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AMYOTROPHIC LATERAL SCLEROSIS WITH GENERALIZED NEUROAXONAL DEGENERATION AND SELECTIVE INVOLVEMENT OF THE NIGRO-PALLIDAL SYSTEM

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Apart from the classic form of amyotrophic lateral sclerosis (ALS), characterized by clinical symptoms of simultaneous involvement of both upper and lower motor neurons, there exists quite a number of atypical forms of the disease (Hudson 1981). These, occurring both in sporadic and familial variants combine in addition to the leading motor neuron symptomatology, clinical features indicating involvement of other systems of the neuraxis. Among them, combination of amyotrophic lateral sclerosis with dementia and/or extrapyramidal syndrome seems to be the most common (Greenfield, Matthews 1954; Boudouresques et al. 1967; Bonduelle et al. 1968, 1970; Moya et al. 1969; Munset, Bradley 1979; Hudson 1981). The latter cases are clinically similar to those endemically occurring on the Guam island and Kii peninsula in Japan, as combination of ALS with the Parkinsonism-Dementia complex (Kurland, Brody 1975; Shiraki, Yase 1975; Mitsuyama, Takamiya 1979).

The pathomorphology of the disease shows even greater variability. Even in its classic form, in a large proportion of cases, neuropathological abnormalities exceed widely the structures of upper and lower motor neurons (Smith 1960; Brownell et al. 1970). The pathomorphological variability is considerably greater in atypical forms of the disease, in which involvement of other structures of the brain and spinal cord is as common as alterations of both neurons of the motor pathway (Greenfield, Matthews 1954; Boudouresques et al. 1967; Moya et al. 1969; Brownell et al. 1970; Bots, Staal 1973; Finlayson et al. 1973; Kaiya, Mehraein 1974; Kosaka, Mehraein 1978; Hudson 1981).

Our intention is to present a clinical-pathological analysis of a case of amyotrophic lateral sclerosis with atypical clinical picture and course and unusually rich and complex neuropathological findings.

CASE REPORT

Clinical data *

The case concerned a 47-year-old man with negative family history, in whom general asthenia and apathy, mental and psychomotor slowness, difficulty in walking with weakness of lower extremities, slurred speach and writing abnormalities had been progressively developing in the course of the last year prior to hospitalization. Neurological examination, in addition to mild dementia, speach difficulty and writing abnormality revealed increased muscle tone in all extremities, fine tremor in upper limbs, bilateral lack of ankle jerks and Babiński sign on the right side. Due to lowered ceruloplasmine (9.5 mg%) and copper levels in the blood serum (30 μg%) and presence of a delicate Kayser-Fleischer ring found on ophthalmological examination, Wilson's disease was diagnosed and typical therapy with chelating agents was applied with positive subjective results.

Three years later, on second hospitalization, severe deterioration of the patient's state was found. The demented patient was emaciated, he did not speak spontaneously, neither did he answer questions and follow orders. Swallowing difficulties were noticeable. The face was amimic, palmomental and snout reflexes were present. Muscle wasting involving bilaterally shoulder girdle muscles and those of both hands was striking. Fasciculations in the atrophic muscle groups were present. Coarse tremor was observed in both hands. Muscle strength in both lower extremities was decreased. Increased muscle tone of extrapyramidal type was present in all extremities. Tendon reflexes in lower extremities were absent. Plantar reflexes were bilaterally extensor. Ceruloplasmine level was extremely low (0.55 mg%), that of copper, although higher than in previous examination, was lower than normal (70 μg%). A discreet Kayser-Fleischer ring was also seen.

During the 4-month hospitalization the patient progressively deteriorated. He died 4 years after the beginning of clinical symptoms.

Pathological findings

General autopsy findings were irrelevant. Moderate atheromatosis of larger arteries and purulent bronchitis and bronchopneumonia were noted. Liver cirrhosis was not a feature. Microscopic examination of liver revealed moderate vacuolization of hepatocyte nuclei.

Neuropathological findings

Gross brain examination revealed moderate frontal cortical atrophy,

* The patient was treated in the Neurological Department, Postgraduate Medical Education Centre, Military Medical Academy, Warsaw. The authors are indept to Prof. Dr. T. Domżał for kind permission to use clinical data.

atrophy and bilateral cavitation of substantia nigra, some atrophy of cervical spinal enlargement and poor outlines of grey spinal structures. In addition an inveterate hemorrhagic focus was found in the temporo--parietal region of the right hemisphere.

Microscopic examination. Microscopic neuropathological examination was carried out on representative sections of the brain, brain stem, cerebellum and spinal cord. Paraffin sections were stained with hematoxylin--eosin and according to Klüver-Barrera, van Giesen, Griedley, Kanzler--Arendt and PAS methods. Silver-impregnation according to Bielschowsky was performed on frozen sections. Histochemical reaction for iron was run according to Pearle's method.

Microscopic examination revealed severe loss of large motor neurons in the anterior horns of the spinal cord, being the most pronounced in the spinal enlargements, first of all the cervical one. Here, practically the whole population of large motor neurons was absent, with only some small nerve cells preserved (Fig. 1). In other spinal segments neuronal loss concerned mostly antero-medial groups of large motor neurons. The preserved motor nerve cells showed severe degeneration in the form of lipochromatosis, chromatolysis, shrinkage and vacuolar degeneration (Fig. 2a). Some cells showed features of granulovacuolar degeneration (Fig. 2b). Similar abnormalities, but much less pronounced, concerned posterior horn neurons. Neuronal loss and degeneration were accompanied by cellular and fibrous gliosis. Neuronal loss and degeneration involved also motor nuclei of the cranial nerves, mostly those of the hypoglossus and vagus nerves (Fig. 3). Changes in the motor cortex were less advanced, although there was moderate rarefaction of large pyramidal neurons in the fifth cortical layer. There was no noticeable demyelination of the pyramidal tracts on their whole length, except slight pallor of some pyramidal bundles in the pons. However, under higher magnification some rarefaction and spongiosis, with no macrophagic activity, were seen in the lateral cortico-spinal tracts in the cervical and thoracic segments of the spinal cord. Similar abnormalities were present in the dorsal spino-cerebellar tracts and in the central portion of the posterior funiculi.

Substantia nigra in addition to macroscopically seen bilateral cavitation revealed almost complete neuronal loss in both compact and reticular portions. The only melanin-bearing neurons left were those located in the most lateral part of the structure. Coarse and fine melanin granules were lying loosely in the neuropil, often in perivascular aggregations (Fig. 4). This was accompanied by severe cellular and fibrous gliosis. Numerous yellowish-brown, fine granular deposits were spread widely over the structure (Fig. 5). Their accumulation arround astrocytic nuclei suggested their intracellular location. Most of them revealed a positive iron reaction (Fig. 6).

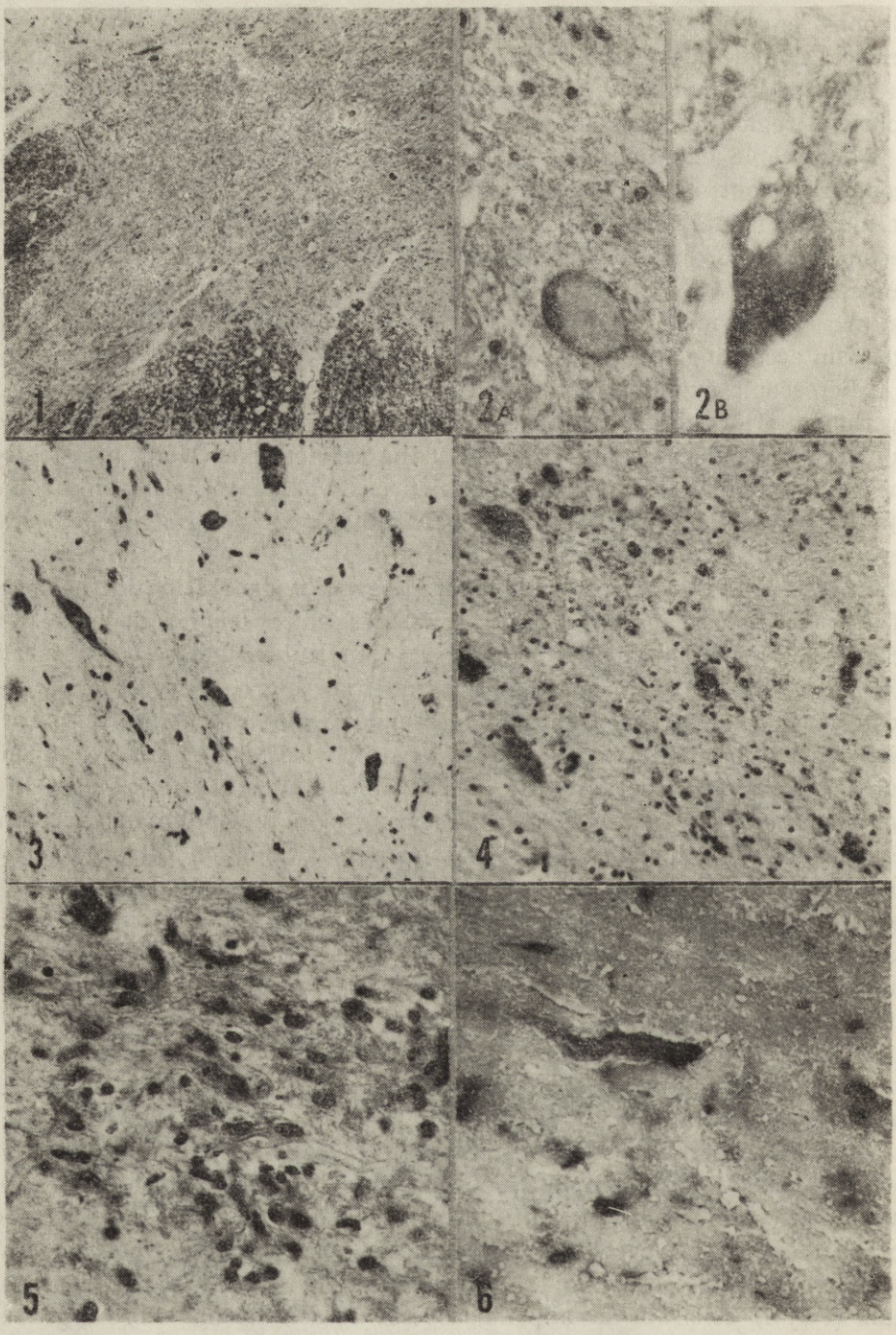


Fig. 1. Spinal cord, cervical segment. Almost total loss of large motor neurons with secondary gliosis. Klüver—Barrera. × 60

Ryc. 1. Rdzeń kręgowy, odcinek szyjny. Prawie całkowity zanik dużych neuronów ruchowych z wtórną fibroglejozą. Klüver—Barrera. Pow. 60 ×

Globus pallidus was bilaterally shrunken and fibrous (Fig. 7). There was severe neuronal loss and degeneration and glial proliferation and hypertrophy (Fig. 8). Numerous fine and coarse granular deposits, similar to those seen in substantia nigra, were spread widely in the neuropil and aggregated arround astrocytic nuclei. Most of them revealed a positive reaction for iron, although some of them were negative (Fig. 9). There was strong adventitial siderosis of medium-size pallidal arteries. Cytology of the putamina, caudate and subthalamic nuclei was apparently normal. Thalami showed moderate neuronal loss and degeneration. In both putamina and thalami some delicate iron-positive deposits were seen. Frontal cortex showed patchy and laminar neuronal loss, confined in most instances to the II and III cortical layers, with no remarkable astrocytic proliferation (Fig. 10). There was some pallor of myelin in the frontal subcortical white matter. Neurofibrillary tangles, Pick's argentophilic degeneration and senile plaques were not a feature. The most striking finding consisted in the presence of numerous neuroaxonal spheroids spread all over the central nervous system. Varying greatly in size and morphology they were most numerous in both grey and white structures of the spinal cord (Fig. 11), substantia nigra (Fig.

Fig. 2. Degeneration of large motor neurons. *A*) Severe lipochromatosis and shrinkage of large motor neurons in the cervical segment of spinal cord. H—E. × 400. *B*) Vacuolar and granulovacuolar degeneration of large motor neuron in the lumbar segment of the spinal cord. H—E. × 1200

Ryc. 2. Zwyrodnienie dużych neuronów ruchowych. *A*) Stłuszczenie i obkurczenie zachowanych dużych neuronów ruchowych w szyjnym odcinku rdzenia kręgowego. H—E. Pow. 400 ×. *B*) Wodniczkowe i ziarnisto-wodniczkowe zwyrodnienie dużego neuronu ruchowego w lędźwiowym odcinku rdzenia kręgowego. H—E. Pow. 1200 ×

Fig. 3. Neuronal loss and degeneration in the nucleus of hypoglossal nerve. Klüver—Barrera. × 200

Ryc. 3. Ubytki komórek nerwowych i zwyrodnienia neuronalne w jądrze nerwu podjęzykowego. Klüver—Barrera. Pow. 200 ×

Fig. 4. Substantia nigra: loss of pigmented cells, cellular gliosis, loose granules of pigment lying free in the neuropil. H—E. × 200

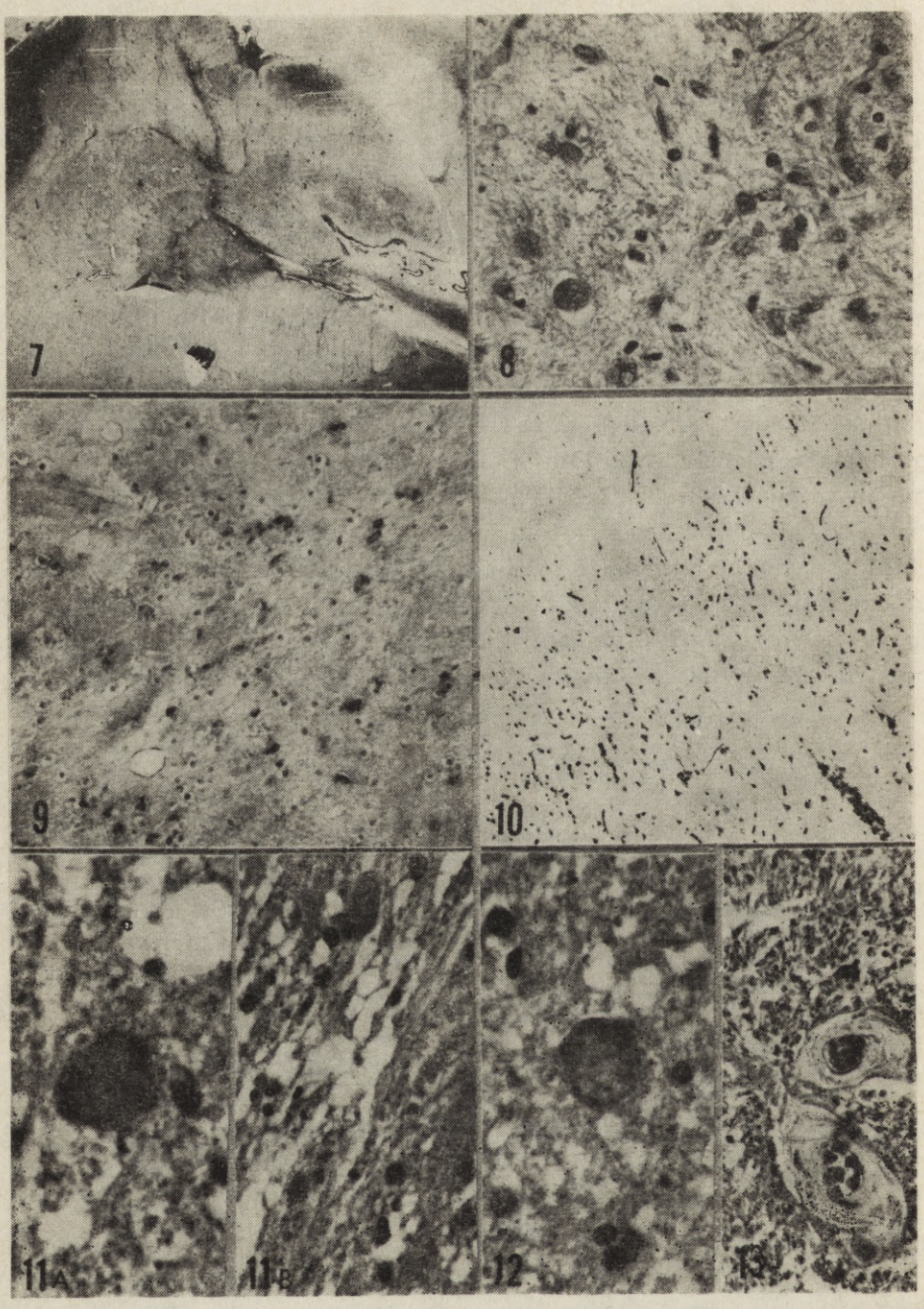
Ryc. 4. Istota czarna: zanik komórek barwnikowych, glejoza komórkowa, ziarna barwnika rozsiane w neuropilu. H—E. Pow. 200 ×

Fig. 5. Substantia nigra: glial proliferation and hypertrophy. Fine granular deposits seen in neuropil. H—E. × 400

Ryc. 5. Istota czarna: proliferacja i przerost gleju. Drobnoziarniste złogi w neuropilu. H—E. Pow. 400 ×

Fig. 6. Substantia nigra: coarse and fine granular iron-positive deposits. Pearle. × 400

Ryc. 6. Istota czarna: grube i delikatne żelazo-dodatnie złogi. Pearle. Pow. 400 ×



12) and pallidum. They were less numerous in the medulla, being not limited to the nuclei of the posterior funiculi, in basal ganglia, thalami, cerebral cortex and the subcortical white matter. The neuropathological picture of the case was completed by severe fibrosis and hyalinization of the small blood vessel walls (Fig. 13); this being most advanced in the white matter of the spinal cord and putamina.

Chemical data

The copper content in basal ganglia, cerebral cortex and subcortical white matter was 24.43, 11.74 and 7.02 mg of copper/g of the dry tissue weight, respectively. Lead content, estimated as that of copper, spectrophotometrically (atomic absorption standard method of Jarrall-Ash) was markedly increased in all examined structures of the central nervous system as compared with that found in identical CNS areas in a non-neurological patient of the same age group as ours. The comparative data are shown in Table 1.

Fig. 7. Globus pallidus: shrinkage and fibrogliosis of medial and lateral segments. Kanzler—Arendt, Magnif. glass.

Ryc. 7. Gałka blada: obkurczenie i glejoza włóknista obu segmentów jądra. Kanzler—Arendt. Pow. lupowe

Fig. 8. Globus pallidus: glial proliferation and hypertrophy, fine granular material spread over neuropil. Axonal spheroid seen in the lower part of the picture. H—E. × 400

Ryc. 8. Gałka blada: proliferacja i przerost gleju, drobnoziarniste złogi rozsiane w neuropilu. Sferoid aksonalny widoczny w dolnym fragmencie ryciny. H—E. Pow. 400 ×

Fig. 9. Globus pallidus: granular, iron-positive deposits spread over neuropil. Pearle. × 200

Ryc. 9. Gałka blada: ziarniste, żelazo-dodatnie złogi w neuropilu. Pearle. Pow. 200 ×

Fig. 10. Frontal cortex: neuronal loss in II and III layers. Klüver—Barrera. × 100

Ryc. 10. Kora czołowa: ubytki neuronalne w II i III warstwie. Klüver—Barrera. Pow. 100 ×

Fig. 11. Spinal cord: *A*) axonal spheroid from the lateral funiculus. H—E. × 800. *B*) axonal spheroids from the posterior spinal root. H—E. × 400

Ryc. 11. Rdzeń kręgowy: *A*) sferoid aksonalny z bocznych powrózków. H—E. Pow. 800 ×. *B*) sferoid aksonalny w śródrdzeniowym odcinku korzenia tylnego. H—E. Pow. 400 ×

Fig. 12. Spheroid in the reticular part of substantia nigra. H—E. × 800

Ryc. 12. Istota czarna: sferoid aksonalny w części siatkowatej H—E. Pow. 800 ×

Fig. 13. Fibrosis of blood vessel walls in the posterior funiculus of the spinal cord. H—E. × 400

Ryc. 13. Rdzeń kręgowy: zwłóknienie ściany drobnego naczynia tętniczego w powrózku tylnym. H—E. Pow. 400 ×

Table 1. Lead content in various structures of the central nervous system (μg/g of dry tissue weight)

Tabela 1. Zawartość ołowiu w różnych strukturach ośrodkowego układu nerwowego (μg/g suchej masy tkanki)

Structure of the CNS Struktura oun	Patient Pacjent	Reference case Przypadek referencyjny
Cerebral cortex Kora mózgu	7.20	3.15
Subcortical white matter Istota biała podkorowa	5.62	2.11
Basal ganglia Jądra podstawy	8.68	4.10
Spinal cord Rdzeń kręgowy	21.90	7.20

DISCUSSION

In the presented case, the 4-year-long disease process began with progressive psychoorganic changes concomitant with an extrapyramidal syndrome with some features of pyramidal involvement. Muscular atrophy with fasciculations, involving bilaterally upper limbs appeared in the further stage of the disease. The extrapyramidal syndrome with psychoorganic changes, accompanied by both laboratory and clinical exponents of copper metabolism abnormalities inclined the clinician to diagnose hepato-lenticular degeneration. Further development of the disease, especially appearance of the amyotrophic syndrome, shook this diagnosis, which was neither proven at the postmortem examination. This revealed lack of liver pathology and neuropathological exponents of Wilson's disease as well as an apparently normal copper level in the brain tissue. However, the question of copper metabolism disturbances, manifested by reduced blood content of both copper and ceruloplasmine and presence of the Kayser-Fleischer corneal ring remains open. The same concerns the transitory positive clinical response to copper-chelating agents, while House et al. (1978) pointed out negative results of penicillamine treatment in amyotrophic lateral sclerosis.

Light-microscopic examination revealed a variety of neuropathological abnormalities involving practically the whole central nervous system. Neuronal loss and degeneration concerning spinal and bulbar motor neurons are classic neuropathological exponents of amyotrophic lateral sclerosis. Involvement of the upper motor neurons, although present, was mild. This, however, has been observed in quite a number of the most classic cases of ALS. In the series of Brownell et al. (1970) in 20 per cent of classic cases there were no changes in pyramidal tracts and motor cortex. On the other hand slight involvement of the posterior horn neu-

rons and abnormalities in the posterior funiculi and spino-cerebellar tracts are not unusual components of both classic and atypical forms of the disease. So are neuronal loss and degeneration, in globus pallidus and substantia nigra (Malamud et al. 1961; Boudouresques et al. 1967; Moya et al. 1969; Bonduelle et al. 1968; Bots, Staal 1973; Kaiya, Mehraein 1974; Shiraki, Yase 1975; Kosaka, Mehraein 1978; Hudson 1981). Both of these structures, alongside with the cerebral cortex, belong to those most commonly affected in ALS combined with dementia and/or extrapyramidal syndrome. In our case nigral and pallidal lesions were particularly intensive. Damage to substantia nigra resulted in its cavitation. The clinically extrapyramidal syndrome preceded the appearance of amyotrophy. Neuronal loss, secondary gliosis, neuroaxonal dystrophy and accumulation of iron-positive deposits in the substantia nigra and globus pallidus, observed in our case, constitute a typical neuropathological background of the Hallervorden-Spatz disease. Concomitance of morphological abnormalities characteristic of the Hallervorden-Spatz disease, with amyotrophic lateral sclerosis was described by Hirano et al. (1961), Staat and Bots (1969), Bots and Staat (1973) and Kosaka and Mehraein (1978). More striking neuropathological features of Hallervorden-Spatz disease were demonstrated by Shiraki and Yase (1975) in two Japanese cases combining amyotrophic lateral sclerosis and the Parkinsonism-Dementia complex. Contrary to our case, pallidal changes were more advanced than nigral ones. However, in Hallervorden-Spatz disease pigmentary alterations concern selectively the reticular portion of the substantia nigra, while in our case severe tissue disintegration with pigment deposition involved both its reticular and compact parts. Cavitation of substantia nigra, being the most advanced tissue abnormality, was located in its reticular portion. Similarly, neuroaxonal spheroids, although numerous in both substantia nigra and globus pallidus, were spread widely all over the central nervous system. The distribution of neuroaxonal degeneration in our case resembled more that described in cases of neuroaxonal dystrophies than that characterictic o Hallervorden-Spatz disease (Seitelberger 1971). Spheroid localization exceeded also the topistic sides of their accumulation connected with either physiological or pathological brain ageing (Jellinger, Haub 1968; Jellinger, Jirasek 1971; Seitelberger 1971; Fujisawa, Shiraki 1980). Neuroaxonal spheroids were very common in most of the cases described by Shiraki and Yase (1975), including those of both classic type and ALS combined with the Parkinsonism-Dementia complex. However, their distribution, contrary to our case, was limited to the affected areas of the spinal cord and typical topistic sides of their accumulation. It seems that in our case generalized neuroaxonal dystrophy can be considered either as an exponent of a multisystemic dystrophic process (Blakemore, Cavanagh 1969; Koenig 1968; Jellinger, Jirasek 1971; Fujisawa, Shiraki 1980) or

as an indicator of precocious presenile changes (Jellinger, Jirasek 1971). The latter assumption is supported by the appearance of widespread granulovacuolar degeneration of neurons. In general the neuropathological pattern of our case resembles most that of two previously mentioned cases from the series of Shiraki and Yase (1975). However, the most substantial difference between them consists in a lack in our case of intracytoplasmic neurofibrillary tangles, which were the typical finding in the Japanese cases. The second essential difference consists in the presence of vascular abnormalities in the form of fibrosis and hyalinosis of small vessel walls, with consecutive perivascular damage to the brain parenchyma. They occurred in a relatively young man with no arterial hypertension or renal pathology, mild atheromatosis of larger peripheral vessels and complete lack of atheromatosis in larger cerebral arteries. This type of vascular abnormalities, although described in some cases of amyotrophic lateral sclerosis (Rafałowska, Bunina 1969) does not belong to typical elements of the neuropathological picture of the disease.

The question of increased lead content in the tissue of the central nervous system requires a short comment, because of the possibility of professional exposure of our patient to the action of this metal. The problem of the role of lead in the pathogenesis of amyotrophic lateral sclerosis, opened at the beginning of the century with Wilson's paper (1907), has revived in the seventies, despite the changing general concepts concerning the etiopathogenesis of this disease (Campbell et al. 1970; Petkau et al. 1974; Conradi et al. 1976, 1978). The concept of the pathogenetic role of lead is based on observations of ALS cases indicating its increased content in blood serum, cerebro-spinal fluid and in several tissues and organs, first of all in muscles and the peripheral and central nervous systems (Conradi et al. 1976, 1978; Petkau et al. 1974). The observation of Petkau et al. (1974) are of special interest, as they have demonstrated increased lead levels in various parts of the central nervous system, with the striking preponderance of the spinal cord in patients with amyotrophic lateral sclerosis exposed and not exposed to contact with the metal, exceeding that of an average population. According to the hypothesis of Conradi et al. (1976, 1978) lead penetrates to the central nervous system either through damaged blood vessels or via peripheral nerves, transported with a retrograde axonal flow from motor-end-plates to the perikarya of large motor neurons. Involvement of the upper motor neuron, secondary in nature, is supposed to be brought about via transsynaptic metal transport from motor neurons localized either in the spinal cord and/or medulla.

It seems extremely difficult to draw any conclusions in this respect basing on the data concerning the presented case, despite its unusually rich clinical picture and neuropathological abnormalities. However, it

seems worthwhile to point out several questions. A striking increase of lead content was found in all examined structures of the central nervous system, being not limited to the spinal cord. This corresponds well with generalized neuropathological changes, extending beyond both lower and upper motor systems. Goldstein et al. (1974) have shown that chronic lead intoxication produces disturbances in the metabolism of catecholamines. This seems interesting in the light of extrapyramidal symptomatology, dominating alongside with the dementia clinical picture of the disease in its initial stage. Severe neuronal loss within the cerebral cortex, by no means limited to the motor area, which could be considered as structural basis for the psychoorganic syndrome in the relatively young man without morphological features of presenile dementia, was the only neuropathological alteration, common with the described up till now, verified cases of lead encephalopathy (Whitefield et al. 1974; Nyka et al. 1978). It should be added, however, that neuropathology of lead encephalopathy is neither specific nor diagnostic. All the above discussed questions cannot be considered as indicating pathogenic participation of lead in the development of amyotrophic lateral sclerosis, although in the particular case presented it could have played some role in complicating and enriching both the clinical picture of the disease and its pathomorphological exponents.

Summarizing, we would like to consider our case as one more example of the coexistence of motor neuron disease with other systemic degenerative processes of the central nervous system with unusually rich and diversiform neuropathology.

STWARDNIENIE ZANIKOWE BOCZNEJ Z UOGÓLNIONĄ DYSTROFIĄ NEUROAKSONALNĄ I WYBIÓRCZYM USZKODZENIEM UKŁADU NIGRO-PALIDARNEGO

Streszczenie

Przedstawiono przypadek 47-letniego chorego, u którego w okresie czterech lat rozwinął się ciężki, prowadzący do zejścia śmiertelnego, zespół neurologiczny, składający się z otępienia, objawów pozapiramidowych, przypominających w okresie początkowym obraz choroby Wilsona, dyskretnych objawów piramidowych oraz symetrycznych zaników mięśni obręczy barkowej i rąk. Objawy zajęcia obwodowego neuronu ruchowego były zjawiskiem stosunkowo późnym, poprzedzonym zespołem pozapiramidowym i cechami postępującego otępienia.

W obrazie neuropatologicznym stwierdzono zaawansowane objawy uszkodzenia obwodowego neuronu ruchowego na poziomie opuszki i rdzenia kręgowego, przede wszystkim w obrębie zgrubienia szyjnego, bez wyraźnego zajęcia dróg korowo-rdzeniowych. Dominującym zjawiskiem uzupełniającym było wybiórcze, symetryczne uszkodzenie gałki bladej i istoty czarnej, w jej części zbitej i siatkowatej, wyrażające się zanikiem neuronów, wtórną fibroglejozą oraz nagromadzeniem ziarnistych złogów żelazo-dodatnich. W całym ośrodkowym układzie nerwowym, z wyraźną przewagą układu nigropalidarnego, pnia mózgu, a przede wszystkim rdze-

nia kręgowego, występowały liczne, różniące się kształtem i wielkością sferoidy neuroaksonalne. W korze mózgu występowały uogólnione i rozsiane ubytki komórek nerwowych, bez wyraźnej predylekcji topograficznej. Zmian starczych, typu płytek i zwyrodnienia włókienkowego Alzheimera, nie stwierdzono. Obecne były natomiast stosunkowo liczne neurony z cechami zwyrodnienia ziarnisto-wodniczkowego, głównie w formacjach rdzenia kręgowego. Obraz neuropatologiczny uzupełniały zmiany naczyniowe o typie zwłóknienia i zeszkliwienia drobnych naczyń tętniczych. Badanie chemiczne wykazało bardzo znaczny wzrost zawartości ołowiu w korze mózgu, jądrach podstawy, a przede wszystkim w rdzeniu kręgowym, przekraczającej wielokrotnie odpowiednie wartości kontrolne.

Autorzy uważają przedstawiony przypadek za przykład współistnienia stwardnienia zanikowego bocznego z innymi układowymi procesami zwyrodnieniowymi ośrodkowego układu nerwowego, o niezwykle bogatym i zróżnicowanym obrazie neuropatologicznym. Ze względu na zawodową ekspozycję chorego na działanie ołowiu, specjalną uwagę zwrócono na możliwą rolę patogenetyczną tego metalu w opisanym zespole chorobowym.

БОКОВОЙ АМИОТРОФИЧЕСКИЙ СКЛЕРОЗ С ОБОБЩЕННОЙ НЕВРОАКСОНАЛЬНОЙ ДИСТРОФИЕЙ И СЕЛЕКТИВНЫМ ПОВРЕЖДЕНИЕМ НИГРО-ПАЛЛИДАРНОЙ СИСТЕМЫ

Резюме

Представлен случай 47-летнего больного у которого появился и в течение 4 лет привел к смерти неврологический синдром, состоящий с деменции, экстрапирамидных симптомов (с клинической картиной напоминающей болезнь Вильсона), слабо выраженного пирамидного синдрома и симметричной атрофии мышц плечевого пояса и рук. Симптомы повреждения периферического двигательного неврона появились относительно поздно, предшествовал экстрапирамидный синдром и прогрессирующая деменция.

Невропатологический образ выявил выдвинутый синдром повреждения периферического двигательного неврона на уровне продолговатого и спинного мозга, особенно в шейном утолщении, без отчетливого нарушения корково-спинальных пучков. Дополняющим доминирующим явлением было селективное симметричное повреждение бледного шара и черного вещества (как *pars compacta* так *pars reticularis*) проявляющееся полным отсутствием невронов, пролиферацией волокнистой глии и скоплением зернистых железопозитивных отложений. Во всей центральной нервной системе с отчетливым преобладанием нигро-паллидарной системы, ствола мозга и особенно спинного мозга, были обнаружены многочисленные, разные по форме и величине, невроаксональные сфероиды. В коре мозга выступали обобщенные и рассеянные клеточные убытки, без особой локализации. Старческих бляшек и неврофибриллярной клеточной дегенерации Alzheimera не найдено. Вместо того были обнаружены многочисленные невроны с зернисто-вакуолярной дегенерацией, выступающие особенно в структурах спинного мозга. Невропатологическую картину дополняли обобщенные изменения сосудов в виде фиброза и гиалиноза артериол. Химическое исследование обнаружило очень большое количество свинца в мозговой коре, белом веществе, подкорковых ганглях и, особенно, в спинном мозге. Количество это много раз превышало контрольные данные.

Авторы рассматривают представленный случай как пример сосуществования бокового амиотрофического склероза с другими системными дегенерационными процессами, отличающийся необычным разнообразием невропатологической картины. В связи с профессиональной экспозицией больного на влияние свинца, особое внимание было обращено на возможную патогенетическую роль этого метала в формировании болезненного симптомокомплекса.

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