Glaucoma

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Abstract: Glaucoma is a disease characterized by “glaucomatous optic disc atrophy” such as enlargement of the cupping of optic disc and retinal nerve fiber defects, with resultant visual field defect. Visual field defect gradually progresses in an irreversible manner, ultimately leading to blindness. While a high intraocular pressure (IOP) is the greatest and most decisive risk factor in its development and progression, glaucoma is not rare in patients with IOP within the normal range (21 mmHg or lower). Therefore, high IOP is not a prerequisite for the diagnosis of glaucoma. Glaucoma is roughly classified into open-angle glaucoma and angle-closure glaucoma, according to the size of the chamber angle that is formed by the cornea and the iris. Congenital glaucoma that develops immediately after birth or by the age of 2 or 3 years is classified separately. Since the cause, clinical course, and treatment policy may vary depending on the disease type, each type of glaucoma should be treated in a different way. Among these, the most common type of glaucoma is open-angle glaucoma. Open-angle glaucoma should be first treated in a conservative manner by pharmacotherapy. When pharmacotherapy fails to prevent progression of the disease, laser therapy and invasive surgical therapy should be considered.

Key words: Glaucoma; Optic disc; Visual field defect; Open-angle glaucoma; Angle-closure glaucoma

Definition of Glaucoma and Its Changes

Glaucoma is a disease in which visual information obtained by retinal neurons cannot reach the brain due to damage of the retinal nerve fiber axons at the optic disc (Fig. 1), and is characterized by visual field defect (Fig. 2). Secondary to axonal damage, the death of retinal ganglion cells and ganglion cells in the lateral geniculate body is induced by the mechanism of apoptosis.

One of the most well-known causes of glaucoma is elevation of the intraocular pressure.
Glaucoma

(IOP). In the past, glaucoma was regarded as a condition in which elevation of the IOP elevation resulted in visual functional disorder. The term “glaucoma” is believed to have been first used by Hippocrates around 400 B.C. to refer to eyes that have turned blue-green due to high IOP and opacity of the cornea.

In recent years, however, many patients with IOP within the normal range, i.e., not higher than 21 mmHg, have been encountered who exhibit almost the same visual disc atrophic changes and resultant visual field defects as those induced by high IOP. Thus, currently, high IOP is no longer included in the definition of glaucoma.

Prevalence of Glaucoma

According to a national epidemiological survey conducted in 1988 and 1989, the prevalence of glaucoma in the population aged over 40 years is 3.56%, and the actual number of patients in Japan is estimated to be about two million. Open-angle glaucoma, or so-called chronic glaucoma accounts for three-quarters of these patients, and normal-tension glaucoma with IOP within the normal range accounts for more than two-thirds of the patients (Table 1).

After diabetic retinopathy, glaucoma is the second most common cause of blindness in advanced countries, and it is predicted that it will become the most common cause of blindness in the near future.

Causes of Glaucoma

As mentioned earlier, high IOP is the most important cause of glaucoma. When the optic disc becomes unable to resist the pressure load-

Table 1 Prevalence of Glaucoma in the Population Aged Over 40 Years

<table>
<thead>
<tr>
<th>Disease type</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary open angle glaucoma</td>
<td>0.58</td>
</tr>
<tr>
<td>Normal-tension glaucoma</td>
<td>2.04</td>
</tr>
<tr>
<td>Primary angle-closure glaucoma</td>
<td>0.34</td>
</tr>
<tr>
<td>Secondary glaucoma</td>
<td>0.32</td>
</tr>
<tr>
<td>Capsular glaucoma</td>
<td>0.16</td>
</tr>
<tr>
<td>Others</td>
<td>0.12</td>
</tr>
</tbody>
</table>

Fig. 1 Optic disc in a case of glaucoma
Enlargement of the cupping is noted.

Fig. 2 Results of perimetry in a case of glaucoma presented in Fig. 1
Visual field defect (black area) corresponding to atrophy of the optic disc is noted.
Glaucoma can be roughly classified into open-angle glaucoma and angle-closure glaucoma. In addition, glaucoma that develops immediately after birth or by the age of 2 or 3 years is distinguished as congenital glaucoma. While primary glaucoma without specific cause accounts for the majority of the cases, glaucoma resulting from uveitis, injury or IOP elevation induced by steroid eyedrops, or other causes is classified as secondary glaucoma.

Symptoms and Natural Course

Naturally, chronic cases and acute cases much differ in the symptoms and natural course. In the cases with sudden IOP elevation, such as attacks of acute angle-closure glaucoma, marked ocular pain, congestion, declined visual acuity, headache, nausea, and vomiting occur. Persistent IOP elevation at such high levels for several days could lead to blindness. If immediately treated by pharmacotherapy and surgical therapy, the condition could be cured with almost no sequelae or only mild visual field impairment and irregularity of the pupil. However, severe IOP elevation may impair the aqueous outflow, and the possibility of re-elevation of IOP on a subsequent occasion should be borne in mind.

Classification of Glaucoma (Table 3)

Glaucoma can be roughly classified into open-angle glaucoma and angle-closure glaucoma. In addition, glaucoma that develops immediately after birth or by the age of 2 or 3 years is distinguished as congenital glaucoma. While primary glaucoma without specific cause accounts for the majority of the cases, glaucoma resulting from uveitis, injury or IOP elevation induced by steroid eyedrops, or other causes is classified as secondary glaucoma.

Table 2  Genes and Loci Responsible for (Primary) Glaucoma Identified to Date

<table>
<thead>
<tr>
<th>Disease type</th>
<th>Loci</th>
<th>Position on the chromosome</th>
<th>Causative gene</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary open angle glaucoma</td>
<td>GLC1A</td>
<td>1q24.3-q25.2</td>
<td>MYOC</td>
</tr>
<tr>
<td></td>
<td>GLC1B</td>
<td>2cen-q13</td>
<td></td>
</tr>
<tr>
<td></td>
<td>GLC1C</td>
<td>3q21-q24</td>
<td></td>
</tr>
<tr>
<td></td>
<td>GLC1D</td>
<td>8q23</td>
<td></td>
</tr>
<tr>
<td></td>
<td>GLC1E</td>
<td>10p15-p14</td>
<td></td>
</tr>
<tr>
<td></td>
<td>GLC1F</td>
<td>7q35-36</td>
<td></td>
</tr>
<tr>
<td>Congenital glaucoma</td>
<td>GLC3A</td>
<td>2p21</td>
<td>CYP1B1</td>
</tr>
<tr>
<td></td>
<td>GLC3B</td>
<td>1p36</td>
<td></td>
</tr>
</tbody>
</table>

The occurrence of glaucoma is relatively strongly related to genetic factors. The brothers and sisters of patients with open-angle glaucoma have a 25–35% risk of developing glaucoma, although the figures vary among reports. Primary angle-closure glaucoma is also associated with a high risk of occurrence in siblings, because this disease is related to the morphology of the eye.

As a result of recent linkage analyses, numerous genes and loci responsible for glaucoma have been discovered. While great advances in this area are expected in the future, caution must be exercised before informing the patients about the genetic risks of the disease as it may cause severe anxiety in the patients and their families. Appropriate systems for supporting the patients, such as genetic counseling, need to be established.

The genes and loci responsible for glaucoma that have been identified to date are listed in Table 2. Diagnosis by screening for genetic variations is possible in about 3% of the total number of cases diagnosed.
On the other hand, when the glaucoma follows a chronic course without marked IOP elevation, the patients are usually unaware of the condition during the early stages. Impairment of the retinal nerve fiber axons at the optic disc progresses gradually. It is often marked at the top and bottom areas of the cribriform lamina of the optic disc that are structurally weak. The visual field impairment corresponds with this disorder. Relative scotoma appears on the superior and inferior nasal sides and in Bjerrum area 10 to 20° away from the point of foveal fixation, and gradually enlarges to progress to absolute scotoma. Patients are not aware of the visual field defect until very late stages of the disease, because the central visual field is preserved to a considerable extent until the late stage of the disease.

The visual field defect progresses gradually until only the central visual field and a small area of the temporal visual field is preserved. In the advanced stage, the central visual field is also lost and the visual acuity declines at this stage. Unfortunately, however, when the condition is discovered at this late stage, the prognosis is not good. Although some part of the temporal visual field remains until the very late stage, the visual acuity achieved by this visual field is 0.1 or less.

### Diagnosis of Glaucoma

Glaucoma is usually diagnosed on the basis of tonometry, optic disc findings, and perimetry. High IOP is an obvious risk factor of glaucoma. When the IOP is much higher than the upper limit of the normal, i.e., greater than 21 mmHg, for example, higher than 30 mmHg, a high likelihood of development of glaucoma should be borne in mind even if the optic disc findings and perimetric findings are normal, and treatment should be started.

Thus, tonometry is crucial for the diagnosis of glaucoma. However, tonometry alone is insufficient. As discussed at the beginning of this article, glaucoma is defined as impairment of the retinal ganglion cell axons at the optic disc and resultant visual field defects, and the disease is not diagnosed unless both of these abnormalities are observed. More specifically,
abnormal findings in the optic disc, such as the enlargement of optic disc cupping, and visual field impairment that can be explained by these findings should be present in order for glaucoma to be diagnosed.

Gonioscopy is also important from the point of view of prevention of glaucoma. The chamber angle is the space created by the cornea and iris, and the aqueous humor circulating in the eye is excreted here. Since angle-closure glaucoma is likely to develop if the chamber angle is shallow, examination of the chamber angle by gonioscopy is very important for preventing acute attacks of angle-closure glaucoma. Needless to say, gonioscopy is essential for the diagnosis of angle-closure glaucoma and secondary glaucoma.

**Treatment of Glaucoma and Follow-up of the Clinical Course**

At present, lowering of the IOP is almost the only way to treat glaucoma. Calcium channel blockers for improving the blood flow at the optic disc as well as vitamins are used occasionally, but their roles are only supplementary. Therefore, the main goal of treatment of glaucoma is to lower the IOP, evaluate the effects of the treatment by perimetry, and aim at further lowering of the IOP when the effects are judged to be insufficient.

The initial target IOP to be achieved by the treatment is usually set at 21 mmHg, which is the upper limit of the normal range, or 17 to 18 mmHg. If the IOP is lowered to this level, but still not associated with clinical benefits, further lowering of the IOP is attempted.

The treatment of normal-tension glaucoma is usually aimed at lowering the IOP by more than 30% from the baseline. However, a more realistic goal should be set if the baseline IOP is low, and the treatment should aim at lowering the IOP further if marked visual field defects are present and the structure of the optic disc appears to be very fragile.

Specific methods of treatment shall not be discussed here, as they are already described in numerous textbooks. As a general rule, the treatment should be started with pharmacotherapy using eye drops, and then argon laser trabecuoplasty or where indicated, surgical therapy should be attempted if the treatment effects are insufficient. In the event of surgical therapy, trabeculectomy for draining aqueous humor into the subconjunctival space is often performed. However, as a general rule, this procedure should be avoided as far as possible as it may be associated with various complications, including postoperative shallow anterior chamber, ocular hypotony, cataract development, and infection which may develop long after the operation.

**Conclusion**

Glaucoma is a disease that occurs at a high prevalence (at least one in 30 people, in the population aged over 40 years). Because of the paucity of subjective symptoms, the patients may not notice the disease until the late stages. Therefore, early diagnosis through the effective use of ophthalmological examination techniques, as well as health check-ups for detecting adult diseases is important.

**REFERENCES**
