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Cerebellar Cortex Lesions in Cases with Subtentorial Neoplastic Changes

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The aim of the study was to perform neuropathological examinations of the brains of children and adults with various types of neoplasms situated in the subtentorial area. In view of the varied opinions on the central nervous system (CNS) lesions in the course of neoplastic diseases, it was interesting to analyze the cerebellar cortex damage. The study material included fifteen primary tumors in children and fourteen tumors in adults. In the former, two primary and three metastatic tumors were treated with irradiation and chemotherapy (ChTh). In the remaining cases such a treatment was not employed because of the clinical course of the disease. Among adult cases, eight primary and six metastatic tumors were observed. In all metastatic cases irradiation and ChTh were used, other primary tumors were untreated because of the short follow-up period. In all the investigated cases, cerebellar cortex damage was observed. Except for lesions surrounding the neoplastic proliferation, two types of changes were found: one with a prevalence of Purkinje cell loss was similar to the first type of paraneoplastic cerebellopathy, while in the other a granular cell layer lesions predominated. In the entire material the changes were particularly severe in the children, mostly in those with the damage of the granular cell layer, contrary to the prevalent opinions that the CNS damage in the course of neoplastic diseases is more common in adults. Another interesting observation was that the changes did not correlate with the type of tumor and the employed therapy. The results of this study may be interesting for clinicians who perform neurological examinations in pediatric long-survivors of subtentorial tumors.

Introduction

We had the opportunity of performing neuropathological examinations of the brains of children and adults with various types of neoplasms situated in the subtentorial area. Among them there were primary and metastatic tumors. It seems that the cerebellar cortex damage observed in nearly all patients from this series deserve to be discussed, particularly in view of the diversified opinions on neoplastic disease-associated brain lesions and their occurrence in children [1, 4, 8].

Material and Methods

The study material consisted of two groups. The first one included 15 brains of children aged 1 - 14 years (Table 1). In twelve of them, tumors located in the subtentorial region were primary. Five patients were operated on, irradiation and chemotherapy (ChTh) were employed only in two cases, and the other ten children were not treated because of the clinical course of the disease or the patient's death during the diagnostic procedures. In the last three cases metastatic tumors were found. They were treated with irradiation and ChTh.

The second group consisted of fourteen adult brains (Table 2). In eight of them, tumors with the subtentorial localization were primary. Three patients were operated on; irradiation and ChTh were not employed because of the short follow-up period after the final diagnosis. In six cases, primary cancers originally situated within the internal organs metastasized to the brain stem, cerebellum or only to the subtentorial meninges. One patient was treated surgically, while in the others the primary tumor was irradiated and ChTh was employed.

Clinical observations revealed meningismus in some cases, while other patients presented with signs of increased intracranial pressure and disturbances of consciousness, a few manifested convulsions or some neurological signs difficult to precisely define in such severely ill patients as belonging to a specific syndrome. Both groups of patients were administered anti-edematous agents when necessitated by their clinical course.

General autopsy and gross neuropathological examinations confirmed the topography of neoplastic proliferation, including that in the subtentorial area of the CNS described earlier.

For microscopic examination the brains were fixed in formalin and the specimens from representative parts of brain tumors and the surrounding areas of the cerebellum, brain stem and - in some cases - of the hemispheric structures were stained using routine methods, i.e. HE, cresyl-violet and Kluver-Barrera.

TABLE 1

The brains of children

	No	Age (years)	Primary tumor of subtentorial area		Metastatic tumor treated with irradiation or/and ChTh	Cerebellar lesions	
			Not treated with irradiation or/and ChTh	Treated with irradiation or/and ChTh		P	Gr
1	19/71	1.5	cerebellar glioma	–		+/-	+/-
2	55/74	2	non-differentiated neuroepithelial neoplasm	–		+	+
3	94/79	3	hemangioblastoma	–		+	+
4	59/87	4	astrocytoma	–		+	+/-
5	52/83	5	medulloblastoma	–		+	+++
6	84/79	9	astrocytoma of the brain stem	–		+	+
7	128/70	9	medulloblastoma	–		+	+/-
8	18/80	11	astrocytoma of the brain stem	–		+/-	+
9	44/84	11	malignant astrocytoma	–		+	+
10	12/71	14	hemangioblastoma	–		+	+
11	24/84	4	–	medulloblastoma		+	+
12	24/70	11	–	medulloblastoma		+	+
13	37/80	3	–	–	lymphoma	+	+
14	96/79	7	–	–	lymphoma	+	+
15	14/89	14	–	–	lymphoma	+	+++

P - Purkinje cell damage; Gr - granular layer damage; ChTh - chemotherapy

TABLE 2

The brains of adults

	No	Age (years)	Primary tumor of subtentorial area		Metastatic tumor treated with irradiation or/and ChTh	Cerebellar lesions	
			Not treated with irradiation or/and ChTh	Treated with irradiation or/and ChTh		P	Gr
1	24/86	22	hemangioblastoma	–		+	+
2	113/70	24	neurinoma of the ponto-cerebellar angle	–		+	+++
3	11/98	–	cerebellar medulloblastoma	–		+	+/-
4	76/70	51	cavernous hemangioma of the ponto-cerebellar angle	–		+	+
5	112/70	–	neurinoma of the ponto-cerebellar angle	–		+	+
6	20/70	58	schwannoma	–		+/-	+
7	28/77	71	cerebellar astrocytoma	–		+	+/-
8	85/70	75	astrocytoma of the brain stem	–		+/-	-
9	110/67	38	–	–	multiple myeloma	+	+
10	3/84	39	–	–	breast carcinoma	+	+
11	35/70	55	–	–	bronchial carcinoma	+	+/-
12	92/72	59	–	–	lung carcinoma	+	+
13	106/86	79	–	–	breast carcinoma	+	+
14	5/83	39	–	–	breast carcinoma	+	+

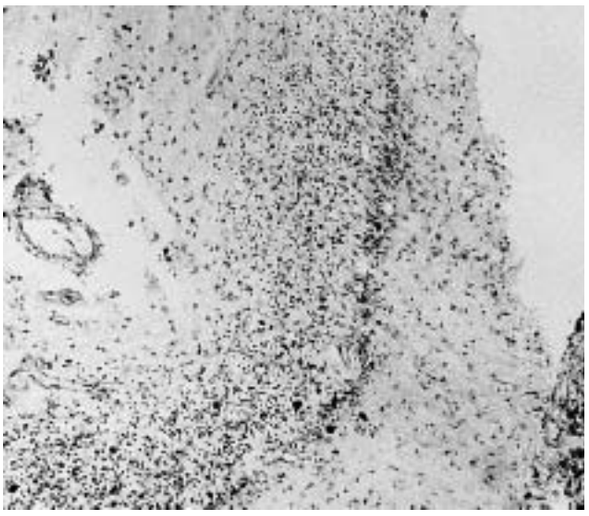

Fig. 1. Focal damage of cerebellar cortex adjacent to the neoplastic changes in meninges. Cresyl-violet. Magn. 200x.

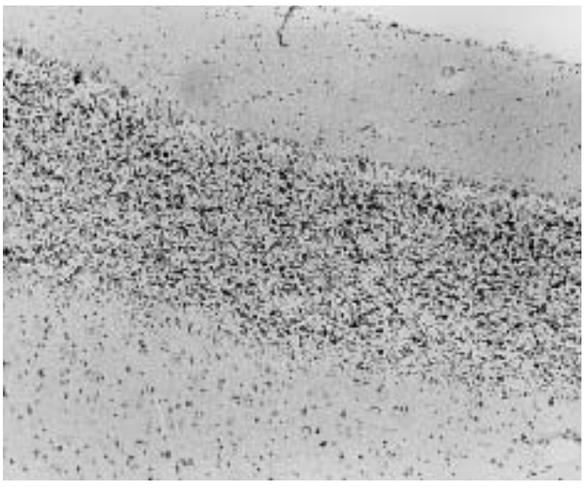

Fig. 2. Severe loss of Purkinje cells and less severe damage to the granular layer. Cresyl-violet. Magn. 200x.

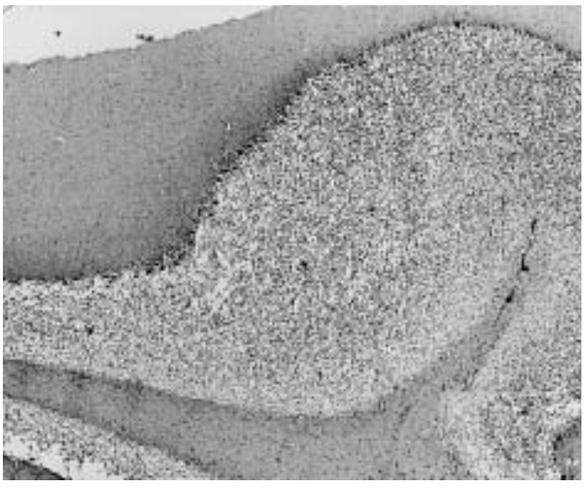

Fig. 3. Cerebellar cortex damage more severe in the granular cell layer. Cresyl-violet. Magn. 200x.

Results

In the brains of three children and one adult, the proliferation of neoplastic tissue in the subtentorial area was limited to the meninges, in others specimens it involved focally the cerebellar tissue or/and the brain stem.

The changes observed in the immediate vicinity of the tumors consisted of more or less advanced necrotic lesions with typical perivascular infiltrations in some cases and with proliferation of microglial and astroglial cells.

In the nervous tissue of the subtentorial structures and also (if available for examination) of the hemispheres, edema was rather moderate and nerve cell damage in areas situated distally to the tumors differed from one case to another, depending on the age of the patient and the clinical data, but generally the phenomena were not very severe.

The changes in the cerebellar cortex presented three various types of lesions. The first type was seen in the vicinity of the neoplastic proliferation and showed a severe damage of some cerebellar folia with a loss of neurons in all the cortical layers, in some cases amounting to subtotal necrosis (Fig. 1). The changes diminished with the growing distance from the neoplastic proliferation. They were seen in 4 children and 8 adults. Another type of cerebellar cortex damage, less frequent in children (three cases) and more common in adults (five cases) was the degeneration and loss of Purkinje cells, which was less evident in the granular layer (Fig. 2). Such changes were found in two cases with metastatic neoplasms, in others they coincided with primary subtentorial tumors. The last type of cerebellar cortex changes, rare in adults and observed in eight brain samples originating from children, mostly very young, consisted of cerebellar folia damage more pronounced in the granular than in the Purkinje cell layer (Fig. 3) or of similar severity in both layers.

The lesions occupied smaller or larger areas and their topography did not correlate with the proliferation of the tumor.

The changes occurred regardless of the treatment used and were evident in patients who had and had not received irradiation and chemotherapy.

Also the severity of edematous changes seen in the subtentorial structures did not show any correlation with cerebellar cortex damage.

Discussion

Having analyzed the character and topography of cerebellar cortex damage in the presented group of patients with subtentorial tumors, we can state that the damage seen directly around neoplastic proliferation does not need a more detailed discussion. Necrotic and reactive lesions, as well as subtotal necrosis of some cerebellar folia in the vicinity of the neoplastic foci can be considered as resulting from the proximity of the tumor [5].

Two types of changes situated independently of the topography of neoplastic proliferation were visible. The cerebellar cortex damage with the prevalence of Purkinje cell loss and less severe lesions of the granular layer, although concomitant only with a moderate edema without perivascular infiltrations, were similar to the first type of carcinogenic cerebellopathy [6]. The changes observed in two adults with metastatic neoplasms may correspond to this diagnosis. In other patients with primary subtentorial tumors, the presence of such changes was not correlated with prolonged irradiation treatment or chemotherapy (ChTh) or the lack of such management.

The last type of cerebellar cortical changes, predominant in the granular layer, prevailed in the majority of children, either untreated or in some cases placed on chemotherapy. Such changes were similar to the second type of paraneoplastic cerebellopathy [6]. Therefore, it should be borne in mind that neoplastic degeneration considered a possible immunologic event [2, 3] was observed by Posner and Tourneaux [7] as more common in the CNS of adults. Similar observations of this syndrome associated with cerebellar changes were made by Tarnawska-Dziduszko [9].

Our cases with particularly severe changes in the cerebellar cortex in children with subtentorial tumors and the damage particularly involving the granular layer, were comparable with those described as paraneoplastic cerebellopathies in children by Laure-Kamionowska [4] and Dąmbska and Laure-Kamionowska [1].

This similarity prompts us to recognize the susceptibility of the cerebellar cortex in children to damage in various situations occurring during neoplastic diseases.

We have to remember about various pathological and damaging factors (toxic, immunological, circulatory) involved in the development of such lesions in nearly all cases of neoplastic diseases situated in the subtentorial area in children.

We publish our observations hoping that they may be of interest to clinicians managing children with subtentorial neoplasms, who often survive for many years.

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