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Acute retinal pigment epitheliitis and dosimetric follow-up: a case report

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Acute retinal pigment epitheliitis (ARPE; also known as Krill disease), a disease first described in the nineteen seventies, is characterized by fine pigment stippling in the macular area, surrounded by hypopigmented halo. The etiology of the disease is not yet known. The patient reported that he used to eat berries picked from the forest in the radioactive contaminated area in late June to early July, 2023. He complained of transient metamorphopsia and reduced vision in the left eye, and received eye examination including optical coherence tomography, general check-up, blood cell counts and whole body radionuclide content study. He was diagnosed with bilateral APRE. On the basis of measurements with the expert whole-body counter, the whole-body burden of Cs-137 for the patient was 505 Bq, and the estimated annual effective dose from internal radiation was 0.011 mSv/y. The estimated dose value was substantially lower than the basic dose limit for the population of 1 mSv/y as per requirement of the Law of Ukraine. Because APRE is a rare disease with an unknown etiology, careful attention deserves to be given to the finding of the disease in a patient who has sustained short-term exposure to ionizing radiation due to the incorporation of Cs-137 into his body tissues. For the first time it has become possible to assess adequately doses from internal radiation in a patient with APRE, which will allow to optimize efforts for further research on the etiology of this rare disorder.

Keywords: acute retinal pigment epitheliitis, ionizing radiation, macula, retina, optical coherence tomography, morphological changes, incorporation of radioactive isotopes, whole-body counter

Introduction. Acute retinal pigment epitheliilitis (APRE; also known as Krill disease) was first described in the nineteen seventies [1]. It is a rare idiopathic inflammatory disease which was first diagnosed and separated as a clinical entity by Alex E. Krill and August F. Deutman. Retinal lesions appear as fine pigment stippling in the macular area, surrounded by hypopigmented halo. APRE had an acute onset with fairly fast resolution in 6-12 weeks, and recovery to normal or almost normal vision was achieved in all patients [1].

The disease typically affects young healthy adults in the age range 20-50 years, and its incidence is unknown [2]. Men and women are equally affected. In a case series of 18 patients from South Korea, the male-to-female ratio was 6:4 [2]. No racial predisposition has been described. Although the exact etiology and pathophysiology is still to be elucidated, a relationship between viral infection and the disease has been suggested. Flu-like symptoms have been reported to occur before the onset of ARPE, suggesting a possible role of infection in the pathogenesis [3]. A case series of 18 patients [2], however, showed that only 17% of patients had prodromal influenza-like symptoms before the onset of the disease [2]. To the best of our knowledge, there have been no reports on (1) ARPE developing in individuals after radiation exposure or (2) individual radiation doses in patients with the disease. Due to the insufficient number of reported cases, there seems to be no consensus regarding the exact nature of the condition [4].

Early spectral-domain optical coherence tomography (OCT) revealed an inflammatory lesion not in the retinal pigment epithelial (RPE) layer, as it had been hypothesized, but in the photoreceptor outer segment layer displacing the external limiting membrane [5].

The involvement of the choroid, RPE and inner retinal layers in the development of APRE is of no doubt. Careful attention deserves to be given to the finding of APRE in a patient who has sustained exposure to ionizing radiation due to the incorporation of Cs-137 into his body tissues. Ophthalmological studies [6–10] have demonstrated that

the retina is sensitive to the effect of ionizing radiation. Although sparse, the studies that have looked at the response of animals to radiation exposure confirmed the presence of ultrastructural changes in the retina [11].

The rarity of this disease with unknown etiology has triggered our search for the possible causes of APRE.

Case description

A male patient born in 1963 is under our regular supervision. On June 9, 2023, he had his annual routine eye examination including uncorrected and best corrected visual acuity assessment, tonometry, and automated refractokeratometry. In addition, slit-lamp biomicroscopy, lens examination and red reflex photography, ophthalmoscopy, and fundus photography (VISUCAM lite, Carl Zeiss AG, Oberkochen, Germany) were conducted with dilated pupils.

The patient had no visual complaints at the time of examination, and his uncorrected visual acuity (UCVA) and best corrected visual acuity (BCVA) was 1.0 (Snellen equivalent 20/20) on both eyes. There was mild cortical lens opacity in both eyes. Both optic discs were unremarkable, the arteries slightly narrowed, and the central and peripheral retina showed no changes of note.

The patient reported that, in late June to early July, 2023, he used to eat berries picked from the forest close to the settlements of the third zone of radioactive pollution (also known as the "zone of guaranteed voluntary resettlement").

The patient reported that, in late June to early July, 2023, he used to eat berries picked from the forest close to the settlements of the third zone of radioactive pollution (also known as the "zone of guaranteed voluntary resettlement"). He also reported that, in late July, 2023, he suddenly began experiencing transient metamorphopsia and reduced vision in the left eye. In addition, the patient experienced an increase in metamorphopsia over time.

The patient had a repeat examination on Aug. 1,2023. UCVA and BCVA were 1.0 (Snellen equivalent 20/20) on the OD and 0.7 (Snellen equivalent 14/20) on the OS. Metamorphopsies were detected with the help of the Amsler grid only on the left eye. There was no change in the optic media as compared to previous examination.

Ophthalmoscopy of the left eye revealed a typical picture of ARPE, with a round lesion surrounded by a hypopigmented halo in the macula (Fig. 1).

The patient underwent OCT and OCT angiography (REVO FC, Optopol Technology Sp. z.o.o., Zawiercie, Poland). The characteristic OCT feature was a domeshaped hyperreflective lesion at the photoreceptor outer segment layer disrupting the ellipsoid zone and interdigitation zone [2, 5] (Fig. 2).

Fundus autofluorescence showed increased autofluorescence in the macula and in the areas corresponding to the hypopigmented dots in the left eye (Fig. 3).

The examination of the right eye showed the picture characteristic of APRE (Figures 4 and 5), but the patient did not complain of this eye.

Therefore, APRE was diagnosed on the basis of history and clinical and OCT findings. The disease was bilateral, although the metamorphosia was self-reported and detect-

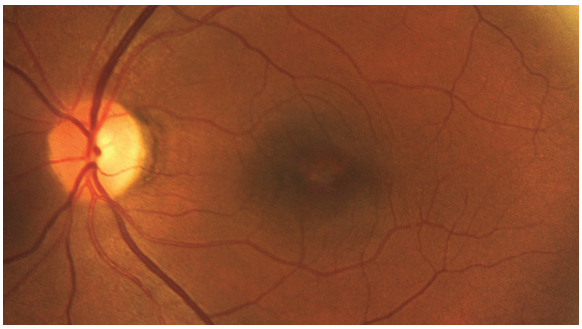

Fig. 1. Ophthalmoscopy image showing the central retina of the left eye after the onset of metamorphopsia

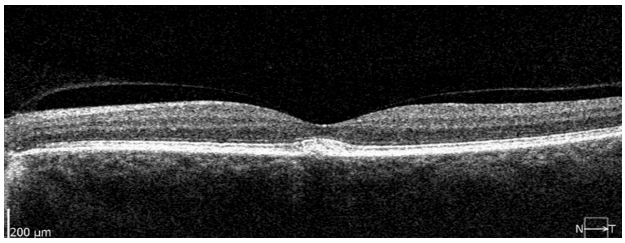

Fig. 2. Optical coherence tomography image for the macular region in the left eye

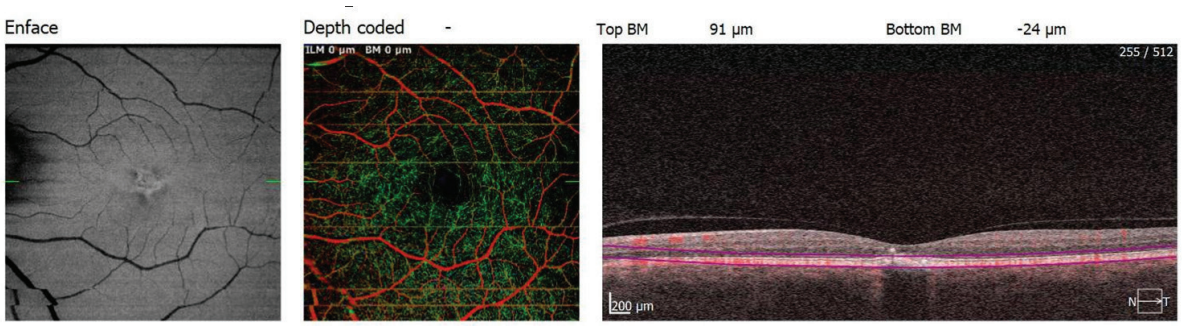

Fig. 3. Fundus autofluorescence image and optical coherence tomography (OCT) and OCT angiography images for the macular region in the left eye

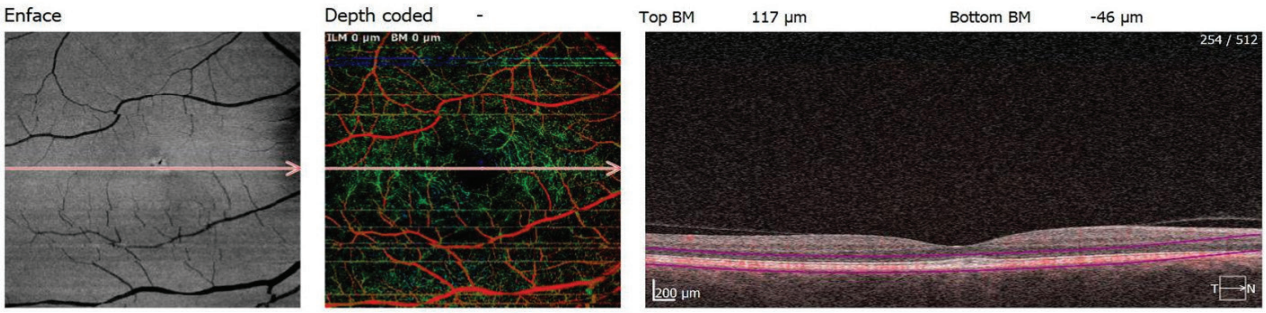

Fig. 5. Fundus autofluorescence image and optical coherence tomography (OCT) and OCT angiography images for the macular region in the right eye

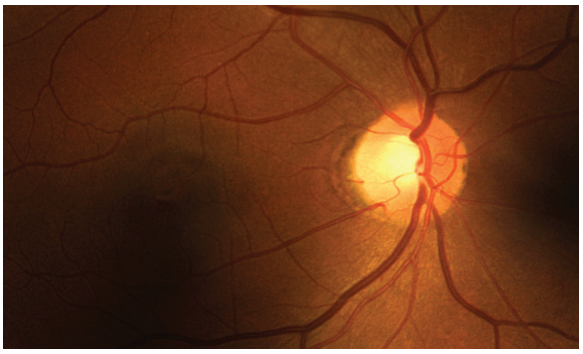

Fig. 4. Ophthalmoscopy image showing the central retina of the right eye

Control of body content of a radionuclide, (MDA, Bq): ^{137}Cs(18)

Measurement results					
Nuclide	Content (Bq)	Measurement error	MDA (Bq)	Net, pulse/min	*Annual effective dose (mSv/y)
^{137}Cs	505	8.8%	18	245	0.011

Group: Group A Measurement duration: 982 s
Measurement date: September 5, 2023
Note: *, pattern of intake of a radionuclide into the body: ^{137}Cs, chronic daily intake; MDA, minimum detection activity

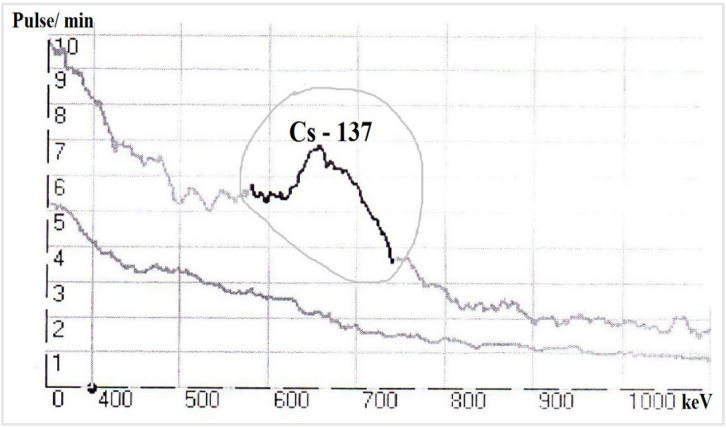

Fig. 6. Expert whole-body counter examination results. The ordinate displays the number of pulses per minute, and the abscissa displays gamma energy in kilo-electron Volts (keV)

ed in the left eye, but not in the right eye, and reduced vision was found only in the left eye. Of note was the presence of substantial changes in retinal and choroidal circulation.

The general check-up and blood cell counts were conducted in an attempt to find out the possible cause of the disease, but were unremarkable.

The whole-body burden of radionuclides was measured with the expert whole body counter (WBC) by the WBC Laboratory, Institute of Radiation Hygiene and Epidemiology, SI "National Research Center for Radiation Medicine, Hematology and Oncology of the National Academy of Medical Sciences of Ukraine" using a standardized method [12, 13].

On the basis of measurements with the expert WBC, the whole body burden of Cs-137 for the patient was 505 Bq (Fig. 6).

The distributions of incorporated Cs-137 and K-40 were obtained using the spectrometric line of the expert WBC (Fig. 7).

The pattern of distribution of incorporated Cs-137 was found to be similar to that of the natural K-40 incorporated through food. This indicates that Cs-137 enters the body by the same route (i.e., oral) as K-40.

The patient is still being followed and the results of further observations will be reported at a later date.

Discussion

This is the first report on APRE in a patient with evidence of the radiation dose due to incorporated Cs-137. Since the etiology of the disease is unknown, all possible causes of the disease should be carefully analyzed. Although the value of changes in the retinal and choroidal circulation in the development of APRE is unknown, a relationship of changes in the retinal circulation with the effect of ionizing radiation has been demonstrated previously [14, 15].

The individual effective dose of internal radiation caused by the intake of Cs-137 through the consumption of food contaminated with

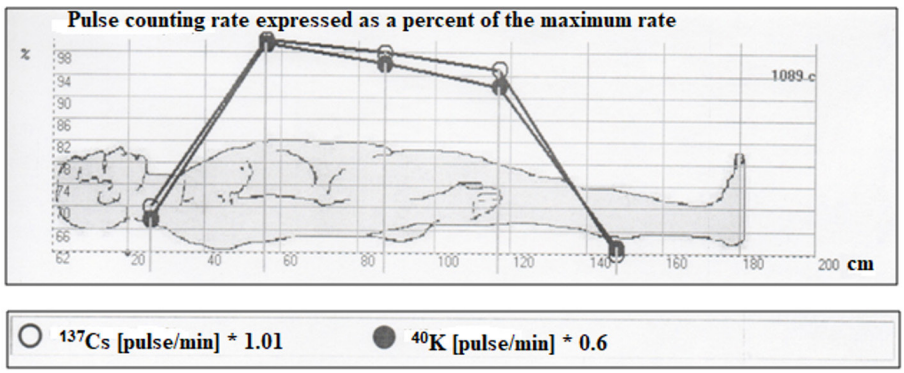

Fig. 7. Distributions of the radionuclides Cs-137 and K-40 obtained using the spectrometric line of the expert whole-body counter

Cs-137 was calculated for the two most likely radionuclide intake scenarios (chronic daily intakes and a single intake).

The average annual dose for the first most likely radionuclide intake scenario was calculated as per the guidelines [16], assuming the equilibrium Cs-137 content in the body, with the average daily Cs-137 intake corresponding to the average daily Cs-137 excretion (Fig. 6). This situation is currently seen in the radioactively contaminated territories of Ukraine, where Cs-137 is a primary contributor to the internal radiation dose and is constantly present in the diet consumed by the local population. The estimated annual effective dose from internal radiation was 0.011 mSv/y.

The dose for the second most likely radionuclide intake scenario was calculated as per International Commission on Radiological Protection Publication 137 [17], assuming that the measured value of the whole body burden of Cs-137 for the patient was obtained through a single intake of forest berries. July 1, 2023, was assumed to be the day of intake. The estimated individual effective dose from internal radiation for the second most likely radionuclide intake scenario was 0.015 mSv.

Both estimated dose values were substantially lower than the basic dose limit from man-made sources for the population of 1 mSv/year as per requirement of the Law of Ukraine "On Protection of Humans from the Influence of Ionizing Radiation" [18].

The distributions of radioactive isotopes, chemical analogues of sodium, potassium and calcium in the human eye have not been sufficiently investigated. Previous studies (1) assessed the morphological changes in other structures of the human body after exposure to stable isotopes, chemical analogues of sodium, potassium and calcium, and (2) demonstrated a substantial impact of these isotopes on functions of human body tissues [19–20]. Changes in vitamin levels in the diet and other factors may affect the macular structures [21]. There have been no reports in the literature on the assessment of possible dose loads for patients with APRE; to the best of our knowledge, such an assessment has not been conducted previously.

Conclusion

Therefore, a low dose of internal residual radiation due to incorporated Cs-137 in the reported case gives no ground to expect an association between radiation exposure and this rare disease. However, this report is of importance for a strategy for further research on the etiology of the disorder, since it deals with the only known case of ARPE in a patient who has sustained exposure to ionizing radiation due to incorporated Cs-137 and received adequate dosimetry using an advanced high-sensitive meter (the expert whole-body counter).

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Disclosures

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Ethical Declaration. *The conducted examination procedures adhered to the principle of minimum risk. Appropriate measures were taken for compliance with the Declaration of Helsinki, the European Convention on Human Rights and Biomedicine and relevant laws of Ukraine. Informed consent for the publication of the reported results in the science literature was obtained from the patient.*

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Abbreviations: *ARPE – acute retinal pigment epitheliitis; OCT – optical coherence tomography; WBC – whole body counter*