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MYOCARDITIS IN FATAL POLIOMYELITIS

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None of the numerous publications dealing with myocarditis in fatal poliomyelitis appears to be studying it in its relation to the nervous system, which the virus is known to be capable of penetrating. Nor is proper account taken of those changes due to lesions in the innervation which, owing to the altered trophism may give rise to diverse pathological processes on the periphery without any direct action of the pathogenic agent. *Konovalov* [10] is one of the authors to point out the probability of such penetration to the nervous system. In view of this situation we decided to investigate in a great part of our material not only the myocardium but also the neural elements that participate in its innervation.

First *Robertson* and *Chesley* [14], then *Abramson* [1], and later on *Cowie*, *Parsons*, *Löwenberg* [5] as well as *Saphir* and *Wile* [15] furnished reports on myocarditis in poliomyelitis. *Saphir* [16] observed myocarditis in 10 of 17 cases of poliomyelitis, of which 2 were severe diffuse, 6 circumscribed, and 2 moderate. *Dolgopol* and *Cragan* [7] found myocarditis in 18,4 to 27,2 per cent of 87 cases. They distinguished three types ; the first was found to be characterized by an increase in the number of nuclei and a thinning out of fibres ; the second by the presence of mainly mononuclear infiltration among almost intact muscle fibres ; the third by histiocytic, lymphocytic, mononuclear, and leucocytic infiltrations. *Ludden* and *Edwards* [12], *Connel* [4], *Laake* [11] arrived at similar conclusions. According to the literature, different authors have found myorcaditis in from 12,5 to 86 per cent of their poliomyelitis cases. Commenting on the wide difference between these figures, *Teloh* [16] thought it probable that certain virus strains had a greater affinity to the myocardium. *Fox*, *Sennet*, *Kuzma* [17] stated the same view. *Jungeblut* and *Edwards* [9] successfully passaged to monkeys virus from the myocardium of patients who had died of poliomyelitis, and thereby proved the presence of the virus in the muscular tissue of the human heart.

Material and observations

In the years 1950—53, necropsy was performed in 27 cases of acute poliomyelitis at the László Hospital. The youngest subject was 15 months, the oldest 52 years of age. In the series, 20 were male patients and 7 females. The

TABLE I

Number	Clinical form	Number of days elapsed since paralysis	Inflammatory infiltration						
			Myo-cardium	Peri-cardium	Nerves of pericardium	Vagal plexus	Nodose ganglion	Superior cervical ganglion	Central nervous system
1	b	4	+/+	+	+				+
2	b	2	+	+	+				+
3	b	3	+	+	−			+	+
4	b	5	+	+	−				+
5	b	1	+	+	+				+
6	sb	3	+	−	−				+
7	b	4	+	−	−				+
8	sb	3	+	+	−				+
9	sb	4	+	+	−		++	+	+
10	b	5	+	+	−				+
11	sb	3	+	−	−				+
12	sb	2	+	−	−		++		+
13	bp	4	+	−	−		+−		+
14	L	10	+/+	+	+				+
15	sb	2	+/+	+	−			+	+
16	s	3	+/+	−	−		++	+	+
17	sb	2	+	+	+	⊖	++	+	+
18	b	2	+/+	+	+	⊕	++	+	+
19	b	5	+	−	−	+	++	+	+
20	e	7	+	−	−		++	+	+
21	sb	3	+	−	−		++	−	+
22	sb	7	+/+	+	+	⊕		+	+
23	sb	4	+/+	−	−	+ ⊖	++	+	+
24	b	4	+	−	−		++	v	+
25	sb	7	+	−	−		++	−	+
26	sb	5	+/+	−	−		++	+	+
27	sb	4	+	−	−		++	−	+

Signs and abbreviations used:
b = bulbar, sb = spinobulbar, bp = bulbopontine, L = Landry, s = spinal, e = encephalitic, + = inflammatory infiltration, (+/+ = muscle destruction, − = no inflammation, ⊕ = destruction of the myelin sheath, ⊖ = no destruction of the myelin sheath, v = haemorrhage. In places left vacant no examination was performed.

clinical manifestations of the disease varied (Table 1). The sections prepared from the central nervous system confirmed the diagnosis of poliomyelitis.

On gross examination the hearts showed no distinct characteristics. The myocardium was found to be red, the muscular pattern somewhat blurred. The cardiac veins and the cardiac cavity were replete with coagulated blood. Punctate or even lentil-sized haemorrhages were frequently found under the visceral membrane of the endocardium and pericardium. In one case a thrombus was recorded in the auricle of the right atrium and a haemorrhagic infract in the lung (case 1). From 8 to 10 samples were taken from each heart's left anterior and posterior ventricular wall, from the apex of the ventricle, from the left posterior papillary muscle, from the ventricular septum, from the wall of the right ventricle and that of the right and left atrium.

Myocardial lesions were most frequent in the left ventricle. In relatively fewer instances was infiltration found in the papillary muscles and in the left atrial wall. The predominant finding was the presence of infiltrate in the interstitial connective tissue, often situated around vessels (Fig. 1). The infiltrate consisted mainly of lymphocytes, plasma cells, mononuclears, fibroblasts, histiocytes, mast cells, with occasional neutrophile and somewhat more eosinophile leucocytes. Pericapillary haemorrhages, serous infiltrates were observed almost invariably. In milder cases, there was no loss of striation. In more severe ones, in addition to the cellular infiltration described above, the degenerative changes scattered over small areas included myofibrillary fragmentation ; vacuolisation of the myoplasm, sometimes its disintegration into a dust of granules or its saturation with serum ; then swelling or vacuolisation of the nuclei. In these limited areas also leucocytes were present (Fig. 2).

On the basis of these findings two classes of myocarditis were distinguished. The cases of moderate severity, where interstitial inflammation was observable but no muscle damage, made up the majority (70,4 per cent), the rest comprising the more severe acute cases displaying muscular destruction (29,6 per cent).

Occasional perivasculitis was observable around small vessels. The adventitia was broadened, fragmented, with lymphocytic, histiocytic infiltrations around it. The intima was found to be normal.

In the pericardium infiltrations were encountered in 13 cases occasionally around the vessels, more frequently in the region of the nerve plexuses, as if accompanying them. Often they were visible closely on the capsule of the neural plexuses, at other times in the interneural space (Fig. 3). The infiltrations were found to contain only lymphocytes and plasma cells. In the invaded areas the structure of the nerve plexuses was observed to have lost its density, the fibres shifted apart, the interneurum widened. In two instances intensive lymphoid cellular infiltration in the cervical vagal trunk was seen. In four cases the plexuses of the cervical vagus, were slained for myelin sheaths ; in two of them destruction of the myelin sheath was present.

Vegetative ganglion cells in the anterior wall of the right atrium and in the pericardial neuroplexuses have often been investigated. On no occasion were

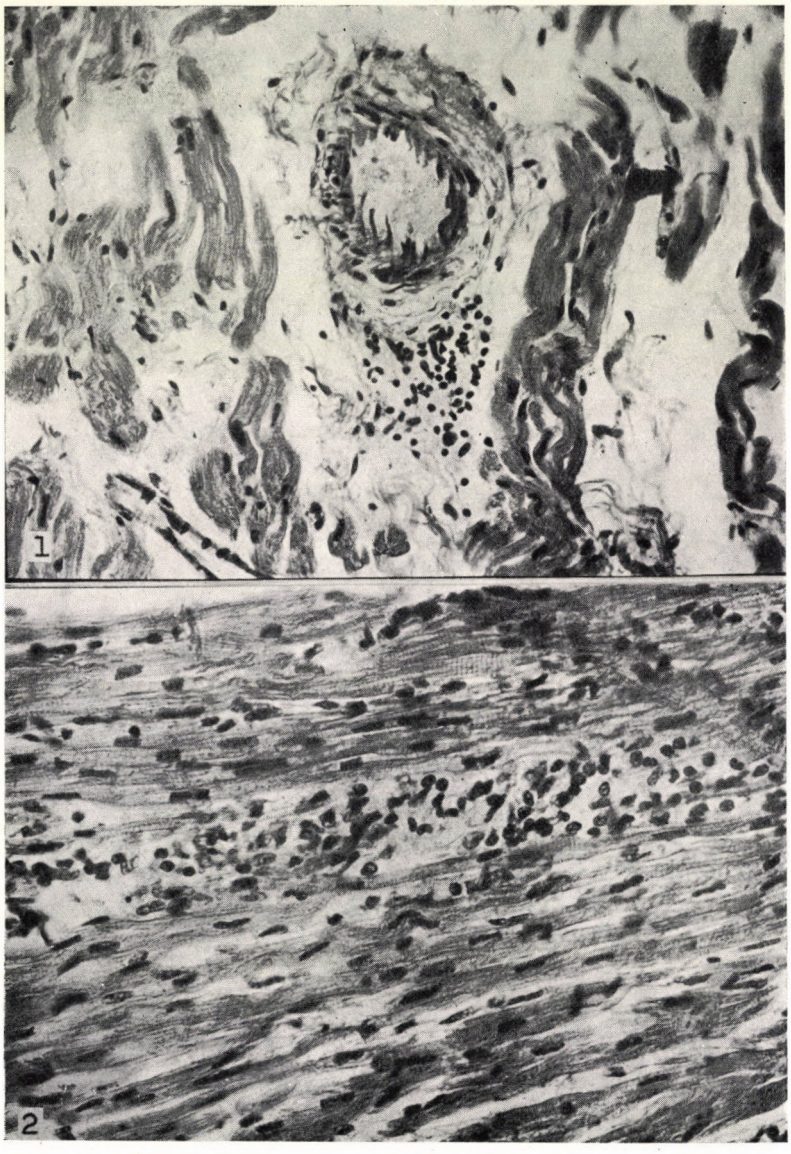

Fig. 1. Lymphocytic infiltration along a vessel in the right atrial wall
Fig. 2. Muscle destruction with mixed round cell infiltration in the wall of the left ventricle

any inflammatory or degenerative changes observed in them. The nodose ganglion has been studied on both sides in 13 cases, on one side in one case only. Inflammatory changes were found in every one of them. Not infrequently

the sections revealed massive perivascular infiltration or inflamed cellular congestion in the interstitium, in the state of neuronophagy (Fig. 4), or the one

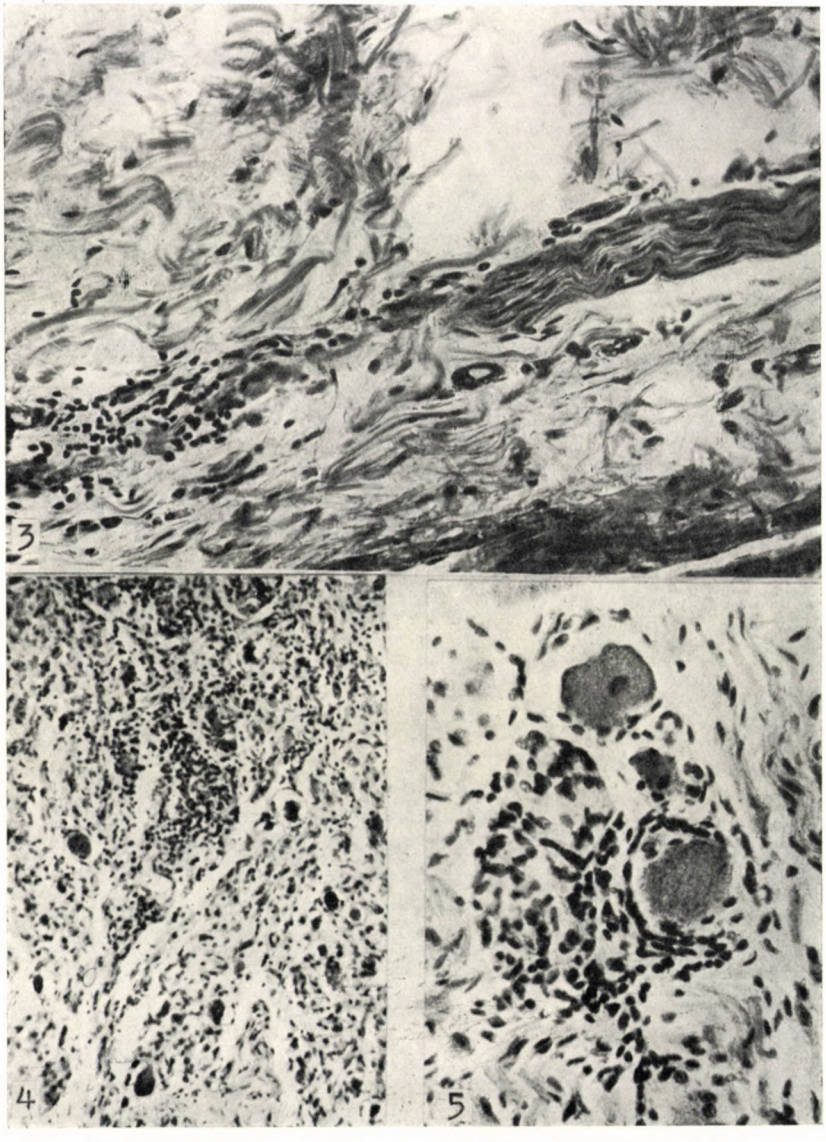

Fig. 3. Lymphocytic infiltration in the pericardial nerve plexus in the left ventricle
Fig. 4. Diffuse mononuclear infiltration in the nodose ganglion
Fig. 5. Destruction of ganglioncells in the nodose ganglion

following it (Fig. 5). In addition, degenerative changes were observable in the ganglion cells. The nuclei were seen to be swollen, vesical, or vacuolated, in places fragmented or dissolved. Large vacuoles were visible on the edges of the cyto-

plasm or throughout it. The tigroid had disappeared, or showed on the marginal parts in the form of some dust of granules, or it was found to be dissolved. Now and then the ganglion cells contained a large mass of brown pigment granules. The superior cervical ganglion has been studied in 14 cases. In 10 of these mild perivascular, interstitial, lymphocytic infiltrations, as well as interstitial haemorrhages could be observed. In one instance, extensive bleedings exclusively were found, and in three the ganglion was intact.

Discussion

Myocardial infiltrations were encountered in each of the cases in this series (Table I). According to the data in literature, the incidence of myocarditis in poliomyelitis varies widely (19). Apparently, the number of specimens taken to examine the myocardium was frequently insufficient (7), and thus the lesions consequent upon the scattered interstitial or intermuscular infiltrations escaped the notice of the investigators.

Our own material presented evidence similar to that of the earlier authors, namely, that myocarditis in poliomyelitis was of interstitial character and in the majority of cases did not involve muscular damage further, that the infiltrate in the interstitial connective tissue, consisting of lymphocytes and mononuclear cells, may be characteristic of viral infection ; and finally, that this type of myocarditis probably healed without leaving any traces, or only those of a very slight proliferation of connective tissue. Similarly to other authors, muscle destruction was observed in a few cases only, and these involved small regions of myocardium, but myocarditis is known to be attended sometimes by muscle destruction so extensive as to cause even perforation of the ventricle (12). This type of the disease evidently leaves scars behind. Irrespective of the classifications by *Saphir* or by *Dolgopol* and *Cragan*, we believe, only the two classes which have been mentioned above are justified, and even they represent but differences in degree. Interstitial infiltration, namely, is to be found in all cases, including those where muscle damage is present as well. From the practical aspect the distinction is important, because it is probable that physical examination and E. C. G. findings do not indicate myocarditis definitely, unless muscular damage is manifest, this being the only type of myocarditis to leave traces after healing.

Assumptions that viruses concomitant to the poliomyelitis virus may also play a role in producing myocarditis can in our opinion be ruled out ever since the polio virus was isolated from the myocardium (9). That this or that strain of the poliomyelitis virus might show a greater affinity for the myocardium than the others do is likewise improbable [18, 19]. The necropsy material of four years seems to admit of the conclusion that in our cases several different strains can be assumed to have been playing the role.

Bodian [3] ascribes poliomyelitic lesions in the vagal and sympathetic ganglia to the centrifugal spread of the virus. *Pette* [13] maintains the same opinion. In the cases under investigation the inflammatory lesions of the nodose ganglion and the vagal trunk and of the nerve plexuses to be found in the pericardium, respectively, do not show an appreciable chronological difference as compared either to the inflammatory lesions of the central nervous system, or to those of the myocardium. This should not be taken to mean, however, that we refute the idea of a possible centrifugal spread of the virus, for, although it seems probable that this is the route of transmission to the cardiac musculature, it may yet be possible that the virus had reached the myocardium previously, during viraemia.

The question arises as to whether myocarditis can occur in poliomyelitis when the cardiac nerve elements are not pathologically effected. The literature furnished no data concerning this problem. In our own cases there was inflammation in both the heart and the neural elements. It may be assumed, however, on the strength of earlier investigations *(Horányi-Hechst*, [8]), that changes of neural elements do not follow any regular pattern, and it may be that in such a case there is no myocarditis either.

It appears from the above that the role of the poliomyelitis virus as the causative agent in myocarditis cannot be discarded. Moreover, inflammatory and degenerative changes in the cardiac neural elements are significant from another aspect too. As has been mentioned above, lesions were found in the sensory ganglion of the vagus nerve and in the superior cervical ganglion, while the vegetative ganglia of the vagus were intact. These neural lesions seem to point at the possibility of a neuroreflex origin of myocarditis. *Alpern* [2], *Speransky* and *Chernukh* [6], as well as *Tonkikh* [19], in performing experiments concerning other organs, have found that lesions of the nodose ganglion, the vagal trunk, or the superior cervical ganglion were leading to pneumonia. The work of *S. Vayl* [20] might be considered to confirm our assumption that inflammatory reactions, muscle fibre disintegration, and lymphocytic infiltrations in the myocardium were of neuroreflex origin. The experimentally induced myocardial lesions described by *Vayl* are in many respects similar to the lesions of the myocardium in poliomyelitis observed by us. The entire problem requires, however, further experimental work to be settled.

Summary

Morphological findings in 27 cases of acute poliomyelitis studied in 1950—53, inclusive, are reported. In each case, interstitial mononuclear infiltration was found in the myocardium.

Two forms of myocarditis are distinguished, depending on the presence or absence of muscular damage.

In 14 cases, in addition to inflammatory changes in the central nervous system, lesions in the peripheral neural elements of the heart have been demonstrated. On this basis a reflex, neurodistrophic origin of myocarditis is suggested, due to neural lesions arising during the centrifugal spread of the virus.

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О МИОКАРДИТЕ УМЕРШИХ ВСЛЕДСТВИЕ ПОЛИОМИЭЛИТА

Л. ЛИСКАИ

Автор исследовал в 27 случаях poliomyelitis anterior acuta сердечную мускулатуру а в половине случаев нервные элементы, участвующие в иннервации сердца: блуждающий нерв и ganglion cervicale superius симпатической нервной системы.

Автор разобщает две формы заболевания миокардитом. Одна форма представляет собой интерстициальное воспаление (70,4%) без разрушения мышц, а во второй форме разрушение мышц также имеет место (39,6%). В интерстициальных инфильтрациях можно обнаружить лимфоциты, плазматические клетки, гистоциты, тучные клетки, в то время как в случаях, сопровожденных разрушением мышц, наблюдаются, наряду с вышеупомянутыми, также и нейтрофильные и эозинофильные лейкоциты и фибробласты. Вокруг маленьких кровеносных сосудов иногда появляется perivasculitis.

Автор обнаружил в 13 случаях в перикардии, или же в перикардиальном нервном сплетении, или в окрестности последнего, инфильтрации с лимфоидными клетками. В двух случаях обнаруживалась клеточная инфильтрация в шейном стволе блуждающего нерва.

В 14 случаях был исследован ganglion nodosum и в каждом из этих случаев наблюдались воспалительные явления. В верхнем шейном узле были в 10 из 14 случаев обнаружены воспалительные ифильтрации, в одном случае интерстициальные кровоизлияния, а в трех случаях узлы оказались невредимыми.

Подобно другим исследователям, автор также рассматривает воспалительные изменения нервных элементов как следы пути неврального распространения вируса. Однако, непосредственное патогенное действие вируса полиомиэлита при заболевании миокардитом автор не считает доказанным. Ссылаясь на экспериментальные работы других авторов, он выдвигает вопрос о возможности рефлекторного, нейродистрофического механизма в патогенезе миокардита.

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