Nuclear vacuoles in nuclear cataract

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Abstract. The human lens nucleus has always been described as a homogeneous part of the lens, and if any distinct opacities are found, these are considered to be congenital. However, in lenses with nuclear cataract, both of senile type and those induced by hyperbaric oxygen, we have found relatively transparent vacuoles in the nucleus of similar appearance as cortical vacuoles. In cataracts induced by hyperbaric oxygen the vacuoles were reversible to some extent. The vacuoles have been investigated with slit-lamp photography and quantitative microradiography. Nuclear vacuoles were found in 11 out of 25 patients treated with hyperbaric oxygen compared to 19 out of 100 pre-operatively examined senile nuclear cataracts. In the microradiographs the vacuoles appeared as dark rounded areas with a lower dry mass content (−0.30 g · cm⁻²) than the surroundings (−0.50 g · cm⁻²).

Key words: human cataract – nucleus – vacuoles – quantitative microradiography.

In an earlier study of hyperbaric oxygen induced nuclear cataracts (Palmquist et al. 1984), we have noticed vacuole-like formations in the nucleus. The same type of vacuoles have also been found in the nucleus of patients with grey-white nuclear cataracts of senile type. These vacuoles will now be described in detail using slit-lamp photography and quantitative microradiography.

Material and Methods

At the pre-operative slit-lamp (Haag-Streit 900) examination of patients with cataracts the lenses were classified consecutively. Of those patients where a judgement of the lens nucleus was possible, 100 consecutive nuclear cataract patients were studied according to the presence of nuclear vacuoles as well as the degree of turbidity and colour.

Slit-lamp examination was also performed in 25 patients treated with hyperbaric oxygen and an age matched reference group of 19 patients (Palmquist et al. 1984). Most of the patients treated with hyperbaric oxygen suffered from peripheral ischemic ulcers of arteriosclerotic origin. The examination period lasted at least 12 months during which the lenses were examined every two months. The reference group, also followed during 12 months, consisted of patients on the waiting list for hyperbaric oxygen treatment, and were comparable to the oxygen treated group with respect to age, sex and state of circulation. The frequency of nuclear

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vacuoles was studied in these 3 groups of patients. Lenses with nuclear vacuoles were photographed in vivo in a Nikon photo slit-lamp.

Twelve lenses were selected for quantitative microradiographical examination. Six of these were senile nuclear cataracts without visible vacuoles at the slit-lamp examination. Of the 6 selected lenses with vacuoles, 2 were cataracts developing during hyperbaric oxygen treatment, and 4 were senile grey-white nuclear cataracts. After intracapsular cryoextraction the lenses were transported in Eagle’s MEM tissue culture medium for less than 60 min before further processing. Quantitative microradiography is a method for determination of the concentration of dry mass, i.e. mainly protein, within small volumes of the lens (Philipson 1969). The method includes freezing of the lens in isopentane, pre-cooled in liquid nitrogen to \(-140^\circ\text{C}\), freeze-sectioning to 15–25 \(\mu\text{m}\), followed by freeze-drying of the sections. The sections are then mounted together with a reference system in close contact to a fine-grained photographic emulsion and exposed to soft X-rays generated at 3 kV. The microradiograms are then densitometrically evaluated in order to determine the dry mass in different parts of the lens.

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**Table 1.**

<table>
<thead>
<tr>
<th></th>
<th>Hyperbaric oxygen treated</th>
<th>Untreated</th>
<th>Pre-op. nuclear cataracts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>25</td>
<td>19</td>
<td>100</td>
</tr>
<tr>
<td>Age distribution</td>
<td>23–94 (mean 66)</td>
<td>43–90 (mean 69)</td>
<td>47–93 (mean 76)</td>
</tr>
<tr>
<td>Number of patients</td>
<td>11</td>
<td>1</td>
<td>19</td>
</tr>
<tr>
<td>with nuclear vacuoles</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
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**Fig. 1a.**
Slit-lamp photo of a lens from a 83-year-old female patient with senile nuclear cataract. Note the prominent nuclear vacuoles.

**Fig. 1b.**
Slit-lamp photo of a lens from a 67-year-old female patient with hyperbaric oxygen cataract. Note the shadow of decreased turbidity behind the vacuoles.
Results

Nuclear vacuoles were first noticed in patients undergoing treatment with hyperbaric oxygen, often increasing in number when the treatment was intensified. However, they were found to decrease in number or even disappear when the oxygen treatment was reduced or terminated. A complete disappearance was seen only in lenses with few nuclear vacuoles, whereas a reduction in number was found when they were frequent. Out of 25 patients treated with hyperbaric oxygen, 11 developed nuclear vacuoles. No vacuoles were found in the nucleus before the treatment. In the reference group of 19 patients, one had nuclear vacuoles. Pre-operative examination of 100 patients with senile nuclear cataracts revealed 19 with nuclear vacuoles (Table 1).

In the slit-lamp rounded vacuoles were recognized in the nucleus, most often in the anterior part. The nuclear vacuoles were found in grey or yellow-grey nuclear cataracts but not in solely brown ones. The nucleus is here defined as the central grey or yellow-grey part of the lens seen in the slit-lamp. The number of vacuoles varied from a few to more than 50, giving the nucleus the appearance of a Swiss cheese. The diameter of most of the vacuoles was around 0.1 mm, with a few up to around 0.2 mm as calculated from slit-lamp photos (Fig. 1). The slit-lamp appearance was the same in senile grey nuclear cataracts as in hyperbaric oxygen cataracts, although the vacuoles were more frequent and more distinct in all the lenses of the latter type. No cortical vacuoles were found except for some anterior subcapsular vacuoles in 4 lenses.

In the microradiographs the vacuoles of the most affected lenses were seen throughout the entire nucleus. When a smaller number was present, they were found in the outer part of the nucleus. In the microradiographs the vacuoles appeared as dark rounded areas with a lower dry mass content (~0.30 g \cdot cm^{-2}) than the surroundings (~0.50 g \cdot cm^{-2}) (Fig. 2). The diameter of the dark areas varied from 0.02–0.10 mm. In the microradiographs from the 6 nuclear cataracts without visible vacuoles at slit-lamp examination no dark areas of similar appearance could be found.

Discussion

To our knowledge this type of nuclear vacuoles have not been described before, although they should have been observed. The vacuoles were found in the grey nuclear cataracts in contrast to the crystalline spheres formed by calcium phosphate described to be typical for the 'red' or brown nuclear cataract (Pau 1984). The slit-lamp appearance was similar to subcapsular or cortical vacuoles although these are much more distinct. This is probably due both to their more superficial location and to their more transparent surroundings. A shadow of decreased turbidity often was seen behind the vacuoles indicating that light was refracted or absorbed to some extent by the vacuoles (Fig. 1b). If the vacuoles were present in normal lenses, they would most probably be seen in the clear nucleus in conformity with subcapsular vacuoles. In epidemiological studies comprising more than 900 persons (50 years or older) a few punctate opacities were relatively frequently (30–40%) found in the normal transparent nucleus (Lydahl 1984). The opacities were small and located adjacent to the suture lines. No vacuoles of the type described in this study were seen, however.

The microradiographic appearance and the dry mass concentration determined in this study were
in good agreement with an earlier report on the vacuoles of the subcapsular cataract (Philipson & Fagerholm 1981). The vacuoles had a low protein concentration probably due to a locally increased water content. The diameter of the vacuoles was smaller when measured from the microradiographs compared to when measured from the slit-lamp photographs. This may be explained by the fact that in a microradiographic section only a few, if any, of the vacuoles are cut in their center. Thus most of them will appear smaller than their real size. Furthermore, the microradiographs might reveal the smallest vacuoles not seen in the slit-lamp. In a microradiographic study of normal human lenses a high constant dry mass level was determined in the nucleus (Fagerholm et al. 1981). The microradiographs from nuclear cataracts without visible vacuoles also showed a high constant dry mass level without areas of reduced X-ray absorption.

Nuclear vacuoles were most common in hyperbaric oxygen cataracts. The presence of vacuoles in senile nuclear cataracts as well suggests similar mechanisms in these two types of cataract. Whatever the mechanisms behind these vacuoles, intra-cellular, or extracellular the normal relation between water and protein phases is disturbed.

The appearance of vacuoles in the nucleus of hyperbaric oxygen cataracts was related to the intensity of the treatment and seems to be an indicator of an active cataractogenic process. The fact that a reduction in number or even a complete disappearance of the vacuoles was found, when the oxygen treatment was terminated does not necessarily mean a normalization of the fine structure of the lens. One possible event could be a gradual diffusion of the local hydration when the stress is eliminated. Being less well-defined, the local hydration might not be seen as a vacuole but instead contribute to the general light scattering. The nuclear vacuoles were more common in hyperbaric oxygen treated patients. Hyperbaric oxygen has been shown to cause nuclear cataract within a very short time (Palmquist et al. 1984). Experimentally, oxidative stimuli have been shown to cause serious injury to the lens (Spector 1984). Oxidative damage to the lens epithelium as well as to the lens fiber membrane would affect the permeability and the water balance. The concentration of the various protective systems of the lens against oxidative damage are generally higher in the cortex than in the nucleus which might explain the nuclear localization of the vacuoles.

The appearance of vacuoles in hyperbaric as well as senile nuclear cataracts points to similar etiologic factors, such as oxidative trauma to the lens in these two types of cataract. The appearance of the vacuoles also indicates that the lens nucleus is a much more dynamic structure than is generally considered.

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References


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