Cytotoxic Damage to the Ridge of the Corpus Callosum. Cerebral Polyopia, A New Symptom of “Split Brain”?

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Abstract
A clinical description is given of a 31-year-old patient who experienced unusual visual sensations: episodes of simultaneous loss of vision in the left field with multiple replication of the image in the right field. The above described arose on the 21st day after suffering a coronavirus infection (COVID-19), accompanied by memory impairment, anxiety. MRI revealed cytotoxic edema of the corpus callosum ridge. There is a rapid recovery by the 6th day of illness with neuroimaging improvement. Based on the nature of visual disturbances, clinical and radiological data, cerebral polyopia is diagnosed. Differential diagnosis is carried out with other causes of visual perseveration. Dissociation of interhemispheric visual connections in case of cytotoxic damage to the ridge of the corpus callosum can be the cause of cerebral polyopia.

Keywords: Cytotoxic lesion of the corpus callosum; Polyopia.

Introduction
Cytotoxic Lesion of the Corpus Callosum (CLOCCs) is a polyetiological clinical and radiological condition, with a predominant lesion of the Ridge of the Corpus Callosum (RCC) [1]. This definition has replaced the former names MERS (mild encephalopathy with reversible isolated lesion of the corpus callosum ridge) and RESLES (reversible lesion of the ridge syndrome), which, as previously assumed, denote a mild, transient neurological disorder with selective damage to the RCC [2]. With the accumulation of clinical material, an understanding arose that the damage to the corpus callosum could be more significant with the spread of cytotoxic edema both to the body and to adjacent neurological structures, which is often associated with the severity and residuality of clinical and radiological changes [3]. Given the above, the authors proposed the term CLOCCs, focusing on the features of radiological changes in the corpus callosum, defining them as nonspecific and always secondary to a whole range of pathologies: associated with drugs, malignant diseases, infections, metabolic disorders, subarachnoid hemorrhage, trauma, and others. Diseases [4]. These heterogeneous types of pathologies are united by a common pathogenesis underlying cytotoxic edema of the corpus callosum - this is an enhanced inflammatory reaction (cytokinopathy), endothelial dysfunction, microglia involvement, increased release of glutamate with the penetration of water into the cell, leading to edema. Significant the presence of glutamate receptors in the area of the corpus callosum, namely the ridge, makes it a defenseless target under conditions of massive excitotoxicity [1].

Often, a detailed history, clinical and radiological data help to establish the root cause of the cytotoxic lesion of the RCC, which is important when choosing therapeutic measures. CLOCCs are usually differentiated from infarcts in the zone of
vascularization of the distal branches of the anterior cerebral artery, acute disseminated encephalomyelitis, multiple sclerosis, lymphoma, or glioblastoma involving the corpus callosum. The asymmetry of the ischemic focus, the multiplicity of lesions in autoimmune pathology, and the accumulation of contrast will distinguish these types of pathologies from CLOCCs [3,4].

We give a description of the clinical observation. A 31-year-old European man sought medical help with complaints of episodic visual impairment: when trying to focus on an object, the image disappeared in the left half of his vision, and began to be perceived in the right half as a lot of the same objects. At the same time, the images were perceived clearly, and the ability to see at that moment was impaired. The patient compared his feelings with the image in Figure 1 (Figure 1). What was seen lasted about a minute, then passed and could reappear when fixing the gaze after a while. Up to 30 such episodes could occur per day at the height of the disease. The described visual disturbances disturbed the patient for a little more than 6 days.

He notes instability when walking, memory loss for recent events (does not remember whether he drank medication the day before). He constantly feels anxiety, fear for his future, it seems “as if everything is happening not with him, outside of reality” (depersonalization and derealization). He characterizes his condition as follows: “I don’t understand what is happening to me, I’m afraid that I will lose my job.” The thought appears that this state will remain with me forever. The above accompany general weakness, sweating, increased blood pressure up to 160/90 mm. rt. Art., headache in the occipital region.

On the 4th day of illness (d.i.), he was hospitalized in the neurological department. The general and neurological examination revealed no focal symptoms, significant cerebral symptoms and somatic disorders. Neuropsychological testing (for 11 d.i.): MOCA test - 27 points. The patient did not cope with the task of redrawing the cube, could not reproduce 2 words from memory (but smog when prompted by category). Technique 10 words Luria. After 1 repetition, the patient named only 4 words out of 10. On the next repetition, he was able to reproduce 7 words, then 9, and all 10. Bourdon correction test: volume - 583 characters. Concentration 4.85. It is noted the safety of attention, a decrease in the volume of working capacity.

Laboratory data (only deviations from the norm are reflected): ALT - 53 units / l (up to 45 units / l); ferritin - 272 ng / ml (normal 20-250); coagulogram is not changed, An MRI of the brain with contrast (4 d.i.) was performed: a hydrophilic focus was detected in the ridge of the corpus callosum, 12x18x15 in size, without perifocal changes and accumulation of contrast. May correspond to cytotoxic injury (CLOCCs) (Figure 2.1; 3.1; 4.1; 5). The repeated MRI of the brain (by 17 d.i.) notes a significant regression of the previously identified changes (Figure 2.2; 3.3; 4.2).

![Figure 1](image1.png) Sick, saw objects repeated many times, comparing them “like the old Microsoft splash screen”.

3 weeks before that, he received inpatient treatment with a diagnosis of “Coronavirus infection COVID - 19, moderate form. Bilateral pneumonia. Cytolysis Syndrome. PCR positive for CO-VID-19. Clinical blood tests, total bilirubin, urea, creatinine, cholesterol, HDL, potassium, sodium, magnesium, calcium, fibrinogen corresponded to the reference values; D-dimer -1275 ng / l (N-up to 440), CRP - 144.6 mg / l (N up to 5), PTI - 110.7% (N-80-105%), ferritin 550 ng / l (N-10-120 ng/l), procalcitonin 0.23 ng/l (N-0.046), LDH 625 U/l (N-135-225).

After the illness, the patient was able to return to his job (he worked in the IT field). On the 21st day, the vision problems described above appeared. Mental disorders appeared. He characterized his condition as “I can’t think clearly, I feel stupid compared to the past.” The level of anxiety has increased. An increase in blood pressure up to 150/90 mm Hg was noted. Was consulted by an ophthalmologist. The diagnosis was “Simple astigmatism of the left eye, retinal angiopathy of both eyes”. No visual field studies were performed. Consulted by a psychotherapist, the diagnosis of “Organic anxiety-depressive disorder” was established. Sent to a neurologist.

Figure 2.1: MRI, T2 mode (4 d.i.): on the axial section of the brain in the RCC, a single symmetrical focus of a hyperintense MR signal with fairly even and clear contours is determined. Rice. (2.2). MRI, T2 mode (17 d.i.): there is a significant regression of previously identified changes in RCC.
Figure 3.1: On the ADC-map (4 d.i.): there is a low signal intensity in the projection of the ridge of the corpus callosum. (3.2) On the ADC-map (17 d.i.): the average signal intensity in the RCC projection is noted.

Figure 4.1: FLAIR (4 d.i.): On the sagittal section of the brain in the FLAIR mode, a hyperintense focus in the RCC. (4.2) FLAIR (17 d.i.): on the sagittal section of the brain in the FLAIR mode, a decrease in the intensity of the focus at RCC is noted.

Figure 5: MRI with contrast (4 d.i.). The same level after the introduction of contrast. Contrast does not accumulate. MR angiography is a variant of the development of the circle of Willis. No hemodynamically significant stenoses were found. Hypoplasia of the right vertebral artery.

Discussion

In our observation, visual impairment was the leading one in the clinic. The patient’s inability to focus on an object brought visual impairment of our patient closer to astigmatism, association with an infection - with an acquired one. The very characteristic of visual disturbances did not correspond to astigmatism, the main symptom of which is the blurring of objects. The patient saw clearly. If, with astigmatism, objects double, then in our case they “multiplied” and, as it were, moved away to the right. Visual disturbances were transient and were associated with the results of neuroimaging and neurological examination. The above did not allow explaining the visual disturbances in a patient with astigmatism.

Features of visual disturbances, their short duration, data from neuroimaging and neuropsychological testing, indicated a symptom of dissociation (inability to redraw the cube, mnestic disturbances) made it possible to attribute visual impairment in the patient to cerebral polypia. Cerebral Polyopia (CP) is the vision of two or more images arranged in regular rows, columns or diagonals after fixing the gaze on an object [5]. A frequent combination of CP with homonymous hemianopsia was noted, which was present in our patient “the image disappeared in the left half of vision, and began to be perceived in the right.” The patient’s absence of ophthalmic pathology - corneal opacity, the initial stage of cataract, keratoconus or lenticonus ruled out ocular polyopia. It is based on the formation in the optical media of the eye (cornea, lens) of areas that unequally refract light rays, which is accompanied by the projection onto the retina of several images of one object. In this case, a person sees not one object, but several, one image may seem clear, the other blurry. The visual defect is not related to the fixation of the gaze.

CP was first described in 1908 by the neurologist Giovanni Mingacini in connection with diseases with damage to the occipital lobe [6] and is a fairly rare condition [5]. There are reports of cases of cirrhosis in migraine, epilepsy, trauma, tumors, encephalitis, multiple sclerosis and cerebral stroke [7,8]. The neurophysiological mechanism of palyopia is associated with an increase in the excitability of neurons in the visual cortex [9]. At the same time, local cortical hyperexcitability may be the result of visual deafferentation in case of damage to the visual pathways from the lateral geniculate bodies to the cerebral
cortex with an increase in the sensitivity of cortical neurons to visual impulses ("cortical release"); focal "irritation" of the cortex with the occurrence of spontaneous non-epileptic neuronal discharges. It has been suggested that cerebral polyopia is associated with the recording of visual receptive fields in the primary visual cortex with bilateral lesions in the occipital lobe [10]; - with impaired connections between the posterior parietal cortex, where visuospatial analysis is carried out, and the cortical gaze center, subcortical structures, and the stem gaze center [11].

Previous disorders of visual function associated with cytotoxic lesions of the corpus callosum were characterized as blindness, hallucinations [2], “flickering zigzags” [12], recognition of unfamiliar faces as acquaintances [13]. There was no CP among them, which forced us to turn to research on its functions.

Anatomical data indicate the heterogeneity of the composition of the RCC fibers: its anterior part is represented by thin, late myelinating fibers from the parietal and medial temporal association zones, and the posterior part contains thick, early myelinating fibers connecting the primary/secondary visual fields [14]. In human ontogenesis, slow myelination of the RCC occurs during the first two decades, which reflects its plastic adjustment to heterochronously maturing visual functions in childhood and adolescence: in the first weeks/months of the postnatal period, it coincides with the rapid development of sensitivity to movement and orientation [15]. The next period is accompanied by the improvement of functions related to spatial integration. Myelination facilitates interhemispheric interaction by enhancing the coordination of interhemispheric input, which leads to more efficient involvement of the target neuronal population in overall activity [16]. In adults, cognitive function correlates with the size of the corpus callosum [17], and cognitive impairment correlates with RCC demyelination [18].

The study of the course of RCC fibers according to diffusion-tensor MRI revealed a significant inter-individual variability of connections between the striatal cortex, and a large interhemispheric connection from the right to the left hemisphere was found in the extrastriate cortex [19]. Animal studies have shown that roller fibers, connecting visual fields 17/18 modulate the control thalamocortical input through inhibitory effects during short latent periods and excitatory effects during longer latent periods [20]. In addition to establishing image continuity, one function of the roller is the ability of the visual system to segment images of the outside world into objects and backgrounds. Within a homogeneous region, similarly tuned neurons mutually inhibit their activity, while at the boundaries such neurons are less inhibited due to regional heterogeneity [21,22].

Thus, the above reflects the important contribution of RCC association fibers to the modulation of visual perception. Our description shows that polyopia can occur not only with lesions of the occipital or temporal lobe, but also with lesions of the ridge. Apparently, the developing interhemispheric disconnection, disrupting the interactions between the primary visual cortex and associative visual zones, leads to focal "irritation" of the cortex with perseveration of the visual image. It is to be hoped that this work will arouse interest among neurologists, ophthalmologists, and pathophysiologists dealing with brain problems.

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**Reference**


