

<https://doi.org/10.31288/oftalmolzh202425256>

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

Babenko T. F.,<sup>1</sup> Fedirko P. A.,<sup>1</sup> Saksonov S. G.,<sup>2</sup> Shevchenko I. I.,<sup>3</sup> Pilmane M.,<sup>4</sup> Vasilenko V. V.,<sup>1</sup> Korobova O. V.,<sup>2</sup> Garkava N. A.,<sup>5</sup> Kuriata M. S.<sup>1</sup>

<sup>1</sup> State Institution «National Research Center for Radiation Medicine, Hematology and Oncology of the National Academy of Medical Sciences of Ukraine»

Kyiv (Ukraine)

<sup>2</sup> Donetsk National Medical University of the Ministry of Health of Ukraine

Druzhkivka (Ukraine)

<sup>3</sup> State Institution «Institute of Pediatrics, Obstetrics and Gynecology of NAMS of Ukraine»

Kyiv (Ukraine)

<sup>4</sup> Institute of Anatomy and Anthropology, Riga Stradiņš University

Riga (Latvia)

<sup>5</sup> Dnipro State Medical University

Dnipro (Ukraine)

*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 epitheliitis (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

© Babenko T.F., Fedirko P.A., Saksonov S.G., Shevchenko I.I., Pilmane M., Vasilenko V.V., Korobova O.V., Garkava N.A., Kuriata M.S., 2024

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 refractometer. 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. Metamorphopsias 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.

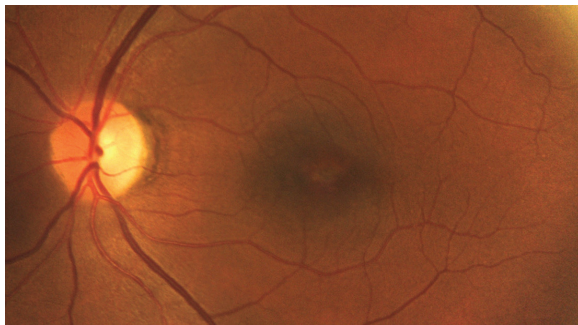
Ophthalmoscopy of the left eye revealed a typical picture of ARPE, with a round lesion surrounded by a hypopigmented halo in the macula (Fig. 1).

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).

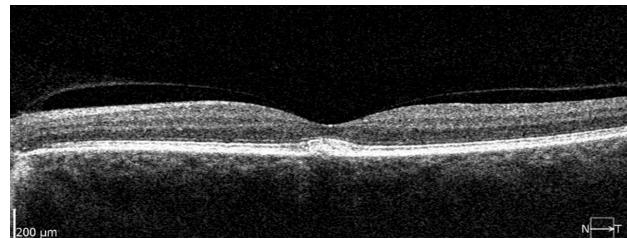
Fundus autofluorescence showed increased autofluorescence in the macula and in the areas corresponding to the hypopigmented dots in the left eye (Fig. 3).

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.

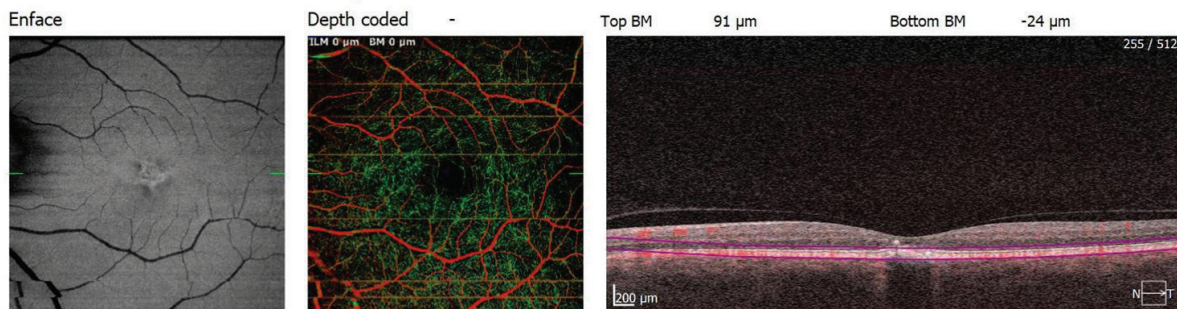
Therefore, APRE was diagnosed on the basis of history and clinical and OCT findings. The disease was bilateral, although the metamorphopsia was self-reported and detect-



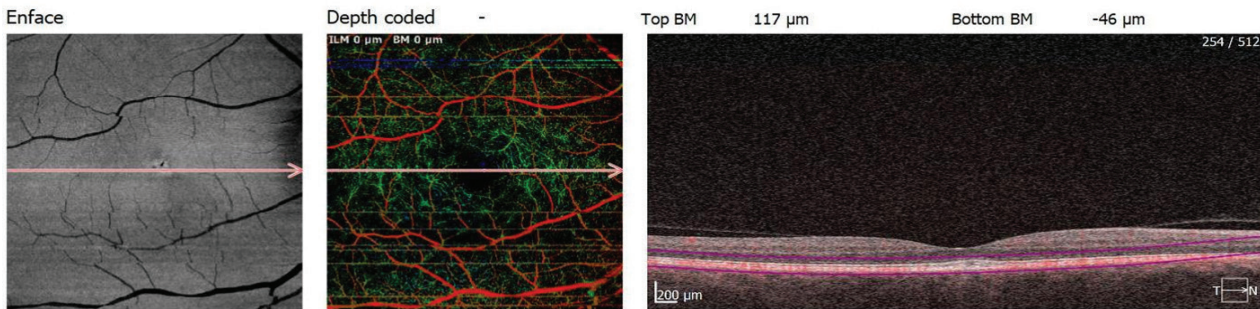
**Fig. 1.** Ophthalmoscopy image showing the central retina of the left eye after the onset of metamorphopsia



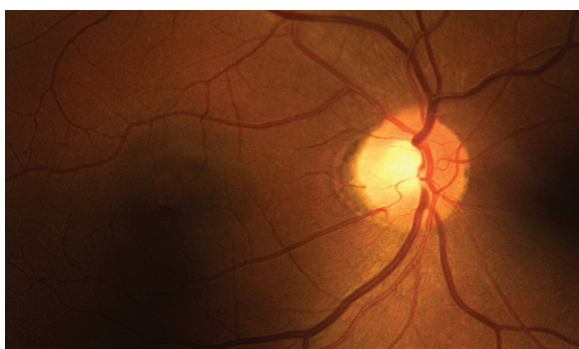
**Fig. 2.** Optical coherence tomography image for the macular region in the left eye



**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

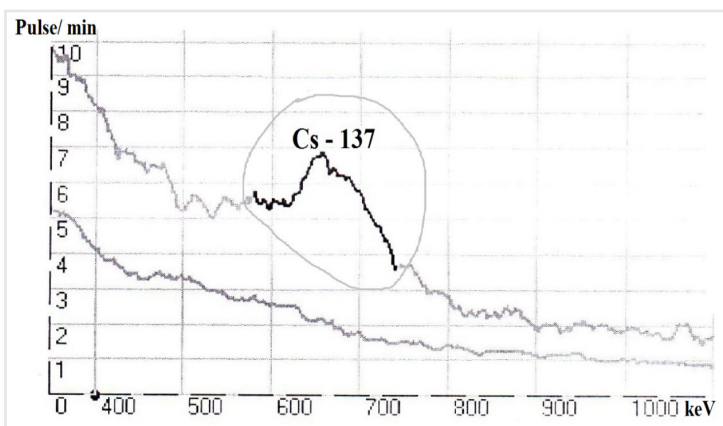
Control of body content of a radionuclide, (MDA, Bq): <sup>137</sup>Cs(18)

Measurement results					
Nuclide	Content (Bq)	Measurement error	MDA (Bq)	Net, pulse/min	*Annual effective dose (mSv/y)
<sup>137</sup> 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: <sup>137</sup>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

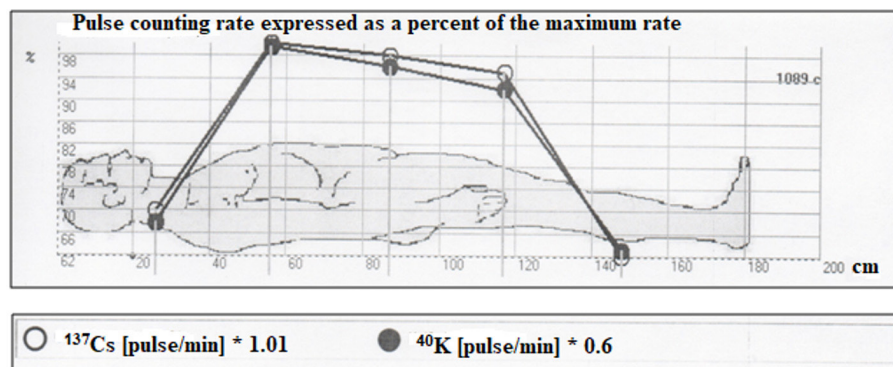


Fig. 7. Distributions of the radionuclides Cs-137 and K-40 obtained using the spectrometric line of the expert whole-body counter

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).

### References

1. Krill AE, Deutman AF. Acute retinal pigment epitheliitis. *Am J Ophthalmol.* 1972; 74:193–205.
2. Han SY, Cho SW, Lee DW, Lee TG, Kim CG, Kim JW. Acute retinal pigment epitheliitis: spectral-domain optical coherence tomography findings in 18 cases. *Invest Ophthalmol Vis Sci.* 2014; 55(5):3314–3319.
3. Kılıç R. Acute retinal pigment epitheliitis: a case presentation and literature review. *Arq Bras Oftalmol.* 2021; 84(2):186–190. doi: 10.5935/0004-2749.20210028.
4. Al-Nofal M, Charbel Issa P. Acute retinal pigment epitheliitis, a diagnostic myth? *Eye.* 2024; 38:238–239. doi: 10.1038/s41433-023-02683-w.
5. Iu LPL, Lee R, Fan MCY, Lam WC, Chang RT, Wong IYH. Serial spectral-domain optical coherence tomography findings in acute retinal pigment epitheliitis and the correlation to visual acuity. *Ophthalmology.* 2017; 124 (6): 903–909.
6. Babenko TF, Fedirko PA, Dorichevska RY, Denysenko NV, Samoteikina LA, Tyshchenko OP. The risk of macular degeneration development in persons antenatally irradiated as a result of Chernobyl NPP accident. *Probl Radiac Med Radiobiol.* 2016 Dec;21:172-177.
7. Mao XW, Boerma M, Rodriguez D, Campbell-Beachler M, Jones T, Stanbouly S, et al. Acute effect of low-dose space radiation on mouse retina and retinal endothelial cells. *Rad Res.* 2018; 190 (1): 45-52. DOI: <https://doi.org/10.1667/RR14977.1>
8. Fedirko PA, Babenko TF, Kolosynska OO, et al. Morphometric parameters of retinal macular zone in reconvalescents of acute radiation sickness (in remote period). *Probl Radiac Med Radiobiol.* 2018;23:481-489. doi: 10.33145/2304-8336-2018-23-481-489.
9. Rios CI, Cassatt DR, Hollingsworth BA, Satyamitra MM, Tadesse YS, Taliaferro LP, et al. Commonalities Between COVID-19 and Radiation Injury. *Rad Res.* 2020; 195 (1): 1-24 DOI: <https://doi.org/10.1667/RADE-20-00188.1>
10. Babenko TF, Loganovsky KM, Loganovska TK, Medvedovska NV, Kolosynska OO, Garkava NA, et al. Brain and eye as potential targets for ionizing radiation impact.

- Part III-Features morphometric retinal parameters, amplitude and latency components of visual evoked potential in radiation exposed in utero. *Probl Radiac Med Radiobiol.* 2021; 26:284–296. doi: 10.33145/2304-8336-2021-26-284-296.
11. **Molchaniuk NI, Dumbrova NE.** [Ultrastructural changes of nerve elements and retinal microvessels in rats exposed to radiation factors of the Chernobyl accident]. *Oftalmol Zh.* 2002;(6):44–49. Russian.
  12. **Vasylenko VV, Zadorozhna GM, Kuriata MS, Lytvynets LO, Novak DV, Mishchenko LP.** Evaluation of main foodstuffs consumption by residents of particular settlements on radiologically contaminated territories of Ukraine. *Probl Radiac Med Radiobiol.* 2019 Dec;24:93–108. doi: 10.33145/2304-8336-2019-24-93-108.
  13. **Bazyka DA, Fedirko PA, Vasylenko VV, Kolosynska OO, Yaroshenko ZS, Kuriata MS, et al.** Results of WBC-monitoring of firefighters participating in response to Chernobyl forest fires in April-May 2020. *Probl Radiac Med Radiobiol.* 2020 Dec; 25:177–87. doi: 10.33145/2304-8336-2020-25-177-187
  14. **Fedirko PA, Babenko TF, Dorichevska RY, Garkava NA.** *Probl Radiac Med Radiobiol.* Retinal vascular pathology risk development in the irradiated at different ages as a result of Chernobyl NPP accident. *Probl Radiac Med Radiobiol.* 2015 Dec; 20:467–573.
  15. **Fedirko PA, Garkava NA.** Patterns of development of retinal vascular pathology at remote time period after radiation exposure. *J Ophthalmol (Ukraine).* 2016;6:24-28. <https://doi.org/10.31288/oftalmolzh201662428>
  16. **Nechayev SY, Vasylenko VV, Pikta VO, et al.** [Monitoring of internal exposure doses of the population in the later stage of the Chernobyl NPP accident using whole body counters]. Kyiv: Research Center for Radiation Medicine of the Academy of Medical Sciences of Ukraine; 2010. Ukrainian.
  17. **Paquet F, Bailey MR, Leggett RW, Lipsztein J, Marsh J, Fell TP, et al.** Occupational Intakes of Radionuclides: Part 3. *Ann ICRP.* 2017 Dec;46(3-4):1-486. doi: 10.1177/0146645317734963.
  18. Law of Ukraine. On protection of the person against influence of ionizing radiation. Information of the Verkhovna Rada of Ukraine (VVR). 1998. № 22 URL: <https://zakon.rada.gov.ua/laws/show/15/98>
  19. **Zarins J, Pilmane M, Sidhoma E, Salma I, Locs J.** The Role of Strontium Enriched Hydroxyapatite and Tricalcium Phosphate Biomaterials in Osteoporotic Bone Regeneration. *Symmetry.* 2019; 11 (2): 229. doi.org/10.3390/sym11020229
  20. **Zarins J, Pilmane M, Sidhoma E, et al.** Immunohistochemical evaluation after Sr-enriched biphasic ceramic implantation in rabbits femoral neck: comparison of seven different bone conditions. *J Mater Sci: Mater Med.* 2018; 29 (8): 119. doi.org/10.1007/s10856-018-6124-7
  21. **Soysal GG, Berhuni M, Özcan ZO, Tiskaoğlu NS, Kaçmaz Z.** Decreased choroidal vascularity index and subfoveal choroidal thickness in vitamin D insufficiency. *Photodiagnosis Photodyn Ther.* 2023; 44: 103767. doi.org/10.1016/j.pdpdt.2023.103767

#### Disclosures

Received 29.11.2023

Accepted 24.03.2024

**Author Contributions.** TFB: Detection and diagnostic assessment of the case, Methodology, Writing – original draft; PAF: Conceptualization, Methodology, Writing – original draft; SGS: Diagnostic assessment of the case, Conceptualization, Writing – review & editing; IISh: Diagnostic assessment of the case, Conceptualization, Writing – review & editing; MP: Conceptualization, Methodology, Writing – review & editing; VVV: Diagnostic assessment of the case, Conceptualization, Writing – original draft; OVK: Conceptualization, Writing – review & editing; NAG: Conceptualization, Writing – original draft, Writing – review & editing; MSK: Diagnostic assessment of the case, Writing – original draft. All authors reviewed the results and approved the final version of the manuscript.

**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.

**Financial support:** no financial support received.

**Conflict of interest statement:** None.

**Financial/proprietary interest:** None.

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