Diabetes mellitus and optic nerve diseases

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Abstract

In addition to diabetic retinopathy (DR), optic nerve diseases (OND) of diabetic origin also have a significant place in routine ophthalmologic practice and they are among the most important complications of diabetes mellitus (DM). The paper deals with the systematization and classification of optic nerve diabetes−induced changes into various clinical entities. Congenital bilateral optic nerve atrophy in hereditary DM, diabetic papillopathy, anterior and posterior ischemic optic neuropathy and retrobulbar neuritis are described as the most common clinical forms of optic nerve diabetes−induced diseases. Possible etiopathogenic mechanisms are discussed, the most important among them being ischemic. 600 diabetic patients were analyzed. Presence of OND was found in 14 of them. Compared to the control group, statistically significant difference regarding the number of patients with OND was demonstrated in the group of diabetic examinees (p<0.01). One of essential characteristics of optic nerve diabetes−induced disease is that the optic nerve involvement is not always associated with evident signs of DR and that in some of the cases OND even precede the occurrence of retinopathy.

Key words: Optic nerve disease – diabetes mellitus.

Background

When discussing fundus changes caused by diabetes, we usually think of diabetic retinopathy (DR). In extensive ophthalmologic literature there is a great number of papers dealing with the problem of DR. The occurrence of optic nerve diseases (OND) caused by diabetes mellitus (DM) is not so often described, in spite of the fact that it has a significant place among diabetes caused complications in the eye. There were several attempts to systematize and classify the optic nerve diabetes−induced diseases and the most appropriate, in our opinion, is the one given by Forofonova et al. Based on this classification, ONDs can be divided into several groups:

1. Early changes in hereditary DM
   Patients with congenital bilateral optic nerve atrophy and juvenile insulin dependent diabetes, where progressive deterioration of eyesight begins in 9–11 month of life, but are usually discovered in the age of 4–5 year, when it becomes obvious to the parents that something goes wrong with the child’s eyesight.

2. Diabetic papillopathy, is rarely described disease, occurring in younger diabetes patients with minimal or completely absent visual disturbances.

3. Anterior and posterior ischemic optic neuropathy occurs as a result of ischemic lesions of anterior or posterior part of optic nerve in the area of diabetic micro and macroangiopathy.

4. Retrobulbar neuritis in DM
   Retrobulbar neuritis associated with diabetes is the subject of controversies, because many authors consider that in these patients we are dealing with posterior or ischemic neuropathy.

The purpose of our research was to find out the incidence of optic nerve diseases in patients with diabetes with us.

Material and methods

We analyzed ophthalmologic findings in 600 consecutive diabetic patients sent to our daily hospital by endocrinologists, as part of one−day research. We performed detailed ophthalmoscopic examination, as well as the visual acuity, perimetry, fluorescein angiography, etc.). As a control group, we used findings in 600 patients examined in outpatient Ophthalmology Clinic in Niš, who came there in order to get appropriate glasses, without symptoms of optic nerve disease. These patients were of approximately similar age and sex compared to patients with DM.
Optic nerve disease – diabetes mellitus

Results
Out of 600 patients with diabetes, 314 were males and 286 females, with the mean age of 61.2 years. 467 patients were on oral anti-diabetic therapy, while the remaining 133 were on insulin treatment. Out of this number, there were 14 (2.4%) patients with OND. In six cases we found anterior ischemic neuropathy, posterior ischemic neuropathy in three, and in one case with juvenile diabetes, the symptoms were consistent with diabetic papillopathy. In four patients unilateral discoloration of optic disc of unknown etiology was found. We did not detect any case of retrobulbar neuritis or hereditary optic atrophy associated with juvenile diabetes (Tab.1). In the control group, we detected only three cases with OND of various genesis.

Table 1. Optic nerve diseases and diabetes

<table>
<thead>
<tr>
<th>Disease</th>
<th>Diabetics</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>Diabetic papillopathy</td>
<td>1</td>
<td>0.17</td>
</tr>
<tr>
<td>Anterior ischemic neuropathy</td>
<td>6</td>
<td>1.0</td>
</tr>
<tr>
<td>Posterior ischemic neuropathy</td>
<td>3</td>
<td>0.5</td>
</tr>
<tr>
<td>Retrobulbar neuritis</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Discoloration of the optic disc</td>
<td>4</td>
<td>0.7</td>
</tr>
<tr>
<td>Total</td>
<td>14</td>
<td>2.37</td>
</tr>
</tbody>
</table>

The difference was tested by $x^2$ test and proved to be statistically significant (p<0.01) (Tab.1).

In the Tab. 2, ophthalmoscopic changes in patients with diabetes are presented, and it is evident that the majority (72 subjects, or 12%) had minimal, initial vascular changes, described as micro and macro diabetic angiopathy. Second largest group were those with signs of mild non–proliferative DR (63 or 10.5%), followed by 28 (4.7%) patients with severe non–proliferative DR and the smallest group of 12 (2%) with proliferative DR (Tab.2).

In 14 patients with the diabetic OND we found microangiopathy in 4, initial non–proliferative DR in 5, severe non–proliferative DR in another 3, and proliferative DR in the remaining 2 (Tab.3).

Table 3. Fundus changes in patients with optic nerve disease

<table>
<thead>
<tr>
<th>Fundus changes</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Micro–macro angiopathy</td>
<td>4</td>
<td>28.6</td>
</tr>
<tr>
<td>Mild non–proliferative DR</td>
<td>5</td>
<td>35.7</td>
</tr>
<tr>
<td>Severe non–proliferative DR</td>
<td>3</td>
<td>21.4</td>
</tr>
<tr>
<td>Proliferative DR</td>
<td>2</td>
<td>14.3</td>
</tr>
<tr>
<td>Total</td>
<td>14</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Discussion
Diabetes mellitus is an extremely important etiological factor for development of various optic nerve diseases$^{10,11}$. Accepting the model proposed by Forofonova et al., we classified them into five groups and analyzed their incidence with us.

The most common optic nerve changes found in our series were anterior and posterior ischemic optic neuropathy. We had one single case of diabetic papillopathy. At least in 3 out of 4 cases with discoloration of optic disc, the most probable cause of descendent atrophy was an underlying vascular disease. Since this was a retrospective study, there was no possibility of further follow up.

When analyzing etio–pathogenic mechanisms for development of these pathological conditions, it became obvious that vascular changes (microangiopathy) were dominant in the form of ischemia in the area of posterior and anterior portions of optic nerve. This is in accordance with data in the literature$^{12}$.

According to Hayreh, diabetes is on the fourth place as etiological factor for development of anterior and posterior ischemic optic nerve neuropathy$^7,8$. In spite of the opinion of some authors that anterior and posterior ischemic neuropathy caused by diabetes are the consequence of toxic effects of prolonged hyperglycemia, nowadays we know that the primary factor for development of anterior ischemic neuropathy is vascular lesion in the area of anterior ciliary arteries, and that posterior ischemic neuropathy is caused by ischemia of posterior parts of the optic nerve$^7,8,11,16,17$. When describing diabetes–induced ONDs, other etio–pathogenic mechanisms are also important, such as hereditary, toxic, metabolic or transudative.

Hereditary factor is important in younger patients with congenital atrophy of the optic nerve and juvenile DM, which is described by some authors$^{10,13,15}$. Toxic–metabolic factor can be responsible for development of diabetic papillopathy, which presents a new and not adequately recognized ophthalmologic entity. It is described as a pathological condition occurring in younger patients with juvenile diabetes, with minimal or completely absent visual disturbances$^{1,2,9}$. There is an ophthalmoscopic picture of bilateral optic disc swelling, peri–papillary haemorrhage—
gies and extensively dilated veins and capillaries on the disc, which is very much similar to obstructive edema of optic nerve. In fundus oculi, one can usually find clinical picture of non-proliferative diabetic retinopathy.

Domination of ischemic factor for development of complications on optic nerve in DM, points once more to the importance of vascular disorders developing in the course of the disease. It is characteristic that in four cases with optic nerve disease, micro and macro-angiopathy were also present, without any signs of retinopathy and that in another five cases a mild form of diabetic retinopathy was detected (Tab.3). This indicates that vascular complications on optic nerve may come first in diabetic patients, before the development of pronounced forms of DR. It is considered that primary involvement of the optic nerve is the consequence of the specificity of it’s sensitive and vulnerable vascular network. The same explanation is offered for the early appearance of the optic disc neovascularisation. As a rule, optic nerve complications indicate progression of primary disease and in the cases of optic nerve involvement progression of DR should be expected.

For that reason, complications occurring on the optic nerve as consequence of DM should be taken seriously and all necessary therapeutic measures should be applied in order to prevent further complications and the development of the disease on the fellow eye. Treatment of other vascular problems such as arterial hypertension, arteriosclerosis, cardiovascular diseases and others also is of great importance for the treatment of the affected eye and prevention of further complications.

**Literature**

Oboljenja vidnog živca prouzrokovana dijabetesom

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Kratak sadržaj
Pored dijabetične retinopatije i oboljenja vidnog živca dijabetične geneze imaju značajno mesto u svakodnevnoj oftalmološkoj praksi i predstavljaju jednu od značajnijih komplikacija dijabetesa. U radu se govori o sistematizaciji i podeli oboljenja vidnog živca prouzrokovanih dijabetesom. Bolesnici sa urođenom atrofijom vidnog živca i juvenilnim insulin zavisnim dijabetesom, dijabetična papilopatija, prednja ishemična neuropatija vidnog živca, zadnja ishemična neuropatija i retrobulbarni neuritis, opisani su kao najčešće forme oboljenja optikusa prouzrokovane dijabetesom. Takodje se analiziraju mogući etiopatogenski mehanizmi, medju kojima su najznačajniji ishemični. Analizirano je 600 bolesnika sa dijabetesom u cilju utvrđivanja znakova oboljenja vidnog živca. Kod 14 pacijenata nadjeno je prisustvo patoloških promena na vidnom živcu, pri čemu je kod 6 ustanovljena prednja ishemična neuropatija, zadnja ishemična neuropatija kod 3, videli smo 1 slučaj dijabetične papilopatije i 4 slučaja dekoloracije papile nejasne etiologije. U grupi bolesnika sa dijabetesom, pokazana je statistički signifikantno veća učestalost onih sa oboljenjem vidnog živca (p<0,01) u odnosu na kontrolnu grupu ispitanika. Jedna od bitnih karakteristika oboljenja vidnog živca kod dijabetičara je ta da nisu uvek praćena izraženim znacima dijabetične retinopatije i da oboljenje optikusa može da predhodi pojavi retinopatije.

Ključne reči: Šećerna bolest – oboljenja vidnog živca.