix and Alajouanine (16), Parker and Kernohan (1) and many others.

The relative paucity of the clinical symptoms of Pick's disease in our case may have been due to the distribution of the cortical changes which failed to involve the frontal lobes and large areas of the temporal lobes. While mental deterioration was evident the prevailing clinical features were those of cerebellar disease. Psychic signs compatible with those of Pick's disease were no doubt present as early as 1940; however no satisfactory mental examination was ever recorded partly because of the inability of the patient to understand or speak English and partly because of cerebellar speech disturbances. There is a possibility that the speech disturbances may have been due, in some degree, to the involvement of the insula as indicated by Economo and Koskinas (21). We admit our inability to arrive at a proper correlation between clinical and pathologic findings, so far as the cerebral involvement is concerned, because of the advanced state of mental and physical deterioration of the patient while in our hospital.

CONCLUSIONS

1. In a case of parenchymatous cortical cerebellar atrophy the loss of Purkinje cells was combined with practically complete disappearance of nerve cells in the rostral three-fourths of the inferior olivary nucleus.

2. The atrophic changes in the cerebellum were associated with similar alterations in certain parts of the cerebrum where they were interpreted as those of Pick's disease.

3. Some features of the clinical history suggest that the condition was familial.

DISCUSSION

Dr. W. R. Kirschbaum, Manteno, Illinois: This is a very rare case of circumscribed brain atrophy and it is all the more unusual as portions of the basal convolutions together with the cerebello-olivary systems were involved. Were the histological findings in the atrophic areas typical of Pick's disease? Were argentophilic deposits present in the degenerated neuron cells?

Dr. K. T. Neubuenger, Denver, Colo.: Argentophilic globules in the nerve cells of the cerebral cortex were not found. The nuclei of the pons were uninvolved. We are dealing with two well-defined, different diseases of the brain that com-
menced at different times and showed the characteristic pathologic lesions usually associated with either of them; if they are to be considered as a unity this can be done only on the ground of their belonging to the group of heredo-familial degeneration.

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