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CASE REPORTS 1964 - PATHOLOGY
症例報告 1964 年 — 病理

HISTOPLASMOSIS OF THE KIDNEY
腎 ヒ ス ト プ ラ ス マ 症

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SUBACUTE NECROTIZING ENCEPHALOMYELOPATHY
亜 急 性 壊 死 性 脳 脊 髄 疾 患

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SUBACUTE NECROTIZING ENCEPHALOMYELOPATHY
亜急性壊死性脳脊髄疾患

HIDEO NAMIKI, M.D.　並木秀男

INTRODUCTION

In 1951, Leigh[1] published a case report of a peculiar neuropathological disorder in an infant. The disease, which he called *subacute necrotizing encephalomyelopathy*, was characterized by: Multiple, frequently symmetrical foci of necrosis with predilection for the periaqueductal and periventricular structures and the tegmentum of the brain stem; breakdown of the interstitial tissue of the nerve parenchyma with relative preservation of the cell bodies of the neurons; and the prominence of small blood vessels. Although Leigh suggested that the disorder might represent Wernicke's disease in infants, there has been no convincing proof as to the etiology of this disorder.*

The case reported here is the first recorded instance of the disease in Japan. The importance of the associated pathology of the peripheral nerves, spinal roots and dorsal white columns of the spinal cord is also stressed.

CASE REPORT

The patient ([redacted]), a 15-year-old Japanese girl, was the first child of parents who were first cousins. It was alleged that the mother's nutritional status during the pregnancy was very poor; the delivery occurred at term and was not complicated. The details of the feeding and development of the patient in early infancy were not available. At four months of age, the patient suffered from bilateral otitis media and for about the year following, she had a relapsing fever, often to 40°C. She started to laugh late and could not hold her head upright for long periods. She sat up at the end of the first year, was able to stand by herself at the age of 22 months and began to walk at 30 months. Around the

緒　言

1951年に Leigh [1] は乳児における特異な神経病理学的疾患の症例報告を行なった．この疾患すなわちかれのいう亜急性壊死性脳脊髄疾患は次のような3つの特徴を持つ．すなわち，中脳水道周囲ならびに脳室周囲の構造および脳幹被蓋に好発する多発性でしばしば対称性の壊死巣を作ること．神経細胞体が比較的よく保存されているのにかかわらず神経実質の間質に崩壊のあること．および小血管が著明になることである．Leigh は，この疾患は乳児におけるウェルニッケ病ではなかろうかといったが，この疾患の病因については今日まで確証がない．*

ここに報告した症例は日本におけるこの疾患の最初の記録例である．この論文では末梢神経，脊髄神経根および脊髄後索における随伴病変の重要性も強調した．

症例報告

患者([redacted])は15歳の日本人少女．いとこ同士の両親の第1子である．妊娠中の母体の栄養状態はきわめて不良であったが，満期分娩で安産であったという．乳児期における患者の栄養，発育状態の詳細は不明である．生後4か月の時に両側中耳炎に罹患した．その後約1年間，間歇的発熱があり，しばしば40℃に達した．普通の乳児よりも笑い始めが遅く，長い間首がすわらなかった．生後1年で起座し始め，生後22か月でひとり立ちができ，30か月で歩き始めた．2歳のころ，脊椎

*Subsequently, Feigin and Wolf(1954),[2] Richter(1957)[3] and Reye(1960)[4] added several cases of a similar neuropathological disease.

その後，Feigin ならびに Wolf (1954年),[2] Richter (1957年),[3] および Reye (1960年)[4] はさらに同様の神経病理学的疾患数例を報告した．

age of two, lordosis appeared. At that time, she could understand her parents but was scarcely able to speak or laugh. Walking required her mother's help and, by the time of her school admission, her walking difficulty had gradually worsened. She swayed to the left, wore her left shoe with difficulty, and her left leg trembled while standing. Her school record indicated gradual deterioration.

When she was 13 years old, she was seen at the eye clinic of the Nagasaki University Hospital. At that time she weighed 29.5 kg and measured 132 cm in height (normal values at this age for Japanese girls are 42.2 kg and 149.0 cm). Both the tuberculin skin test and a Wasserman test were negative. She was said to have had abnormal gaze (strabismus) since the age of three or four. The visual acuity of both eyes was within normal limits. Her right eye was dominant, and when she focused on an object with her left eye, horizontal nystagmus was provoked. A diagnosis of strabismus concomitans divergens sinistra was made. About four months prior to death she was seen at a Nagasaki hospital because of general fatigue. She died at home and the details of her terminal illness are not known.

She was the eldest of four siblings. One of her younger siblings died of pneumonia shortly after birth. The youngest, a boy, was said to have had muscular weakness and difficulty in walking and died at the age of three. Only one of the siblings was living and well.

Autopsy Findings A postmortem examination was done eight hours after death. Examination of the thoracic and abdominal viscera revealed extensive acute necrotizing pancreatitis, chronic pyelitis of the right kidney, mild renal tubular calcification and acute passive congestion of the viscera. The immediate cause of death was acute pancreatitis.

The brain was examined after fixation for one week in 10% formalin solution. It weighed 1460 g. The dura mater and superior sagittal sinus were unremarkable. The cerebral hemispheres were symmetrical and of usual size, except for the superior temporal gyri which appeared slightly smaller than usual as did both the brain stem and cerebellum. Small focal areas of recent subarachnoid hemorrhage were present over the frontal and occipital poles and over the inferior surface of the

前弯が現われた．当時，自分の両親のいうことはわかったが，話したり，笑ったりすることはほとんどできなかった．歩行の際には母の介添えが必要で，就学時までに歩行困難が徐々に悪化した．身体は左方に動揺し，かろうじて左側の靴をはくことができ，立っていると左脚が震えた．学業成績は徐々に低下した．

13歳の時に，長崎大学付属病院眼科において診察を受けた．当時，体重は29.5kg，身長は132 cmであった．(同年齢の日本人少女の正常値は体重42.2kg，身長149.0cmである．) ツベルクリン皮膚反応およびワッセルマン反応はともに陰性であった．3，4歳のころから異常注視(斜視)があったという．両眼視力は正常範囲内であった．通常物体を右眼で注目し，物体を左眼で注視すると，水平眼振を生じた．これを左眼共動性外斜視と診断された．死亡の約4か月前，全身疲労感を訴えて長崎の某病院で受診した．自宅で死亡したため，疾病末期の詳細は不明である．

同胞4人の最年長者である．同胞1名は生後間もなく肺炎で死亡した．最年少の同胞である末弟は筋衰弱および歩行困難があり，3歳の時に死亡したという．同胞1名は健在である．

剖検所見 死後8時間を経過して剖検を行なった．胸部および腹部臓器：広範性急性壊死性膵炎，慢性右腎盂炎，軽度の腎細尿管石灰化および臓器の急性鬱血を認めた．直接死因は急性膵炎である．

脳（10%ホルマリン液に1週間固定したのちに検査を行なった)：重さ1460g．硬膜および上矢状静脈洞に著変はない．大脳半球は対称性で正常大であるが，上側頭回は脳幹ならびに小脳と同様に正常よりもやや小さいように思われる．前頭葉極，後頭葉極，および小脳半球

cerebellar hemispheres. The leptomeningeal blood vessels were slightly congested while the major arteries at the base of the brain were normal in distribution and caliber with delicate walls. The cranial nerves were not grossly abnormal.

Serial coronal sections of the cerebrum and diencephalon were unremarkable. The lateral and third ventricles were not dilated. The substantia nigra was paler than usual. Multiple serial coronal sections of the brain stem revealed an irregular, ill-defined, brown, spongy area in the midline of the tegmentum at the level of the upper medulla. The lesion measured approximately 0.7cm in greatest dimension. Two smaller but similar lesions were identified in the ventral portion of the lower medulla and a fourth, measuring 0.5cm in diameter, was seen in the medial portion of the right dentate nucleus. The spinal cord, spinal roots, dorsal root ganglia of the lumbar area, nerves of the brachial plexus and sciatic nerves were unremarkable. The skeletal muscles showed no gross atrophy.

Histopathology Multiple histologic sections were prepared from the cerebral hemispheres, brain stem, cerebellum, spinal cord, spinal roots, dorsal root ganglia and peripheral nerves (sciatic nerves and nerves of the brachial plexuses). All sections were examined with hematoxylin-eosin (H & E), Holzer, Luxol Fast Blue (LFB), LFB-cresyl violet, Oil Red O, Holmes-LFB and Bodian-LFB stains.

Irregular, discrete lesions sharing identical and unique histological changes were seen in various locations as shown in Figure 1.

The histologic characteristics of these lesions consisted of: Destruction of the ground substance of the neural parenchyma (neuropil), ranging from incomplete staining and loosening of the texture to formation of microcysts; relative preservation of the cell bodies of neurons (perikaryons); and prominence (increase in number and diameter) of small vessels (Figures 2-11). Despite the destruction of neuropil, there were only a few *gitter cells*. There was a mild degree of infiltration with lymphocytes and rod-shaped microglial cells, predominantly in the proximity of small blood vessels, in some of the lesions. The number of oligodendroglia

下面に急性くも膜下出血の小病巣を認める．軟膜血管は軽度に充血しているが，脳底における主要動脈の分布および口径は正常で，壁は菲薄である．脳神経に肉眼的異常を認めなかった．

大脳および間脳の連続的前頭断面には著変を認めない．側脳室および第３脳室の拡張を認めない．黒質は正常よりも蒼白．脳幹連続的前頭断面を見ると延髄上部の被蓋部正中線に不整形，境界不明瞭，褐色，海綿状の１病巣を認める．この病変の最大径は約0.7㎝ある．延髄下部の腹側部にこれよりも小さいが同様の病変を２個認める．右歯状核の内側部に直径約0.5㎝の４番目の同様病変を認める．脊髄，脊髄神経根，腰髄後根神経節，上腕神経叢神経および坐骨神経に著変はない．骨格筋に肉眼的萎縮を認めない．

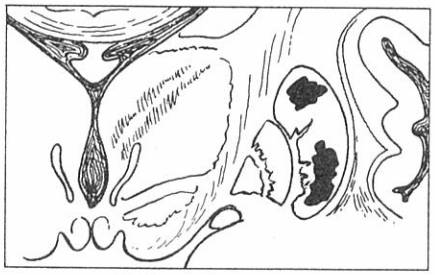
組織病理学的検査所見 大脳半球，脳幹，小脳，脊髄，脊髄神経根，後根神経節および末梢神経（坐骨神経および上腕神経叢神経）から多数の組織切片を作成した．切片はすべて hematoxyline-eosin (H&E) 染色，Holzer 染色，Luxol Fast Blue (LFB) 染色，LFB-cresyl violet 染色，Oil Red O 染色，Holmes-LFB 染色および Bodian-LFB 染色によって検査した．

図１に示すとおり，同じような独特の組織学的変化を示す不整形の分離病変を各所に認める．

これら病変の組織学的特徴は下記の諸点から成る．神経実質の基質(神経網)の破壊，すなわち基質の不全染色性，および粗化から小嚢胞形成に至る病変．神経細胞体(核周囲)が比較的良好に保存されていること．小血管が著明になること(その数および直径の増加)わらず，「gitter 細胞」は少数しか認められない．病変の一部にリンパ球および桿状ミクログリア細胞による軽度の浸潤を認めるが，これは特に小血管の付近において著し

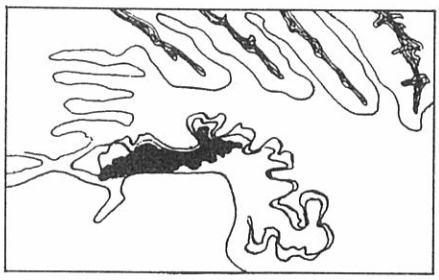
FIGURE 1 DISTRIBUTION OF THE CHARACTERISTIC LESIONS

図1　特異病変の分布



Right Basal Ganglia

右側基底神経節



Right Dentate Nucleus

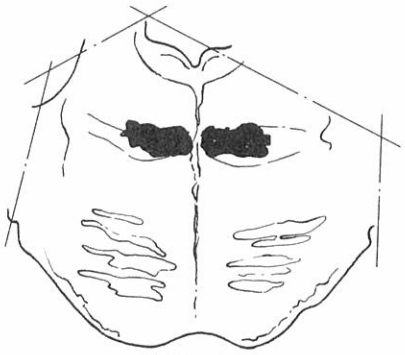
右側歯状核

Midbrain

中脳

Rostral Pons

橋前部

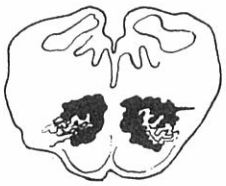


Middle Pons

橋中部

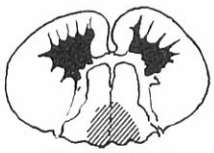
Upper Medulla

延髄上部



Lower Medulla

延髄下部



Cervical Cord

頸髄

Lumbar Cord

腰髄

Rarefaction and vascularization. 粗鬆化および血管新生

Secondary degeneration, dorsal columns. 二次変性，脊柱後索

appeared moderately decreased in these lesions. Although there were only a few *reactionary astrocytes* in and around the lesions, Holzer stained sections demonstrated striking fibrous gliosis involving some of the lesions, especially those in the inferior olives and right dentate nucleus (Figure 10). The cell bodies of the neurons were surprisingly well preserved in these lesions, even in the proximity of the microcysts (Figures 5, 7, 9). Some of the nerve cells in these locations demonstrated features of axonal degeneration. Increased numbers of slightly to moderately dilated, tortuous capillary blood vessels were present in all the lesions. Despite the vascular proliferations, there were no hemorrhages or deposition of heme pigments. With LFB stain, the lesions revealed marked, though incomplete, demyelination. The margins of the lesions were poorly defined. In contrast to the myelin loss, the axis cylinders appeared fairly well preserved in most of the lesions except in those areas with microcyst formation.

These lesions, with predilection for the gray substance, were typically distributed in the periaqueductal structures, floor of the fourth ventricle and tegmentum of the brain stem, right dentate nucleus, and anterior horns of the cervical and upper thoracic cord. There were no lesions in the diencephalon or telencephalic structures with the exception of the right putamen. The corpora mammillaria were not involved. In the brain stem and spinal cord, the distribution of the lesions was roughly symmetrical.

Sections of the spinal cord demonstrated symmetrical degeneration of the gracile fascicles above the level of the lumbar cord. The degeneration was characterized by complete demyelination and loss of axis cylinders and there was no associated infiltration of *gitter* or other inflammatory cells, or gliosis. The cord changes were considered consistent with secondary degeneration (Figure 12).

The dorsal root ganglia of the lumbar and sacral areas were examined and the perikaryons of the ganglia appeared well preserved. There was a questionable increase of neurilemmal cells. Except for a few lymphocytes around the blood vessels, no other inflammatory cells were evident. Intermingled with normal-appearing axons, there were a considerable

い．これら病変においては，希突起神経膠の数は中等度に減少しているように思われる．病変の付近には少数の，「反応性星状膠細胞」を認めるにすぎないが，Holzer 染色を行なった切片では一部の病変，特に下オリーブ核および右歯状核における病変部に著明な線維性神経膠症を認めた(図10)．これらの病変部では，小嚢胞形成病変の付近においてさえも，神経細胞体は非常によく保存されている(図５，７，９)．これら病変部における神経細胞の一部には軸索突起性変性が認められた．いずれの病変部でも軽度ないし中等度に拡張した蛇行性毛細血管が多数認められた．血管増殖があるにもかかわらず，出血またはヘム色素の沈着は認められない．LFB 染色では，病変部に不完全ではあるが著明な脱髄を認めた．病変部辺縁の境界は不明瞭である．ミエリンの減少に比較して，軸索は小嚢胞形成部を除いて病変の大部分においてかなり良好に保存されているように思われた．

これら病変は灰白質に好発するが，中脳水道周囲構造，第４脳室床，脳幹被蓋，右歯状核，および頸髄ならびに上部胸髄の前角に分布しているのが特徴的であった．右被殻を除いて間脳または終脳構造に病変を認めなかった，乳頭体に病変を認めない．脳幹および脊髄においては病変の分布はほぼ対称的である．

脊髄切片では腰髄以上の高さで薄束に対称性変性を認める．この変性は完全脱髄および軸索減少を特徴とし，「gitter 細胞」または他の炎症細胞による随伴性浸潤ないし神経膠症は認めなかった．脊髄のこの変化は二次変性と一致していると考えられる(図12)．

腰髄および仙髄部の後根神経節を検査したが，神経節の神経細胞体は良好に保存されている．神経鞘細胞が増加しているように思われた．血管の周囲に少数のリンパ球を認めたが，他に炎症性細胞は認めなかった．正常と思われる軸索と混在して，不規則な肥厚および断裂を

number of axons showing irregular thickening and fragmentation. Diffuse demyelination of the ganglia was an outstanding feature.

The dorsal roots of the lumbar and sacral segments exhibited conspicuous axonal changes ranging from irregular, sinuous or varicose thickening to fragmentation and disappearance. The axonal changes were associated with marked demyelination. Neither inflammatory cell infiltration nor proliferation of neurilemmal cells was evident in the dorsal roots. Questionable swelling of the axis cylinders was seen in the ventral roots of the thoracic, lumbar and sacral segments.

Changes identical with those seen in the dorsal roots were present in the sections of the peripheral nerves (Figures 13-15). Combined LFB-cresyl violet stains of the peripheral nerves revealed a few mononuclear cells with abundant cytoplasm containing fine violet granules. These cells were found between demyelinated fiber bundles and were thought to be macrophages containing disintegrated myelin.

示す軸索を相当数認めた．神経節の瀰漫性脱髄は非常に明白であった．

腰髄および仙髄分節後根には不規則屈曲性または静脈瘤性肥厚から断裂および消退に至るまでの著明な軸索変化を認めた．この軸索変化は著明な脱髄を伴う．後根においては，炎症性細胞浸潤も神経鞘細胞増殖も認められない．胸髄，腰髄および仙髄分節の前根に軸索腫脹の疑いを認めた．

末梢神経切片に後根に見られる変化と同様の変化を認めた（図13－15）．末梢神経の LFB-cresyl violet 重複染色では，微細な紫色顆粒を含む多量の細胞形質を伴った単核球を少数認めた．これらの細胞は脱髄された線維束の間に認められるので，崩壊したミエリンを含む大食球と思われる．

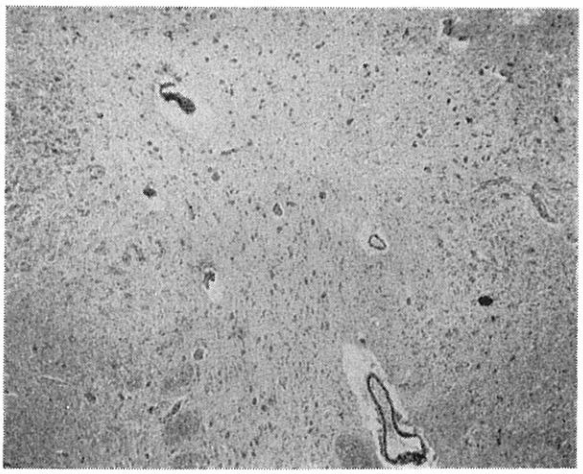


FIGURE 2

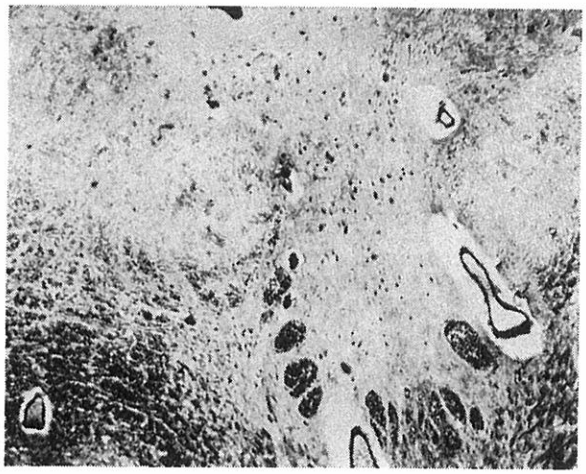


FIGURE 3

FIGURE 2 Tegmentum of the midbrain. Rarefaction of the neuropil and proliferation of capillaries involving oculomotor nerve nuclei and their adjacent structures. H & E stain-scanning.

図2　中脳被蓋．神経基質の粗化，および動眼神経核ならびにその隣接組織に及ぶ毛細血管の増殖．（H&E 染色，極弱拡大．）

FIGURE 3 Tegmentum of the midbrain. Combined Bodian and LFB stain of the area shown in Figure 2 demonstrates marked demyelination involving the longitudinal fascicles - scanning.

図3　中脳被蓋．図2に示す部位の Bodian および LFB 重複染色では縦束の著明な脱髄が証明される．（極弱拡大．）

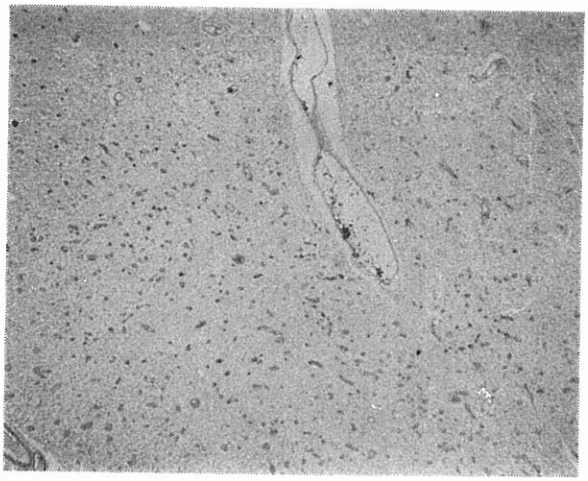


FIGURE 4

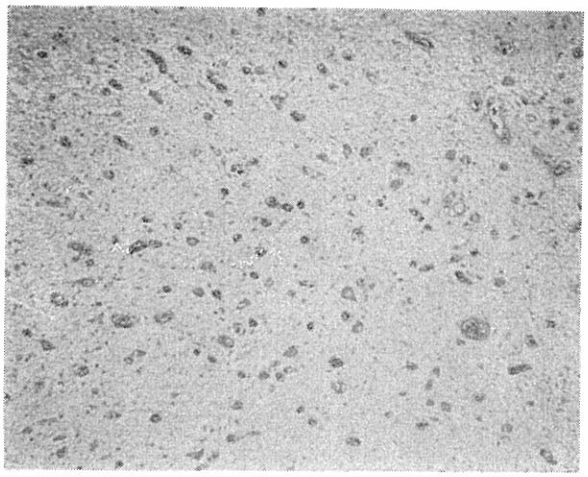


FIGURE 5

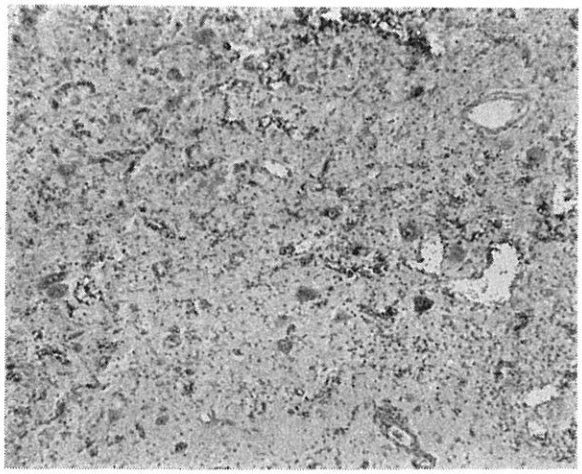


FIGURE 6

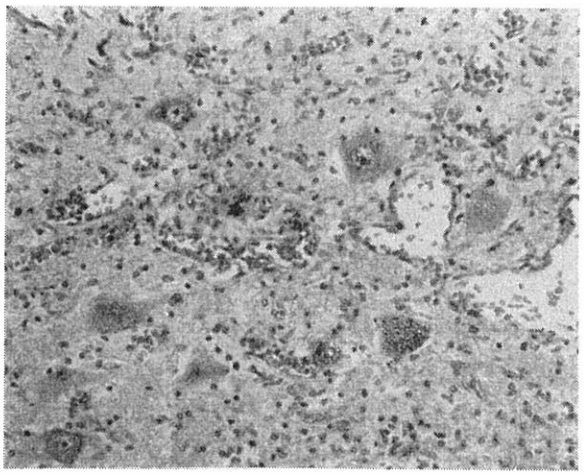


FIGURE 7

FIGURE 4 *Lesion in the inferior colliculus. Note rarefaction and marked proliferation of capillaries. H & E stain - scanning.*

図4　下四丘体における病変．粗化および毛細血管の著明な増殖に注意．（H&E 染色．極弱拡大．）

FIGURE 5 *Lesion in the inferior colliculus. High power view of Figure 4. Despite the rarefaction of the neuropil the nerve cells appear to be well preserved.*

図5　下四丘体における病変．図4の強拡像．神経基質の粗化があるにもかかわらず，神経細胞は良く保存されているように思われる．

FIGURE 6 *Reticular formation of the upper medulla. There is marked capillary proliferation associated with rarefaction of the neuropil. The area is diffusely infiltrated with lymphoid cells and gitter cells. H & E stain - low power.*

図6　延髄上部網様体．神経基質の粗化を伴う著明な毛細血管増殖がある．この部位にはリンパ様細胞および gitter 細胞の瀰漫性浸潤を認める．（H&E 染色．弱拡大．）

FIGURE 7 *High power magnification of Figure 6. Note well preserved perikaryons. Besides lymphocytic infiltration, and microglial proliferation.*

図7　図6の強拡．保持良好の神経細胞，リンパ球浸潤，ミクログリア増殖に注意．

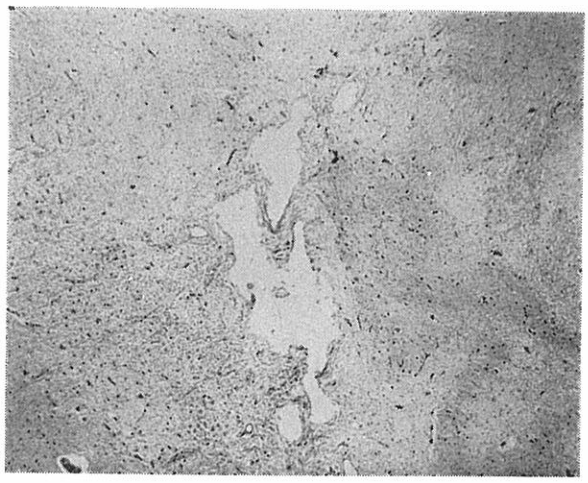


FIGURE 8

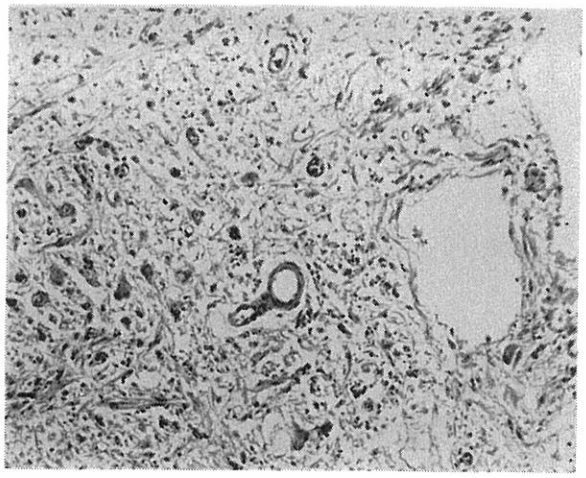


FIGURE 9

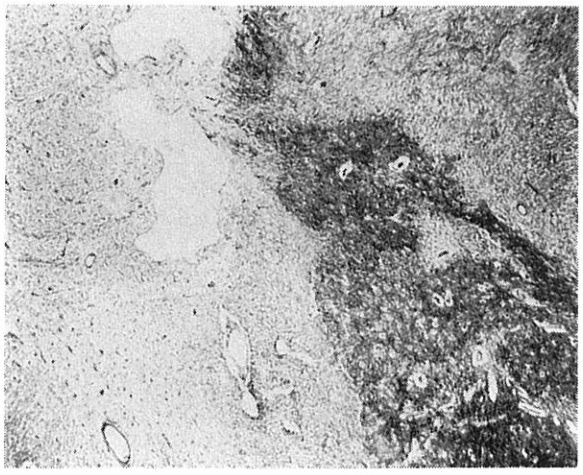


FIGURE 10

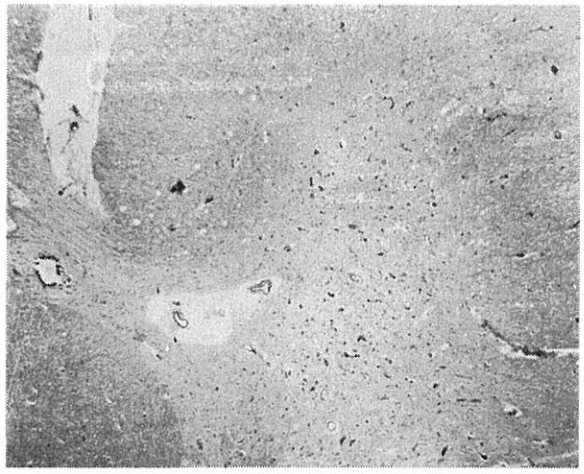


FIGURE 11

FIGURE 8 *Rarefactive lesion in the reticular substance of the lower medulla. The lesion extends into the inferior olivary nucleus. A few irregular microcysts are present. H & E stain - scanning.*

図8 延髄下部網状質における粗化病変．この病変は下オリーブ核内に及ぶ．不整形の小嚢胞が少数ある．（H&E 染色．極弱拡大．）

FIGURE 9 *High power view of Figure 8. Note many well preserved nerve cells within the rarefied lesion*

図9 図8の強拡像．粗化病変内における保存良好の多数の神経細胞に注意．

FIGURE 10 *Fibrous gliosis in the inferior olivary nucleus adjacent to the rarefied lesion of the reticular substance of the lower medulla. Holzer stain - scanning.*

図10 延髄下部網状質の粗化病変に隣接する下オリーブ核における線維性神経膠症．（Holzer 染色．極弱拡大．）

FIGURE 11 *Rarefactive lesion in the ventral gray column of the upper thoracic cord. H & E stain - scanning.*

図11 上部胸髄の前角における粗化病変．（H&E 染色．極弱拡大．）

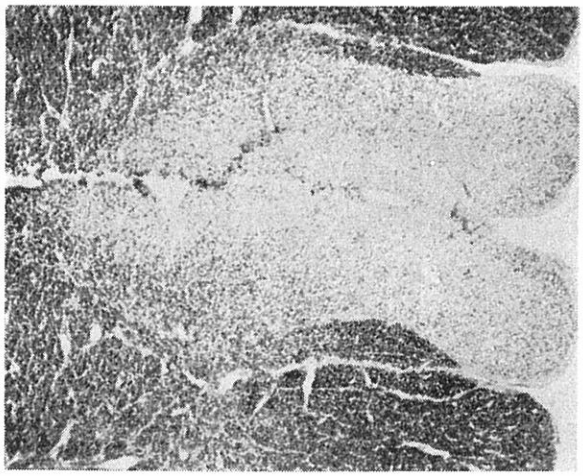


FIGURE 12

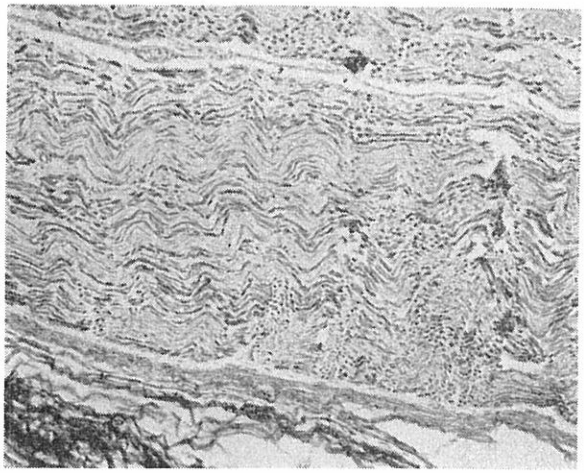


FIGURE 13

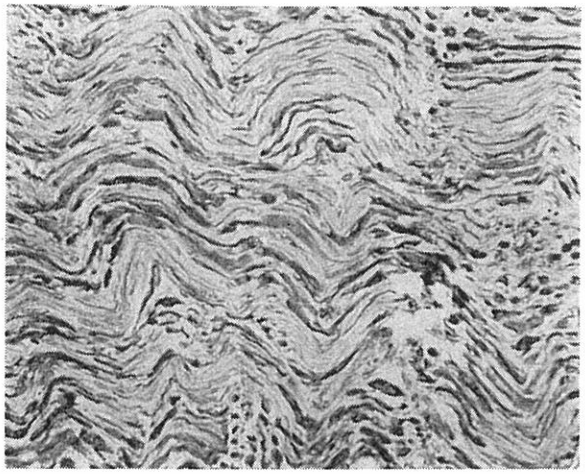


FIGURE 14

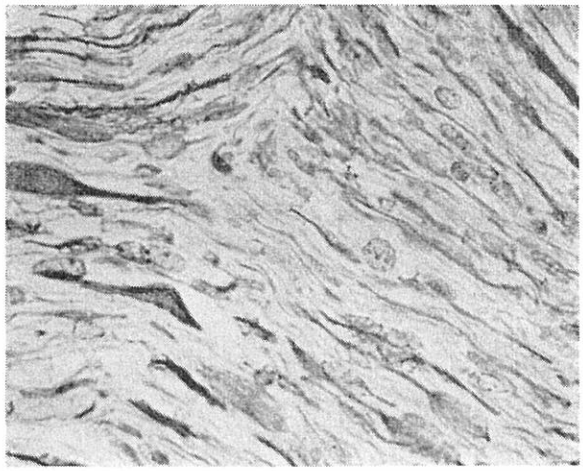


FIGURE 15

FIGURE 12 *Dorsal white column of the cervical cord. Note secondary degeneration confined to the gracile fascicles. Oil Red O stain - scanning.*

図12　頸髄の後索．薄束に限局した二次変性に注意すること．（Oil Red O 染色．極弱拡大．）

FIGURE 13 *Sciatic nerve. Marked axonal degeneration and demyelination are evident. Combined Holmes-LFB stain - scanning.*

図13　坐骨神経．著明な軸索変性および脱髄が明らかに認められる．（Holmes －LFB 重複染色．極弱拡大．）

FIGURE 14 *Sciatic nerve. Low power magnification of Figure 13.*

図14　坐骨神経．図13の弱拡大．

FIGURE 15 *Sciatic nerve. High power magnification of Figure 13.*

図15　坐骨神経．図13の強拡大．

DISCUSSION

Since Leigh's case report of subacute necrotizing encephalomyelopathy (England), ten additional cases with similar neuropathological changes (six from the United States and four from Australia) have been recorded. Richter[3] reported three cases which he called *infantile subacute necrotizing encephalopathy with predilection for the brain stem.* Although the etiology has not been demonstrated, the disorder is generally accepted as an independent disease entity.[5]

The distribution and histopathological characteristics of the lesions in the brain of the presently reported case appear to meet Leigh's criteria of subacute necrotizing encephalomyelopathy. Interestingly, despite the long course of the disease in this case (15 years), there are some lesions indicative of recent activity, as manifested by the presence of inflammatory cell infiltration, in addition to older lesions characterized by extensive fibrillary gliosis. This finding suggests a progressive nature.

The importance of the lesions in the brain, especially in the brain stem, has been stressed in all previous reports;[1-4] hence the disorder has been categorized as an encephalomyelopathy or encephalopathy. As is described in this case report, the pathologic changes in the spinal cord and peripheral nerves appear to be equally prominent.

Table 1 lists reported cases of this disorder in which the spinal cord, spinal roots and peripheral nerves were examined. The descriptions of lesions in the spinal roots and peripheral nerves do not give complete pathologic details of the changes. All of these seven cases except Leigh's demonstrate symmetrical degeneration of the dorsal white columns of the spinal cord, mostly confined to gracile fascicles. The degeneration of the dorsal columns has been described under various names, i.e., secondary degeneration,[3] demyelination and loss of axons,[4] and demyelination.[4] From reviewing the descriptions and photomicrographs, it is felt that the degeneration of the dorsal columns in all these cases may well be interpreted as secondary degeneration.

考　案

Leigh が亜急性壊死性脳脊髄疾患に関する症例報告(英国)を行なって以来，同様の神経病理学的変化を示す症例がさらに10例(６例は米国，４例はオーストラリア)記録された．Richter [3] は**脳幹に好発する小児性亜急性壊死性脳疾患**という名のもとに３症例を報告した．病因は現在まで不明であるが，この疾患は独立の疾病として一般に認められている．[5]

本報告例の脳における病変の分布，および組織病理学的特徴は Leigh の亜急性壊死性脳脊髄疾患に該当するように思われる．おもしろいことには，この患者では疾患の経過が長かったにもかかわらず(15年)，広範な線維性神経膠症を特徴とするやや古い病変に加えて，炎症性細胞浸潤の存在が示すとおり，最近の活動を示す病変を若干認めた．この所見はこの病気が進行性であることを示唆する．

脳，特に脳幹におけるこの病変の重要性は従来の報告全部[1-4] において強調されている．したがって，この疾患は脳脊髄疾患または脳疾患として分類されている．本症例報告書に記載しているとおり，脊髄および末梢神経における病理的変化はともに同じように著明であるように思われる．

表１は脊髄，脊髄神経根および末梢神経の検査が行なわれたこの疾患の報告例を示す．これらの症例においては，脊髄神経根および末梢神経における病変の病理学的詳細についての記載が完全ではない．Leigh の症例を除いて，これら７例にすべて脊髄後索の対称性変性が認められるが，これは主として薄束に限られる．後索の変性については，二次変性,[3] 脱髄および軸索消失,[4] 脱髄,[4] などいろいろな名称のもとに記述されている．これら記述および顕微鏡写真を再検討した結果では，これら全症例における後索の変性は二次変性と解釈してよいように思われる．

TABLE 1 PATHOLOGICAL FINDINGS IN PERIPHERAL NERVES SPINAL ROOTS AND SPINAL CORD IN REPORTED CASES OF SUBACUTE NECROTIZING ENCEPHALOMYELOPATHY

表1 亜急性壊死性脳脊髄疾患の報告例における末梢神経，脊髄神経根，および脊髄の病理学的所見

Author 著者	Peripheral Nerves 末梢神経	Spinal Roots 脊髄神経根	Spinal Cord 脊髄
Leigh (1951)			Demyelination and gliomesodermal reaction, dorsal columns, above thoracic level. 胸髄よりも高位にある後索の脱髄および膠質中胚葉反応
Richter (1957)			Secondary degeneration, descending tracts, lateral collums 側索下行路の二次変性
Reye (1960) Case 1 症例1	Incomplete demyelination 不全脱髄	Demyelination, dorsal roots 後根脱髄	Demyelination and loss of axons, dorsal columns above lumbar. Vascular scar, gray commissure, cervical. 腰髄よりも高位にある後索の脱髄および軸索消失 頸髄灰白交連の血管性瘢痕
Case 2 症例2	Incomplete demyelination 不全脱髄	Demyelination, dorsal roots 後根脱髄	Demyelination, dorsal columns, above lumbar level. Rarefaction, gray matter 腰髄よりも高位にある後索の脱髄灰白質粗化
Case 3 症例3	Incomplete demyelination 不全脱髄	Demyelination, dorsal roots 後根脱髄	Demyelination, dorsal columns, above lumbar level. Rarefaction and nerve cell loss, gray matter, above cervical 腰髄よりも高位にある後索の脱髄，頸髄よりも高位にある灰白質の粗化および神経細胞減少
Case 4 症例4	Slight demyelination, vagus nerve 迷走神経の軽度の脱髄	Unaffected 正常	Demyelination, gracile fascicles, above cervical level 頸髄よりも高位にある薄束の脱髄
Namiki (1964) 並木	Demyelination and degeneration of axons 脱髄および軸索変性	Demyelination and degeneration of axons, dorsal and ventral roots 後根および前根の脱髄および軸索変性	Secondary degeneration, gracile fascicles. Rarefaction, ventral gray columns, above upper thoracic level 薄束の二次変性，上部胸髄よりも高位にある前角の粗化

Reye[4] examined the spinal roots and peripheral nerves in the four cases he reported. He found either *demyelination* or *incomplete demyelination* of these structures in all except for the spinal roots of the fourth case which were considered normal. In the case described here, the spinal roots, especially the dorsal roots, and peripheral nerves demonstrated extensive demyelination and degeneration of the axons. These changes are those seen in the peripheral neuropathies presently classified as primary neuronal degeneration and atrophy.

Although the spinal cord, spinal roots and peripheral nerves have been examined in only a few cases, the constant presence of peripheral neuropathy in all cases in which the peripheral nerves have been studied appears to indicate that in subacute necrotizing encephalomyelopathy, the pathologic changes are not confined to the central nervous system, but involve the peripheral nerves as well. Hence, the name *encephalopathy* or *encephalomyelopathy* does not appear to be an entirely appropriate description for all the features of the disease.

The pathological changes in the spinal roots in the present case are most remarkable in the lumbar and lower thoracic levels and milder in the cervical, upper thoracic and sacral levels, possibly indicating predilection for the longer fibers.

Peripheral neuropathies due to avitaminosis, especially thiamine and pantothenic acid, and arsenical poisoning, both known to prevent pyruvate oxidation in the metabolism of glucose, present pathologic changes in the nerves similar to those described above.[6-11] This fact appears to substantiate the speculation of some authors[1-3] that the lesions of the brain stem in this disorder resemble those of Wernicke's disease, and that the disorder may be caused by disturbances of pyruvate metabolism, due possibly to endodenous toxemia or to an inherent, possibly enzymatic, metabolic defect.

The history of the present case further indicates that the parents are first cousins and that one of the siblings died of a neurological disorder similar to that of the patient. Feigin and Wolf reported cases of two sisters who died of similar neurological difficulties, had identical neuropathological

Reye[4]はかれが報告した4例の脊髄神経根および末梢神経を検査した．そのうち第4例では脊髄神経根は正常と考えられたが，その他の例においては，いずれもこれらの組織に「脱髄」または「不全脱髄」のいずれかを認めた．本症例においては，脊髄神経根，特に後根，および末梢神経に広範な脱髄および軸索変性を認めた．これらの変化は現在原発性神経変性および萎縮として分類されている末梢神経疾患に見られるものである．

脊髄，脊髄神経根および末梢神経は少数例について検査されたにすぎないが，末梢神経の検査を行なった全例に末梢神経疾患が常に見られたことは，亜急性壊死性脳脊髄疾患においては，病理学的変化は中枢神経系に限られないで末梢神経にも及ぶことを示しているように思われる．したがって，「脳疾患」または「脳脊髄疾患」という名称は，この疾患の特徴全部を示す適切な表現とは思われない．

本症例における脊髄神経根の病理的変化は腰髄および下部胸髄神経において最も著明であり，頸髄，上部胸髄および仙髄神経において比較的に軽度であるが，この所見は長い神経線維に病変が好発することを示していると思われる．

ビタミン欠乏症，特にサイアミンならびにパントテン酸の欠乏症および砒素中毒は，いずれも糖代謝における焦性葡萄酸塩の酸化を妨害するものとして知られているが，これらの状態に起因する末梢神経疾患では，以上述べたと同様の病理的変化が末梢神経に発現する．[6-11] この事実は，本疾患すなわち亜急性壊死性脳脊髄疾患における脳幹病変はウェルニッケ病の病変に類似しており，本疾患が内因性中毒症，または先天的の，そしておそらく酵素性の，代謝障害によって起こると思われる焦性葡萄酸塩代謝障害をその発生原因とするであろうという一部の著者[1-3]の推測を立証するように思われる．

さらに，本症例の病歴の示すところでは，本症例の患者の両親はいとこ同士であり，同胞1名はこの患者の疾患と同様の神経疾患で死亡している．Feigin およびWolf は，同様の神経障害で死亡し，神経病理学的所見も同じで，両親がいとこ同士であった姉妹2人の症例に

findings and whose parents were first cousins. One of the four cases reported by Reye, a 23-month-old girl, had an elder sister who died of a similar disease at two years of age; autopsy was not performed on this sister and parental consanguinity is not described. These facts may support Richter's suggestion that the disorder may represent a metabolic defect which is inborn and genetically determined.

SUMMARY

A 15-year-old Japanese girl with a clinical history and postmortem findings of a subacute necrotizing encephalomyelopathy is reported. The patient's parents were consanguinous and a similar disease was also present in one sibling.

This case and those available in the literature indicate that a severe peripheral neuropathy associated frequently with secondary degeneration of the dorsal white columns of the spinal cord constitutes an integral part of the disorder.

The presence of peripheral neuropathy reminiscent of that due to deficiency of thiamine and pantothenic acid, frequent familial occurrence of the disorder and consanguinity in some of the parents give support to the speculation of previous investigators that the disease may represent an inborn error of metabolism especially of pyruvate metabolism.

ついて報告している．Reye が報告した4例のうち1例，生後23か月の女児の姉は2歳の時に同様の疾患で死亡したが，剖検は行なわれなかった．その親の血縁関係についての記載もない．これらの事実は，この疾患は先天的で，遺伝的に決定される代謝障害を示すものではなかろうかという Richter の示唆を裏付けるものであろう．

要　約

亜急性壊死性脳脊髄疾患の臨床歴および剖検所見のある15歳の日本人少女の症例について報告した．患者の両親には血族関係があって，同胞1名にも同様の疾患があった．

しばしば脊髄後索の二次変性を伴う，強度の末梢神経疾患がこの疾患の不可欠部分を構成していることを，この症例および文献上の症例が物語っている．

サイアミンおよびパントテン酸欠乏症による末梢神経疾患に類似する末梢神経疾患の存在と，この疾患の家族性頻発および患者たちの両親に一部血族結婚が認められるということは，この疾患が代謝，特に焦性葡萄酸塩代謝における先天性異常を示すものであろうという従来の研究者の推測を裏付ける．

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