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NEUROPATHOLOGICAL SYNDROMES IN THE COURSE OF FULL BLOWN ACQUIRED IMMUNE DEFICIENCY SYNDROME (AIDS) IN ADULTS IN POLAND (1987–1995)

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Morphological analysis of the brains from 100 cases of full blown AIDS patients observed in the course of 1987-1995 years was performed. The material comprised 96 males, 3 females and 1 infant, 11 months old. Early material consisted almost exclusively of homo- and bisexuals, while in the last years heterosexual drug addicts prevailed.

Gross brain examination revealed focal changes in 25% of cases, most of them being connected either with opportunistic infections or primary proliferating malignancies. Brain atrophy with an evident regional differences was observed macroscopically in 35 cases.

Microscopic examination allowed detection of pathological changes in the brains of 87 cases, although in the remaining 13 cases there occurred some slight abnormalities taking the form of non-specific neuronal degeneration and loss, considered as resulting from perimortal cardio-pulmonary insufficiency or bleeding.

Specific HIV-related changes in the form of HIV-encephalitis, HIV-encephalopathy or coexistence of both and HIV-leptomeningitis as well as HIV-vasculitis were present in 35 cases. They were accompanied by HIV-associated changes (vacuolar myelopathy, vacuolar leukoencephalopathy and selective poliodystrophy). Very seldom they appeared as independent pathological features and were characterized by very low frequency. Opportunistic infections composed the largest group of 59 cases. Proliferative malignancies occurred altogether in eleven cases, 10 of which were primary and secondary brain lymphomas. One case of Kaposi sarcoma completed the neoplastic series. Sixteen cases revealed various types of brain pathology such as hepatogenic encephalopathy, traumatic cortical scars, central pontine myelinolysis etc.

The 59 cases of opportunistic infections consisted of a wide spectrum of viral and bacterial as well as fungal and protozoan infections. Among viral infections cytomegalovirus encephalitis was the most common, way ahead the progressive multifocal leukoencephalopathy. The second in frequency among opportunistic infections was brain toxoplasmosis and some fungal infections such as cryptococcosis and aspergillosis. Bacterial infections were in fact limited to tuberculosis, taking the form of granulomatous leptomeningitis with severe vascular pathology and/or tuberculoma formation.

Many pathological processes appearing in a single case was characteristic feature of our collection. There was coexistence of HIV-specific CNS pathology and opportunistic infections, malignant neoplastic growth and other types of pathology. Various opportunistic infections coexisted without HIV-specific changes as well as malignant proliferation with opportunistic infections. Similarities and differences of our series were compared with data characterizing other, earlier collections of NeuroAIDS.

Key words: *AIDS, neuropathology, HIV-specific changes, opportunistic infections, proliferating malignancies*

Fifteen years which have passed since first publication on previously unknown acquired immune deficiency syndrome (AIDS) brought very rich literature on etiology, pathogenesis, epidemiology, clinical aspects and pathology of this syndrome. A significant that great part of the publications, especially referring to clinical, pathological and selected aspects of etiopathogenesis of AIDS was on its association with the central nervous system (CNS). It was because of early clinical signs of CNS involvement by disease process, high frequency of neurological syndromes in full blown AIDS, estimated at approximately 60-80% of cases (Juszczyk, Gładysz 1992) as well as over 80% frequency of pathological changes in CNS. Human immune deficiency virus (HIV), characterized in its baseline affinity for cells of immune system positive for membrane CD4 receptors, especially helper cells and macrophages (Johnson et al. 1988) shows without any doubt some features of neurotropism. Viral replication and amplification in CNS occurs not only in microglia, representing in here reticulo-endothelial system but also in autochtonous neuroectodermal cells, particularly in astrocytes (Nuovo et al. 1994; Saito et al. 1994; Tornatore et al. 1994).

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Among publications on various aspects of central nervous system involvement in AIDS significant portion consist of reviews of AIDS neuropathology including description of HIV-specific or characteristic pathology as well as a broad spectrum of associated opportunistic infections and primary or secondary neoplastic proliferations. It is obvious that these works deal mostly with countries affected by the AIDS pandemic earlier. It is worth noting the rich material from the United States (Snider et al. 1993; Navia 1986; Petito et al. 1986), Brazil (Chimelli et al. 1992), Italy and Austria (Budka et al. 1987), Switzerland (Lang et al. 1988), Great Britain (Gray et al. 1989) and Berlin (Martinez et al. 1995). Polish material, collected at the Department of Neuropathology, Medical Research Centre of Polish Academy of Sciences in Warsaw, much smaller because of later appearance of AIDS and its less intensive spread has not been analyzed in such manner, yet. It has been partially presented at a few national and international scientific conferences (Mossakowski, Zelman 1990; 1993; Mossakowski et al. 1990) and closed scientific meetings.

The purpose of this article is to analyse AIDS neuropathological material from 1987 – 1995 collection of the Department of Neuropathology of MRC, PAS, obtained from AIDS Centre of Wolski Hospital of Infectious Diseases, Warsaw (ID Department of Warsaw School of Medicine and Centre for Diagnostics and Therapy of AIDS), where initially all the AIDS cases from entire Poland were referred. A few cases from the Infectious Disease Department of Medical Schools in Gdańsk and Wrocław were added. It is without any doubt, the largest collection at present of AIDS neuropathological material in Poland.

Material and methods

The subject for analysis was a hundred brains of patients who died in course of fully symptomatic immunodeficiency syndrome (AIDS); 89 cases from Wolski Hospital for Infectious Diseases in Warsaw (Infectious Diseases Department of Medical School and Centre for Diagnostics and Therapy of AIDS), 8 cases from Infectious Diseases Department, Medical School in Wrocław, and 3 cases from Infectious Diseases Department of Medical School in Gdańsk. There were 96 males, 3 females, 1 child, 11 months old.

Brains were first fixed in 10% neutralized formalin. None of the material contained spinal cord. Formalin fixed brains were weighed and cut in frontal plane into 1-cm-thick slices according to Spielmeyer's method. Blocks from brain stem did not exceeded 5 mm in thickness. Slices for histological examination were routinely taken from left cerebral hemisphere frontal lobe, temporal lobe with hippocampus, central, parietal and occipital regions, basal ganglia and diencephalon, left cerebellar hemisphere, mesencephalon, pons, medulla and subbulbar spinal cord. In a very few cases material includes also upper cervical cord. In case of focal changes, additional samples were taken from all abnormal areas, including damaged areas and their borders. Tissue blocks were routinely processed to paraffin; 6–8 μm slides were stained with hematoxylin and eosin, and by Heidenhain technique. Depending on initial examination, additional stainings were done such as silver impregnations and histochemical and immunochemical reactions. In general, we tried maximal use for diagnosis routine histological methods available in every histopathological laboratory.

Results

Table 1 presents the number of cases each year and mean age of patients examined between 1987-1995. It indicates that number of expirations from AIDS showed a tendency to increase in the last three years. However, our neuropathological data do not reflect current numbers of deaths from AIDS since the number of cases treated and expired in centers outside of Warsaw is increasing as well as number of deaths without autopsies.

Table 1. AIDS-cases examined neuropathologically in 1987–1996 period

Year	Number of cases	Age of patients	
		Mean	Range
1987	2	–	43 and 61
1988	0	–	–
1989	7	36.71	25–51
1990	12	39.25	27–64
1991	9	42.55	30–54
1992	12	39.67	32–46
1993	17	41.30*	26–62
1994	16	40.73**	29–59
1995	25	34.33	23–55

* Eight cases sent for neuropathological examination without full clinical records are excluded
** One case of 11 m old was excluded

Nevertheless, the increase noted in the table is even more convincing, since in earlier years patients were referred from all over Poland (data from patients charts); a contrast to recent years when patients were only from Warsaw and the Warsaw District. In a nine-year period, the age at death did not change significantly, but in the last year the number of younger patients has increased. It is striking, that vast majority are males; the first three cases of woman were from year 1993-95. We suppose, that the only pediatric case, was because our material was from clinical centers without pediatric departments.

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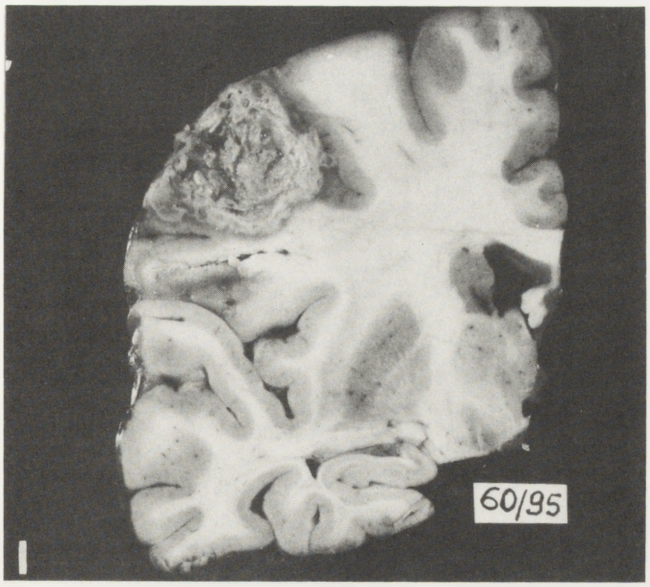

Fig. 1. HIV-encephalitis with aspergillosis. Fungal abscess in F3 gyrus. HE, ×100

It is important, however, to note changing over time risk factors and route of HIV infection in autopsied material. Earlier, almost all cases were of homo- and bisexuals. In following years, the number of drug-addicted heterosexual patients has increased. Cases from the 1980's and 1980/90's were infected abroad; in later years, the source of infection is almost exclusively local.

Macroscopic examination showed focal changes in 25% of brains. In each case they were associated with opportunistic infections (toxoplasmosis, progressive multifocal leukoencephalopathy, cryptococcosis, aspergillosis, etc. (Fig. 1) and neoplastic growth or they were characteristic for vascular or post-traumatic changes. Thirty five percent of cases showed features of cerebral atrophy of different degrees, in most of them without coexisting focal changes in hemispheres. Atrophy characterized by narrowed gyri, wider sulci and fissures showed evident regional differences. They affected most frequently frontal and temporal lobes, sparing usually hippocampus and parahippocampal gyri, and to a lesser extent, parietal lobes. In cases of cortical atrophy, dilatation of ventricles, mostly lateral and third, were noted without focal changes as their possible cause. One should note frequent occurrence of offuscation and thickening of leptomeninges without independent pathological process involving them or associated with parenchymal changes.

Table 2. Neuropathological diagnosis of 100 cases examined in 1987–1995

HIV-specific changes	35 cases
HIV-associated changes	2 cases
Opportunistic infections	59 cases
– cytomegaly	23 cases
– progressive multifocal leukoencephalopathy	11 cases
– herpes zoster encephalitis	1 case
– toxoplasmosis	16 cases
– cryptococcosis	10 cases
– aspergillosis	3 cases
– tuberculosis	2 cases
– cerebral lues	1 case
– matastatic encephalitis	1 case
– micronodular encephalitis	5 cases
– lymphocytic leptomeningits	1 case
Proliferative malignant processes	11 cases
– lymphoma	10 cases
– Kaposi's sarcoma	1 case
Other abnormalities	16 cases
– central pontine myelinolysis	1 case
– hepatogenic encephalopathy	2 cases
– brain trauma	3 cases
– thrombangitis obliterans	1 case
– vasogenic changes	4 cases
– vascular malformations	1 case
– disseminated intravascular coagulation syndrome	3 cases
– respiratory brain	1 case

Microscopic examination allowed detection of pathological changes in CNS in 87 cases (Table 2). Only 13 cases did not show histopathological abnormalities in CNS, in the form of specific neuropathological syndrome. It does not mean that there were no tissue abnormalities such as diffuse neuronal loss, non-specific neuronal degeneration, etc. They were interpreted as perimortal changes, secondary to advanced cardiopulmonary failure which occurred in most of patients.

Specific HIV-related changes in the form of HIV-encephalitis, HIV-leukoencephalopathy or coexistence of both, and HIV-vasculitis, were present in 35 cases. There were also changes of HIV-associated type such as vacuolar myelopathy, vacuolar leukoencephalopathy and selective poliodystrophy (two cases).

Opportunistic infections composed the largest group of 59 cases. Proliferative malignant processes occurred altogether in eleven cases, among which ten were primary and secondary brain lymphomas. Diagnosis of primary malignancy was made based on absence of primary lesion elsewhere on autopsy. One case corresponded by its morphology and immunochemistry to Kaposi's sarcoma. It showed also no detectable primary lesion on autopsy.

In 16 cases other pathological processes were found by neuropathological examination. Two cases of hepatic encephalopathy deserve mentioning; they were characterized by typical astrocyte damage and three other cases with traumatic changes, with characteristic damage of cortical gyri on the base of the hemispheres.

As mentioned earlier, HIV-specific changes such as encephalitis, encephalopathy or both, as well as selective vasculitis, occurred in 35% examined cases.

Diagnosis of HIV-encephalitis was made based on presence of disseminated microglial-histiocytic infiltrates or isolated morphologically characteristic multinucleated giant cells (Figs. 2 and 3). Inflammatory

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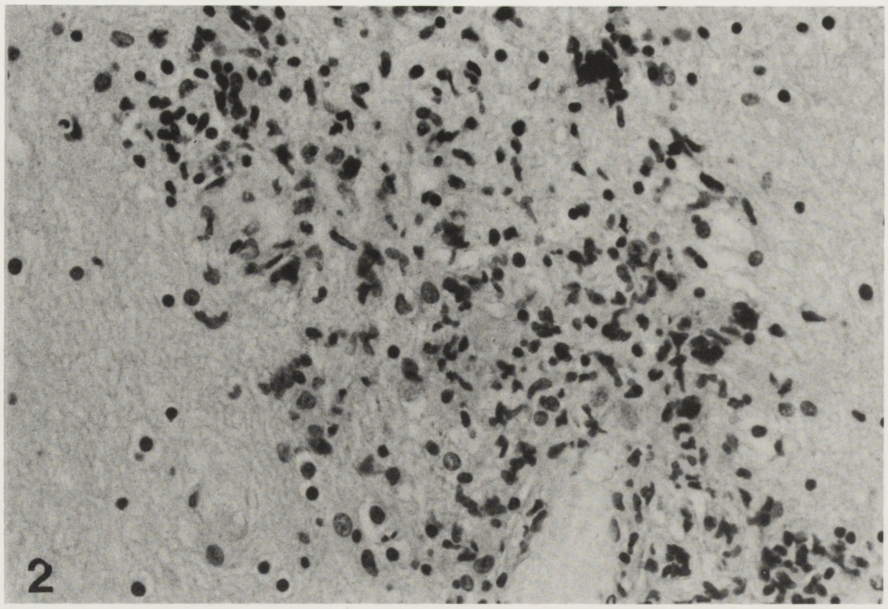

Fig. 2. HIV-encephalitis. Diffuse nodule of microglial/histiocytic proliferation with spread multinuclear giant cells. HE, ×400

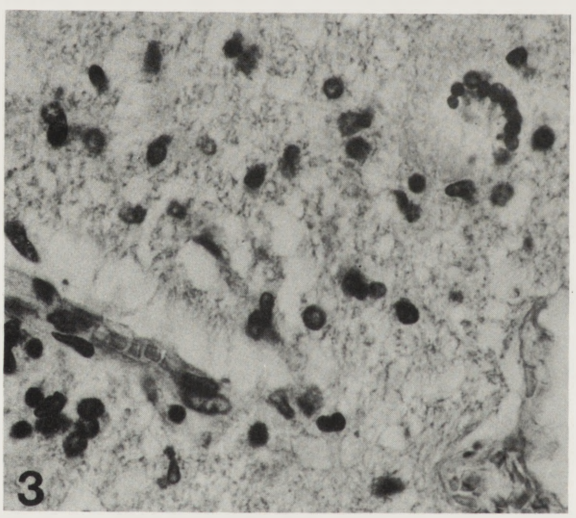

Fig. 3. HIV-encephalitis. Slight microglial activation with typical multinuclear giant cells. Note internuclear bridges. HE, ×600

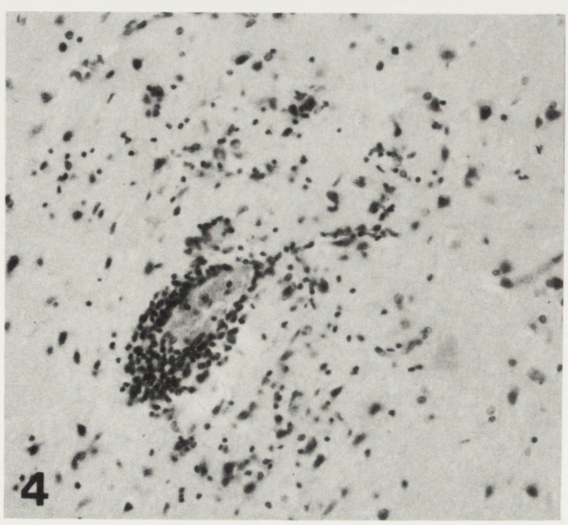

Fig. 4. HIV-encephalitis. Perivascular hematogenic infiltration in the field with microglial proliferation. HE, ×200

infiltrate predominated in white matter, however, sometimes involving grey substance, especially in basal ganglia, diencephalon and brain stem. It was frequently associated with weak perivascular hematogenous inflammatory reaction (Fig. 4). Diagnostic criteria for HIV- leukoencephalopathy were diffuse myelin pallor of hemispheric semioval center with sparing subcortical fibers (Fig. 5), diffuse proliferation of astroglia without hypertrophy and gemistocytic transformation, as well as presence in vascular proximity of multinucleated giant cells, single or in groups (Fig. 6a, b). Some of them showed no association with blood vessels, appearing in areas of myelin pallor as well as in areas otherwise normal. Coexistence of pathological features of HIV-encephalitis and HIV-leukoencephalopathy resulted in a diagnosis of mixed form of HIV-infection. A single case of HIV-vasculitis was characterized by selective involvement of medium and small cerebral blood vessels without parenchymal process of encephalitis or leukoencephalopathy type. Vascular changes were characterized by proliferation of cellular elements of vessel walls leading to a lumen narrowing with intramurally located multinucleated giant cells (Fig. 7). In very few vessels, there were fine intramural or periadventitial hematogenous inflammatory infiltrates. The only case of leptomeningeal inflammation meeting diagnostic criteria of HIV-leptomeningitis, i.e. inflammatory infiltrates with HIV-type giant cell presence, was associated with typical HIV-encephalitis. Similarly, HIV-specific syndromes coexisted with HIV-associated processes such as vacuolar myelopathy and vacuolar leukoencephalopathy. In one case, selective poliodystrophy coexisted with CNS toxoplasmosis, without

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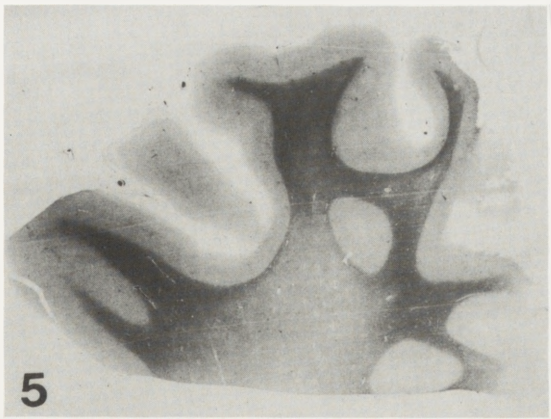

Fig. 5. HIV-encephalopathy. Pallor of myelin in deep hemispheric white matter with relatively good sparing of subcortical fibres. Heidenhain. Magn. glass

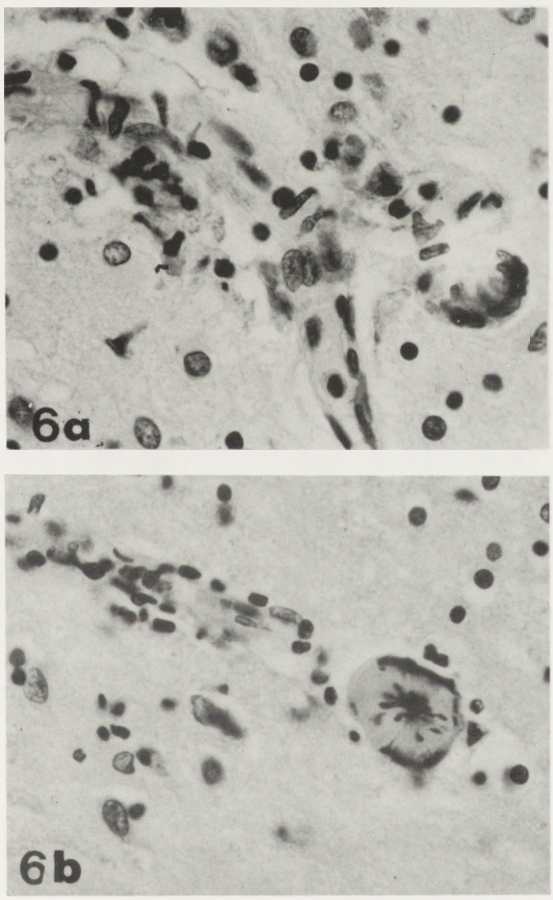

Fig. 6a and **b.** HIV-encephalopathy. Multinuclear giant cells in perivascular position in the cerebral white matter. HE, ×600

HIV-specific changes in CNS. One should emphasize that vacuolar myelopathy with characteristic spongy degeneration of pyramidal tracts, secondary to myelin sheath swelling and lamellar splitting (Fig. 8, 9), extended into brain stem, meeting diagnostic criteria of vacuolar leukoencephalopathy. In one case severe subcortical spongiosis was also seen (Fig. 10). The case of poliodystrophy was characterized by regional almost complete loss of neurons with loss of cortical stratification, extensive neuronal degeneration (Fig. 11) and very significant astrocyte proliferation with metabolic glia predominance (Fig. 12).

In the majority of cases with HIV pathology, obvious neuronal loss occurred in frontal, temporal and to a lesser extent parietal lobes. Good preservation of structures showing selective vulnerability to hypoxia/hypoperfusion, especially hippocampal formation, limits the possibility of explanation of neuronal loss found by premortal hypoxia. The

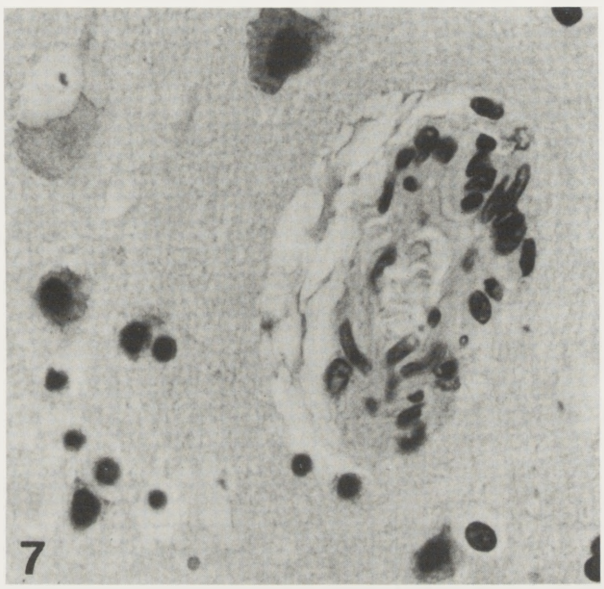

Fig. 7. HIV-vasculitis. Small artery with remarkable wall thickening and intramural multinucleated giant cells. HE, ×600

second general pathological finding was a significant thickening and fibrosis of leptomeninges without an inflammatory reaction in cases without any meningeal pathology as well as without parenchymal changes which could be associated with meningeal reaction.

Analysis of brains with HIV-specific processes observed over consecutive years, indicates that the proportion of cases with changes resulting of HIV infection has been increasing, especially in intensity and extent of disease process (Table 3).

The 59 cases of opportunistic infections (O.I.) consist of a wide spectrum of viral and bacterial infections, as well as those of fungal and protozoan etiology. The most frequent O.I. was cytomegalovi-

Table 3. Distribution of HIV-specific changes in different years

Year	Number of cases	Cases with HIV-specific changes
1987	2	1
1988	–	–
1989	7	2
1990	12	4
1991	9	2
1992	12	3
1993	17	3
1994	16	10
1995	25	10
total	100	35

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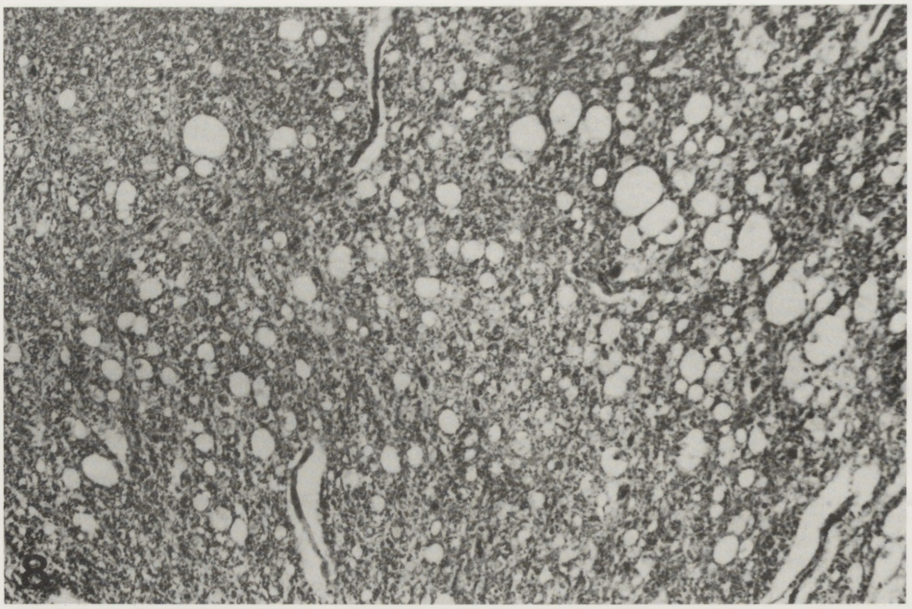

Fig. 8. Vacuolar myelopathy. Spongy degeneration of the pyramidal tract in the subbulbar region of spinal cord. Heidenhain, × 200

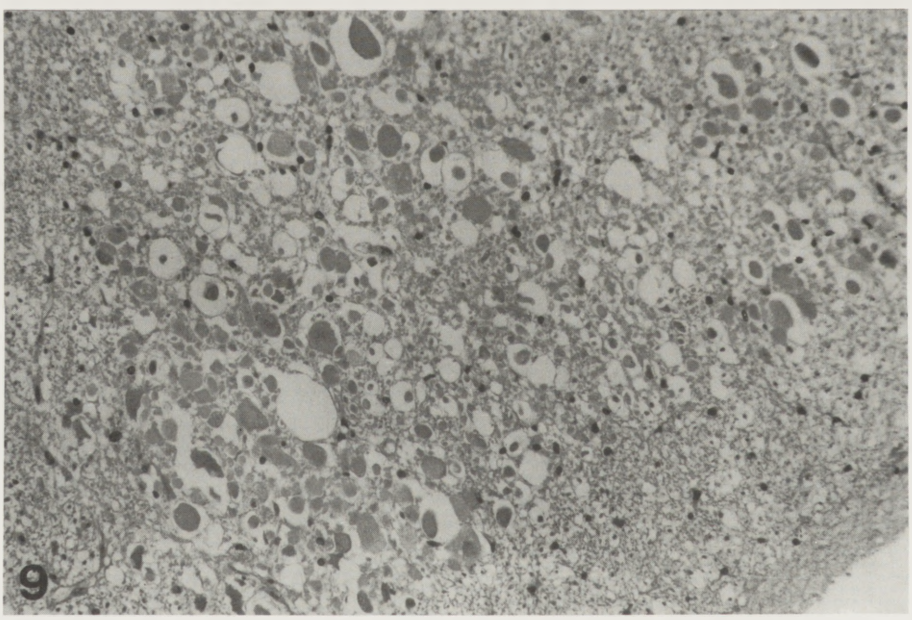

Fig. 9. Vacuolar myelopathy. Spongy degeneration of the pyramidal tract in the medulla. Note either swollen or shrunken axons filling holes in spongiotic tissue. HE, × 200

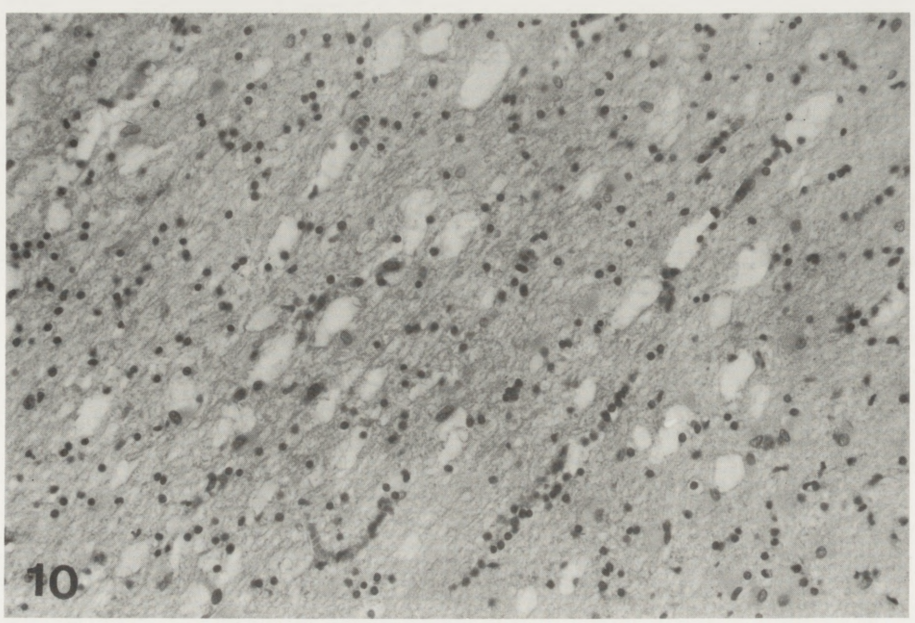

Fig. 10. Vacuolar leukoencephalopathy. Spongiosis of the subcortical white matter. HE, × 200

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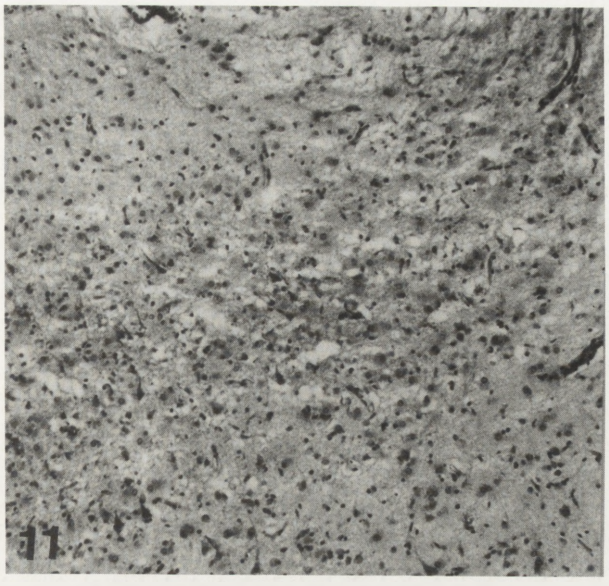

Fig. 11. Selective poliodystrophy. Disintegration of upper cortical layers with glial proliferation and neuronal loss. HE, ×100

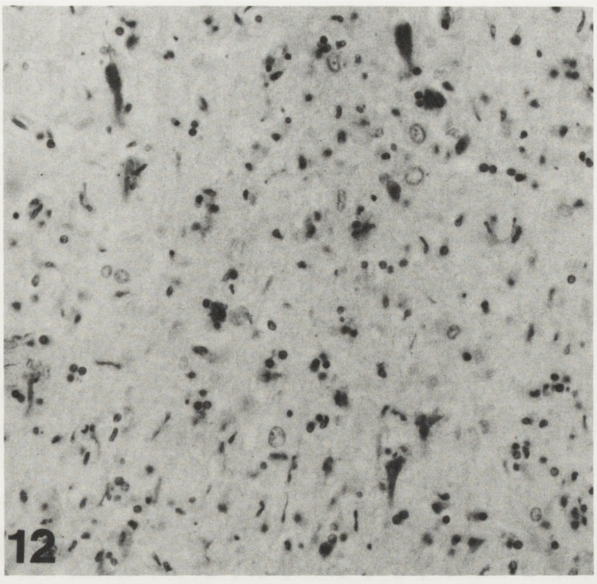

Fig. 12. Selective poliodystrophy. Cerebral cortex revealing neuronal loss, calcification of few preserved neurons and proliferation of microglia and astroglia, with remarkable proportion of metabolic glia. HE, ×200

rus infection (CMV) way ahead of CNS toxoplasmosis and progressive multifocal leukoencephalopathy (PML), associated with pathogenic JC papova virus. Our cases showed a striking degree of demyelination in some cases of PML, involving often entire white matter of one or both cerebral or cerebellar hemispheres. Also, the intensity of the pathological process was significant and characterized by cavitation of involved CNS structures.

Quite frequently O.I. process was CNS cryptococcosis; 10 cases occurring as nonreactive cavitations as well as tuberculosis-like granulomatous inflammation of leptomeninges invading the brain along penetrating blood vessels. Other bacterial or viral infections occurred only in isolated cases.

Separate attention is designated to a small group of cases diagnosed as micronodular encephalitis of unknown etiology. This diagnosis includes 5 cases, and means inability to determine etiological factor based on histological and selected immunohistochemical methods.

Many pathological processes coinciding in single cases was a characteristic feature of our collection. Tables 4 and 5 shows a coexistence of HIV-specific pathology and opportunistic infections, malignant proliferations and other pathologies. It is worth noting that from 35 cases of HIV-specific CNS pathological processes only 14 had one process. Sixteen cases of HIV-specific changes in CNS were accompanied by various O.I., two were associated with lymphomas. In three cases, HIV process occurred simultaneously with malignant proliferation and O.I. HIV-encephalopathy with vacuolar myelopathy and leukoencephalopathy as well as CMV encephalitis and toxoplasmosis would be worth reporting separate. Similarly, various O.I. coexisted without HIV-specific changes as well as malignant proliferation with O.I. Only one case, we had, of Kaposi's sarcoma coexisted with CNS toxoplasmosis for which very extensive areas of tissue necrosis characteristic for cerebral toxoplasmosis including multiple terminal cysts and freely diffused trophozoites involved, large portion of the neoplastic growth.

Table 4. Types of HIV-related brain pathology

HIV-encephalitis	22
HIV-encephalopathy	7
HIV-encephalitis/encephalopathy	5
HIV-angitis	1
Total	35

Table 5. Concomitance of HIV-related changes with other pathological processes

1. Cases with isolated HIV-specific changes	14*
2. Cases with HIV-associated changes	1**
3. Cases with concomitant isolated opportunistic infections	10
– HIV + cytomegalovirus infection	4
– HIV + toxoplasmosis	2
– HIV + progressive multifocal leukoencephalopathy	1
– HIV + cryptococcosis	2
– HIV + micronodular encepehalitis	1
4. Cases with concomitant several opportunistic infections	5
– HIV + cytomegaly and PML	1
– HIV + cytomegaly and toxoplasmosis	2
– HIV + cytomegaly and aspergillosis	2
– HIV + toxoplasmosis and metastatic encephalitis	1
5. Cases with concomitant maligant lymphomas	5
– HIV + malignant lymphoma	2
– HIV + malignant lymphoma and progressive multifocal leukoencephalopathy	1
– HIV + malignant lymphoma and toxoplasmosis	1
– HIV + malignant lymphoma and toxoplasmosis and cryptococcosis	1
6. Others	
– HIV + central pontine myelinolysis	1*
– HIV + vacuolar myelopathy and cytomegaly and toxoplasmosis	1**

* See group "others"
** See group "others"

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Discussion

The above results are the first comprehensive work in Poland on the neuropathological changes in CNS of expired AIDS patients in our country. Frequency of HIV-specific pathology as well as associated opportunistic diseases and neoplasms do not differ significantly from results of earlier descriptions of HIV pandemics such as those from the United States (Snider et al. 1983; Moskowitz et al. 1984; Navia et al. 1986; Petito et al. 1986), Italy and Austria (Budka et al. 1987), Switzerland (Lang et al. 1989) and United Kingdom (Gray et al. 1987). Comparative analysis of our data with data from the United States, Austria and Italy, Switzerland and Berlin are presented in Table 6. Frequency of HIV-specific changes ranged from 16 (Lang et al. 1989) to 38% in the collection of Budka et al. (1987) in which a wide spectrum of immunocytochemical tests were used for detection of HIV-antigens. Showing HIV antigens in macrophages/monocytes had a diagnostic significance in cases, where giant cells, a histopathological marker of HIV damage within CNS, were not found within lesions (Budka et al. 1989).

The statistical data characterizing our material are higher than in Swiss (Lang et al. 1989) and American collections and are closer to those presented by Budka et al. (1987). In our material HIV-leukoencephalopathy alone occurs rarely, while combination of inflammatory and degenerative process, in a sense of HIV-encephalitis and HIV-leukoencephalopathy is more frequent (Kleihues et al. 1985). Leptomeningeal involvement in the form of meningitis with appearance of multinucleated giant cells in inflammatory infiltrate, as described by Gray et al. (1993) was found only in association with parenchymal inflammation. Vascular changes considered as HIV-vasculitis, occurred alone, but they differ remarkably from those described in the literature (Gray et al. 1987).

In contrast to the previously published data, indicating frequent occurrence of vacuolar myelopathy in CNS of patients with full blown AIDS, estimated as 29.6% of cases by Petito et al. (1986) and 11% – by Lang et al. (1989), in our collection this was detected only in 1 case. The vacuolar myelopathy is characterized by most pronounced changes in the thoracic and cervical cord, from where it might extend into medulla and even pons and mesencephalon. However, we are unable to evaluate frequency of the vacuolar myelopathy in our series, since we had only medulla and in few cases upper spinal cord for neuropathological examination.

In the presented collections, similarly to the material from abroad, cytomegalovirus and protozoan toxoplasmosis infections predominated in O.I. They occur in different proportion and sequences in various collections (Strittmatter et al. 1992). They develop, especially toxoplasmosis, as result of reactivation of subclinical infection, the frequency of which varies extensively from 30–90% of total population in different geographic regions. In our material, as in American one, diverse neuropathological forms of cytomegalovirus infections predominated. Toxoplasmosis was second as far as O.I. are concerned and it was almost twice less frequent than in Swiss studies (Lang et al. 1989).

Progressive multifocal leukoencephalopathy (PML) is third among O.I., exceeding that in American and Austro-Italian material (Petito et al. 1986; Budka et al. 1987). In comparison with known description of characteristic PML changes, their extent and intensity in our cases is remarkable reminding some single case reports described in the world literature (Einsiedel et al. 1993). It calls attention to the relative frequency of aspergillosis among fungal infections, with no mentioning of it at all in both American and Italo-Austrian material. Tuberculosis (TB) of CNS was rare in our material. It occurred in only two cases as tuberculous leptomeningitis with massive involvement of meningeal and parenchymal blood vessels and extensive secondary vasogenic changes, as well as small meningeal and parenchymal tuberculomas.

Table 6. Comparison of frequency of different pathological processes in own material with selected data from the literature

	Petito et al. 1986 USA	Budka et al. 1987 Austria/ Italy	Lang et al. 1989 Switzer-land	Martinez et al. 1995, Berlin	Own material, 1995, Poland
HIV-specific changes	28,2%	38,0%	16.0%	35,5%	35.0%
Cytomegaly	26.1%	18.0%	10.0%	13.0	23.0%
Progressive multifocal leukoencephalopathy	2.0%	5.0%	7.0%	8.0%	11.0%
Toxoplasmosis	10.5%	17.0%	26.0%	34.0%	16.0%
Cryptococcosis	2.6%	9.0%	4.0%	1.5%	10.0%
Aspergillosis	–	–	1.0%	–	3.0%
Micronodular encephalitis	17.0%	17.0%	13.0%	20.0%	5.0%
Malignant lymphoma of CNS	7.9%	6.0%	7.0%	14.0%	10.0%
No characteristic changes	19.6%	5.0%	12.0%	–	13.0%

Coexistence of various in some cases results in the fact that sum of percents is not equal to 100

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In US an increase in TB cases was noted among HIV-positive patients. It is estimated that in 10 mil. of TB-infected population, 1 mil concerns HIV-positive patients. This increase includes extrapulmonary TB as well as tuberculous abscesses and tuberculomas within the brain (Barnes et al. 1991).

Important pathomorphological feature of HIV-dependent neurological syndromes is atrophy of CNS, expressed macroscopically as narrowing of gyri and widening of separating sulci; microscopically neuronal loss, especially cortical, is present. Its intensity reveals region-dependent variations. Thirty five percent of our cases showed features of cerebral atrophy. Neuronal loss was frequently present without visible macroscopic focal abnormalities and HIV-specific changes in CNS. It was usually limited to frontal and less frequently to temporal regions. Only in a few cases cerebral atrophy was more severe, occurring together with remarkable widening of ventricles.

One should remember that frequency of brain atrophy in AIDS cases is significantly lower in autopsies when compared to neuroradiological examinations such as CT or MRI. Raininko et al. (1992) in his series of patients examined at different stage of HIV infection showed radiologically that brain atrophy had already appeared in total asymptomatic HIV-carriers as well as in the lymphadenopathy stage of the disease. The percentage of patients with full blown AIDS without O.I. but with cerebral atrophy is as high as 70%. Changes were usually generalized and bilateral.

Parenchymal changes occur usually at later stages of the disease with coexisting advanced clinical symptoms. They are characterized by neuronal loss with astro- and microglial proliferation (Budka et al. 1987). True evaluation of neuronal loss, similar to that described in our studies, requires morphometric quantification taking into account lethal hypoxia associated with present, in most cases, cardiopulmonary failure. Morphometric examination of frontal lobes of patients who died of AIDS showed decreased density of cortical neurons by 18% and decreased neuronal perikaryon volume by 31% (Ketzler et al. 1990). Weis et al. (1993) confirmed neuronal loss in frontal lobe in AIDS without any changes in density of neurons in parietal cortex. Masliah et al. (1992) called attention to differences in preservation of various populations of cortical neurons. Quantitative studies of parvalbumin positive neurons (PV) corresponding to interneurons and neurons immunoreactive with antibodies to neurofilaments, marking large neurons of frontal cortex and hippocampus, showed that none of those cells were responsible for frontal lobe abnormalities. PV neurons atrophy in CA3 sector of hippocampus was statistically significant, thus hypothesizing that cytokines secreted by infected microglia are responsible for PV neurons loss.

Identification of cells sensitive to HIV infection has a key significance in explanation of HIV-specific pathology of CNS. Presence of HIV in monocytes/macrophages and multinucleated giant cells was unquestionably shown in CNS (Budka 1989). Jordan et al. (1991) showed infection of microglia depending on viral strain in dissociated cell culture of human brain. Neuen-Jacob et al. (1993) showed *in situ* presence of p24 antigen in brain microglia of AIDS patients. Data on presence of HIV virus in astroglia were controversial. Results obtained by most researches were negative. Presence of HIV in astrocytes showed Wiley et al. (1986) and Gyorkey et al. (1987) in adults and Epstein et al. (1985) in children. Finely, controversy seemed to be solved by results obtained by four independent groups of investigators in last few years. Nuovo et al. (1994), using polymerase chain reaction, showed presence of HIV-RNA and proviral DNA in astrocytes from adult brains with HIV-encephalopathy. Infection of astrocytes in pediatric cases proved Tornatore et al. (1994) and Saito et al.(1994). Saito et al. (1994) showed it by immunohistochemical method detecting non-structural viral protein nef. Earlier, in 1991, Tornatore et al. (1991) showed that infection of human fetal glial cells, with proviral HIV DNA in culture results in latent infection, activated by TNF-alpha and IL-1-beta. Cultured astrocytes infected with HIV do not show pathological changes (i.e. virus is not cytopathic), perhaps because of low amount of virus produced within cells. Latent infection of cells causes that they can serve as reservoir of virus and in case of cytokine stimulation, they may lead to recurrent viral multiplication. These discoveries, besides basic understanding of HIV pathogenesis in CNS and dynamics of HIV-specific processes, may significantly influence diagnosis of brain disease, changing views on the key value of multinucleated giant cells.

Zespoły neuropatologiczne w oun w przebiegu pełnoobjawowego AIDS u dorosłych w Polsce (1987–1995)

Streszczenie

Przeprowadzono analizę morfologiczną 100 mózgów pochodzących od pacjentów zmarłych w latach 1987 – 1995 w przebiegu pełnoobjawowego AIDS. Materiał obejmował 96 mężczyzn, 3 kobiety i 1 dziecko 11-miesięczne. Materiał z wczesnego okresu pochodził prawie wyłącznie od homo- i biseksualistów, w ostatnich latach przeważali narkomani.

W badaniu makroskopowym ogniskowe zmiany w OUN stwierdzono w 25 przypadkach, w większości związane z współistniejącymi zakażeniami oportunistycznymi lub procesami rozrostowymi. Zanik mózgu z wyraźnie zaznaczonymi różnicami topograficznymi odnotowano w 35 przypadkach.

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Badanie mikroskopowe wykazało obecność zmian tworzących określony zespół patologiczny w 87 przypadkach, w pozostałych 13 przypadkach stwierdzono nieprawidłowości o typie ubytków i nieswoistych uszkodzeń neuronalnych, które odnoszono na ogół do głębokich zaburzeń krążenia i oddychania w końcowym okresie życia.

Zmiany uznane za HIV-swoiste, jak HIV-encephalitis, HIV-encefalopatia, współistnienie obu wymienionych uprzednio oraz HIV-vasculitis stwierdzono w 35 przypadkach. Stosunkowo rzadko obserwowano zmiany uznane za HIV-towarzyszące, jak mielopatia wodniczkowa, leukoencefalopatia wodniczkowa i wybiórcza poliodystrofia, towarzyszące zespołom HIV-swoistym lub innym procesom patologicznym.

Zakażenia oportunistyczne stanowiły najliczniejszą grupę w badanym materiale i występowały w 59 przypadkach. Procesy rozrostowe stwierdzono łącznie w 11 przypadkach: w 10 były to pierwotne lub wtórne chłoniaki mózgu, w 1 przypadku – mięsak Kaposiego. W 16 przypadkach stwierdzono różnego rodzaju zespoły patologiczne, między innymi encefalopatię wątrobową, blizny pourazowe w korze mózgu, mielinozę środkową mostu, zespół wykrzepiania śródnaczyniowego i in.

Wśród infekcji wirusowych najczęściej obserwowano zakażenie wirusem cytomegalii, wyprzedzające znacznie występowanie postępującej wieloogniskowej leukoencefalopatii. Drugie miejsce wśród procesów oportunistycznych zajmowała toksoplazmoza mózgu, mniej często spotykano zakażenia grzybicze, takie jak kryptokokoza, a następnie aspergiloza. Zakażenia bakteryjne ograniczały się w zasadzie do gruźlicy z obecnością typowej ziarniny w oponach miękkich, ciężkim uszkodzeniem naczyń i rozwojem gruźliczaków.

Charakterystyczną cechą naszej kolekcji było współistnienie w obrębie jednego przypadku różnych zespołów patologicznych: zmian HIV-swoistych i zakażeń oportunistycznych, także rozrostu nowotworowego z innymi procesami patologicznymi (zmianami HIV-swoistymi, różnymi postaciami zakażeń oportunistycznych). Zwrócono uwagę na podobieństwa i różnice morfologicznej ekspresji neuroAIDS pomiędzy naszym materiałem i wcześniejszymi opracowaniami zbiorczymi przypadków AIDS z różnych krajów Europy i pozaeuropejskich.

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