II. BIOLOGICAL EFFECTS

H. Cataracts

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Several months to years after exposure to ionizing radiation of the atomic bombs (A-bombs), some survivors developed cataracts. The characteristic clinical finding was a localized lenticular opacity on the inner surface of the posterior polar capsule presenting a polychromatic sheen, and punctate opacities or aggregations thereof in the subcapsular cortical layer of the posterior polar region. In the majority of the affected survivors, the degree of opacification of these radiation cataracts was minimal to moderate and remained unchanged. These cases had no other subjective disturbances associated with this condition.

INTRODUCTIONS

The visual organ exposed to the atomic bombs was subject to burns, and mechanical and radiation injuries. Of these, the radiation injuries of the lens posed the greatest late effect problem. Radiation cataract was the first late effect documented as occurring among those exposed to the atomic bombs.

Reports of such cataracts among survivors were made by Hirose and Fujino in September 1949 and by Cogan, Martin and Kimura in December 1949. Subsequent ophthalmologic studies of survivors were performed at the Atomic Bomb Casualty Commission (ABCC) by Cogan, Martin, Kimura and Ikui (1950), Fillmore (1952), Sinskey (1955), Hall et al (1964), and by Miller et al (1967, 1968). Many surveys for such abnormalities were also conducted by Japanese ophthalmologists.

CLINICAL MANIFESTATIONS

Investigators generally agree that the clinical manifestations of cataracts caused by the neutrons and gamma rays of the atomic bombs are no different than those due to other types of ionizing radiation.

Cogan et al (1952) reported in their study of 20 cases of radiation-induced cataracts, 10 of which were attributed to the ionizing radiation of the atomic bombs, that the findings were identical. They described the clinical characteristics of radiation cataracts as having (1) a doughnut-shaped configuration ophthalmoscopically, and (2) an opacity with a sharply demarcated anterior boundary and bivalved configuration, on slit-lamp biomicroscopy.

Sinskey, in his extensive study of 3,700 A-bomb exposed and nonexposed individuals from May 1951 to December 1963, reported that the presence of granules in the posterior subcapsular axial region of the lens alone was not sufficient evidence to conclude...
that the condition was radiation-induced. He regarded the minimum positive finding to be a minute subcapsular axial plaque as seen only with a slit-lamp. Among 164 controls, 16 (10%) had polychromatic granular plaques on the posterior capsule of the lens. However, among 165 exposed who reported 90 to 100 percent epilation one to three months after the bomb 139 (84%) had such plaques.

Tokunaga14) (1960) ophthalmologically examined 1600 Nagasaki survivors exposed between 100 and 1800 m from the hypocenter. As the major lenticular changes due to radiation, he pointed out (1) punctate opacities in the disjunction zones, (2) vacuoles in the cortex, (3) subcapsular plaque-like opacities at the posterior pole, and (4) tuff-like opacities in the cortex of the posterior pole. He concluded that (1) and (4) were peculiar to radiation cataract, that (2) were also seen in other kinds of cataracts and that (3) were detected in 7.14% of the controls.

The author1,23) (1962, 1967) classified radiation cataracts of Hiroshima survivors into 4 grades of severity, as shown in Table 1.

In May 1959, the author24) (1967) was the first to succeed in photographing images of radiation cataracts in A-bomb survivors on transillumination using a fundus camera. In April 1966, he achieved good results in photographing reproductions of representative cases using a Zeiss photo slit-lamp.

Conditions such as the posterior polar cataract, a complication of pigmentary degeneration of the retina, or certain types of senile cataracts that develop in the posterior polar region, may confuse morphologic characteristics of radiation cataracts in A-bomb survivors.5-15,18)

Table 1. Classification of Radiation Cataracts of Hiroshima Survivors by Severity

<table>
<thead>
<tr>
<th>Findings</th>
<th>Degree</th>
<th>Minute</th>
<th>Slight</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Localized opacity on inner surface of posterior polar capsule</td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Opacities located in subcapsular cortical layer of posterior polar region</td>
<td></td>
<td>-</td>
<td>+</td>
<td>(punctate)</td>
<td>+</td>
</tr>
<tr>
<td>Shadows on transillumination</td>
<td></td>
<td>-</td>
<td>±</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Photographic reproduction by transillumination</td>
<td></td>
<td>Impossible</td>
<td>Impossible</td>
<td>Possible</td>
<td>Possible</td>
</tr>
<tr>
<td>Subjective visual disorders</td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Incidence among 58 eyes with radiation cataract</td>
<td>33 (56.9%)</td>
<td>15 (25.9%)</td>
<td>4 (6.9%)</td>
<td>6 (10.3%)</td>
<td></td>
</tr>
</tbody>
</table>

N. B. "Minute" refers to a localized opacity on the inner surface of the posterior polar capsule presenting a polychromatic sheen depending on the direction of observation, and is visible only by slit-lamp microscopy. "Slight" indicates that, in addition to the "Minute" findings, there were small punctate opacities anterior to the posterior polar capsule, with barely any shadow of opacities visible on transillumination. "Moderate" refers to clumps of opacities anterior to the posterior polar capsule, and with shadows of opacities distinctly visible by transillumination. "Severe" indicates that so-called tuff-like opacities were anterior to the posterior polar capsule. Subjective visual disturbances occurred in this category only.
The first report of histopathological study of cataracts in survivors by Kimura and Ikui\textsuperscript{25} (1951), was followed by several others.\textsuperscript{26-27} Kimura and Ikui reported a case of a twenty-two year old male who complained of visual disturbance commencing 2 years after the bomb and whose left lens was extracted 52 months after exposure.\textsuperscript{25} Study of the posterior capsule of the extracted lens showed its middle third to be wrinkled, thickened, and separated from the underlying cortex by amorphous debris. There was degeneration of epithelium, with irregular morphology and distribution of epithelium and lens fibers at the equator, and thickening and vacuolization of the fibers.

In 3 lenses extracted from 2 Hiroshima cases with severe radiation cataracts more than 10 years after exposure, the author\textsuperscript{15} (1962) found well demarcated granular disintegration and amorphous changes of the lenticular fibers beneath the posterior capsule. Clinically, radiation cataracts first appear at the posterior pole. Histological examination definitely shows that there is more involvement of the posterior than the anterior subcapsular cortex.\textsuperscript{25}

Cogan et al\textsuperscript{22} generally regarded the histologic manifestations of radiation cataracts less type-specific than the clinical ones.

**PREVALENCE**

As with other radiation-induced disorders, the variations in degrees of severity and prevalence of radiation cataracts in A-bomb survivors are dependent upon factors such as dose and age.

According to Fillmore,\textsuperscript{4} Kimura (1949) reported 98 Hiroshima patients with radiation cataracts. Eighty-five (9.8\%) of the 98 were among 869 survivors exposed within 1000 m from the hypocenter. Their estimated air dose\textsuperscript{*} was $\geq 255.5$ rad from gamma rays; $\geq 191.6$ rad from neutrons, and a total dose of $\geq 447.1$ rad.

Kandori and Masuda\textsuperscript{13} (1956) reported 116 cases (26.6\%) with radiation cataracts among 435 Hiroshima A-bomb survivors. By distance there were 87 (54.7\%) among 159 exposed within 2000 m and 30 (10.8\%) with cataracts among 277 exposed beyond 2000 m. The air dose at 2000 m was 1.9 rad from gamma rays, 0.5 rad from neutrons, with a total dose of 2.5 rad. Despite the cataracts, 53.5\% had normal vision.

The author\textsuperscript{15} (1962) found radiation cataracts in 58 eyes (23.4\%) of 32 patients (25.0 \%) among 248 eyes of 128 Hiroshima A-bomb survivors. Prevalence was 70\% among those within 1000 m (*total dose $\geq 447.1$ rad) and 30\% among those between 1000 and 2000 m (*total dose 447.1--2.5 rad). The frequency decreased markedly beyond 1600 m (*gamma rays $\leq 13.2$ rad; neutrons $\leq 5.6$ rad, total dose $\leq 18.8$ rad).

Toda et al\textsuperscript{16} (1964), studying 115 Hiroshima survivors exposed during infancy, found the rate of radiation cataracts to be 55.6\% in those within 1000 m (*total dose $\geq 447.1$ rad), 50\% in those between 1000 and 1200 m (*total dose 447.1--153.3 rad), 22.2\% in those between 1200 and 1400 m (*total dose 153.3--53.3 rad), 12\% in those between 1400 and 1600 m (*total dose 53.3--18.8 rad) and 1.5\% in those between 1600 and 2000 m (*total dose 18.8--2.5 rad). There were no cases beyond 2000 m. All definite cases of radiation cataracts

\* T65D air dose value, Hiroshima\textsuperscript{25}
were less than moderate in degree.

Tokunaga\textsuperscript{14} (1960) studying 1600 Nagasaki survivors found radiation cataracts in 57.4\% of those exposed within 1800 m (estimated air dose\textsuperscript{**}: gamma rays \(\geq 37.6\) rad; neutrons \(\geq 0.3\) rad, total dose \(\geq 37.9\) rad) and in 45.8\% of those exposed within 2400 m (\(\gamma\) gamma rays \(\geq 4.1\) rad; neutrons \(\geq 0.0\) rad, total dose \(\geq 4.1\) rad). Statistically, 1800 m is considered the limit beyond which no radiation cataracts were induced.

Hirose et al\textsuperscript{15} (1960), at ABCC, Nagasaki studied 178 cases whose gamma ray and neutron dose estimates were available and found prevalences of lenticular opacities of the posterior pole by dose, as follows: 0—19 rad (11.9\%), 50—99 rad (26.5\%), 100—199 rad (48.1\%) and 200—499 rad (55.3\%).

From August 1963 to March 1964, Kawamoto et al\textsuperscript{17} ophthalmologically studied those exposed in-utero to the Nagasaki A-bomb. Lenticular opacities, including small vacuoles, were found more frequently in the within-city groups. However, statistically, there was a suggestive (0.05 \(< P \leq 0.10\)) but not a significant difference in the rate of lenticular opacities between those whose mothers had been exposed within 2000 m (11.1\%) and those whose mothers were not in the city at the time of the bomb (3.7\%).

Sinskey\textsuperscript{5} found correlations between the incidence of posterior subcapsular plaques and age,\textsuperscript{7,13} epilation,\textsuperscript{4,15,27} shielding and distances from the hypocenters.\textsuperscript{30} He reported that the loss of vision caused by radiation cataracts was negligible.

The only available report on the estimation of Relative Biological Effectiveness (RBE) of neutrons as compared with gamma rays in A-bomb survivors is that of Jablon et al\textsuperscript{11} (1971). RBE was estimated by seeking concurrence of the Hiroshima and Nagasaki dose response curves for epilation, bleeding, leukemia and axial lenticular opacities. The RBE for epilation and bleeding was about 3 to 5, and that for leukemia was about 6. For axial lenticular opacities the RBE obtained from laboratory animal experiments has been reported to be 4 to 10, or even higher.\textsuperscript{32} Jablon et al\textsuperscript{11} reported the RBE for the A-bomb survivors was between 1 and 2. Moreover, since observations of lenticular opacities were made in a much more subjective manner than were those for other effects, it was concluded that the data for the two cities were not comparable, and a reliable factor for RBE for lenticular opacities in humans based on the data from A-bomb survivors could not be obtained.

\textit{Course}

Cataracts in A-bomb survivors developed several months to years after exposure.\textsuperscript{1,10} Tokunaga\textsuperscript{33} (1962) estimated the latent period of radiation cataracts as within 10 months.

According to Ham,\textsuperscript{24} Donaldson (1951), reexamining 70 survivors 6 years after A-bomb exposure, found moderate regression of lenticular opacities in 2\%, slight regression in 17\%, no change in 36\%, slight progression in 15\%, moderate progression in 26\%, and marked progression in 4\%. Among these cases, 70% experienced complete, 20% partial epilation.

Masuda\textsuperscript{35} (1962), in follow-up observations ranging from one and one-half to nine years, found 21 out of 75 Hiroshima cases to have radiation cataracts. In 4 of them, they remained unchanged; in 8, they became deformed; in 4, there was slight regres-
sion; and in 5, progression. Sinskey\textsuperscript{5}) reported that the posterior subcapsular opacities he observed over a four-year period were increasing in extent only very slowly, or not at all. Fujinaga\textsuperscript{20}) reported that during his 1-10 year case follow-ups from 1959 to 1969, he found no progression of cataracts.

Presently, the general opinion of the courses of cataracts in A-bomb survivors is that the radiation-induced lenticular opacities progress very slowly, after which they become arrested.\textsuperscript{14,20}) However, results of some long-term observations have shown that, in a small number of cases, there has been progression in the degrees of opacities,\textsuperscript{15,35}) and regressions have also been reported.\textsuperscript{19,21,35)

REFERENCES


