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Retinoblastoma - Current Diagnostic Strategies, Treatment Approaches and Long-Term Outcomes

Ewa Witowska-Jeleń[1,2] & Arkadiusz Pogrzebielski,[3,4]

1. Department of Ophthalmology and Orthoptics, School of Allied Health Professions, Nursing and Midwifery, The University of Sheffield, Sheffield, United Kingdom
2. Orto-Optica – Centrum Dobrego Widzenia, Kraków, Poland
3. Oculus Krakowskie Centrum Okulistyczne, Kraków, Poland
4. Prof. Zagórski Eye Surgery Center, Kraków, Poland

Abstract: Retinoblastoma is the most common primary intraocular malignancy of childhood and remains a significant cause of visual impairment, ocular morbidity, and mortality worldwide. Although survival rates have improved substantially in developed countries, delayed diagnosis continues to adversely affect visual and systemic outcomes. This review provides an updated overview of the current understanding of retinoblastoma, including its epidemiology, genetic background, clinical presentation, classification systems, diagnostic strategies, and contemporary treatment approaches. Particular attention is given to the importance of early clinical signs, especially leukocoria and strabismus, which may represent the first manifestation of the disease and facilitate timely diagnosis. Recent advances in eye-preserving therapies, including intra-arterial chemotherapy, intravitreal chemotherapy, focal treatment modalities, and modern imaging techniques, have significantly improved globe salvage and visual outcomes. In addition, the review discusses the long-term ophthalmological, systemic, psychological, and social consequences of retinoblastoma and its treatment. Early recognition, prompt referral, multidisciplinary management, genetic counselling, and long-term rehabilitation remain essential components of care and contribute substantially to improving survival, visual function, and quality of life in affected children.

Keywords: ocular oncology, RB1 mutation, leukocoria, strabismus, childhood blindness

INTRODUCTION

Retinoblastoma is a malignant eye tumour occurring in children, most often diagnosed before the age of 5 [1]. Every year, approximately 7,000–8,000 new cases are diagnosed worldwide, of which 3,000–3,500 children die from the disease [2]. Retinoblastoma was first described by Pawius in the 16th century, but it was not until 1809 that its origin in the retina was demonstrated. Based on the observation of neoplastic lesions in surgically treated patients, this tumour was then termed *fungus hematodes* [3]. Although retinoblastoma is a rare tumour, it remains the most common primary malignant intraocular tumour in children. Its incidence is estimated at 1 in 15,000–20,000 live births, representing approximately 3% of all childhood cancers [4]. In the United States, retinoblastoma accounts for approximately 13% of childhood cancers, with the majority of cases being hereditary [5]. Bilateral forms are usually diagnosed earlier than unilateral ones. Untreated retinoblastoma leads to death within 1–2 years. Survival rate is strongly dependent on place of residence and access to diagnostics and treatment [3].

In high-income countries, the 3-year survival rate for children with retinoblastoma is 99.5%, while in low-income countries it drops to approximately 57.3% [6]. In patients with the hereditary form, as many as 33% develop at least one secondary cancer within 50 years of diagnosis, and 6% develop two or more cancers [7].

Retinoblastoma is a serious medical and social problem. It is a genetically determined cancer, most often inherited in an autosomal dominant pattern. In more than half of cases, it is sporadic, while in the remaining cases, it is associated with an inherited mutation of the RB1 gene and may run in families. The unilateral form is more common, while the bilateral form usually presents earlier. Bilateral retinoblastoma is found in 25–30% of patients. The risk of developing the disease in siblings is 2% and in offspring 45%, even in the absence of a positive family history. In cases of unilateral retinoblastoma without a family history, the risk in siblings and offspring drops to approximately 1% [2].

The unilateral retinoblastoma results from a somatic mutation in 85% of cases, while in the remaining 15% of cases it is hereditary [8]. The incidence does not differ significantly between the sexes, although some studies, including those by Akhiwu and Igbe [9], indicate a slight predominance of the disease among girls. In the long term, the risk of developing secondary cancers is 51% in hereditary forms and 5% in sporadic forms [5].

AETIOLOGY, GENETICS, AND HISTOLOGY

The hereditary form of retinoblastoma is associated with a mutation in the RB1 gene, and the risk of developing the disease in carriers of this mutation is high [1]. Two mutations are necessary for tumour development. According to Knudson's two-hit hypothesis [8], cancer develops only when both copies of the RB1 tumour suppressor gene are lost or mutated. There are two forms of retinoblastoma: hereditary and non-hereditary.

In the hereditary form, a child inherits one defective copy of the gene from a parent, and the second mutation arises somatically in the retinal cells, leading to tumour development. In the non-hereditary form, both copies of the RB1 gene are normal at birth but undergo mutations or deletions in early childhood.

Histologically, retinoblastoma is composed of small, basophilic retinoblasts with large nuclei and scant cytoplasm, which form characteristic Flexner-Wintersteiner rosettes. The tumour infiltrates the retina, destroys its structure, and sometimes also fills the vitreous humour. It can grow endophytically, spreading into the vitreous humour, or exophytically, into the subretinal space, often leading to retinal detachment. As emphasized by Cross [10], the tumour often spreads along the optic nerve or through the sclera, while distant metastases are less common. Due to the rapid growth of retinoblastoma, early diagnosis and prompt treatment remain the most important prognostic factors.

SYMPTOMS AND DIAGNOSTICS OF RETINOBLASTOMA

The clinical presentation of retinoblastoma depends on the size and location of the tumour. Small lesions located peripherally, in the early stages of the disease, may be asymptomatic [2]. On ophthalmological examination, the tumour appears as a white, translucent mass, often with subretinal exudation or spread of tumour cells into the vitreous humour. In more advanced stages, extensive ocular involvement, secondary glaucoma, or optic nerve

infiltration occur. The most common initial symptom, occurring in more than half of patients, is a white pupil (*leukocoria*) [1]. It may be merely photographic (*photoleucocoria*) or visible to the naked eye. In nearly 40% of children, leukocoria coexists with strabismus as the first symptom of the disease [2]. Strabismus is therefore a common clinical symptom of retinoblastoma, observed both at the time of diagnosis and after treatment. Fabian et al. [11] found strabismus in 69% of patients with intact eyes, most often in the form of unilateral esotropia (43%), less frequently exotropia (19%) or alternating horizontal strabismus (12%). Abrams et al. also described strabismus as a possible early symptom, present in 66% of children at the time of diagnosis [12].

Binocular vision in patients with retinoblastoma depends primarily on the location of the tumour, particularly the involvement of the fovea. Stacey et al. [13] showed that 38% of children with the bilateral form had significant visual impairment and 19% met the criteria for legal blindness. Ward's systematic review [14] emphasized that macular involvement is a key factor limiting the development of binocular function, with visual acuity deterioration observed in approximately 10% of patients. Despite these limitations, Hammad et al. noted that vision-related quality of life, assessed using the VFQ-25 and VFQ-39, remains relatively high, regardless of unilateral or bilateral retinoblastoma location [15]. In addition to leukocoria and strabismus, retinoblastoma can sometimes present with a painful, red eye, which is usually associated with advanced stage and secondary glaucoma (often neovascular) [6].

Less common symptoms include pseudohypopyon, idiopathic hyphema, anterior uveitis, orbital cellulitis, including preseptal inflammation, and periorbital oedema. Proptosis may be caused by either compression by the growing tumour or direct invasion of the orbital tissues.

Neurological symptoms, including seizures, usually occur when the tumour spreads to the brain or spinal cord. Loss of vision may result from optic nerve involvement, retinal detachment, or vitreous haemorrhage. Godson [16] also notes the presence of high myopia, significant anisometropia, facial dysmorphic features, retinal detachment, and delayed psychomotor development. Such a broad spectrum of symptoms requires special diagnostic vigilance and close interdisciplinary cooperation to avoid missing early signs of developing cancer. Early diagnosis remains crucial for improving survival and visual outcomes.

A basic ophthalmological examination includes a slit-lamp examination and a thorough fundoscopy with scleral invagination, performed after pharmacological dilation of the pupils. To precisely assess the number, size, and location of lesions, these procedures are often performed under general anaesthesia [17]. According to Prost [18], three main forms of tumour growth can be distinguished based on fundus imaging:

1. *Endophytic form* – growth into the eyeball, towards the vitreous humour. The tumour appears as a whitish or cream-coloured protrusion, often covered with retinal vessels, and varies in size from small foci to masses occupying a significant portion of the eyeball. There is often spread of tumour cells into the vitreous humour, visible as fine, white suspensions.
2. *Exophytic form* – the tumour grows into the subretinal space, leading to retinal detachment due to fluid accumulation; calcifications are often observed beneath the detached retina.

3. *Diffuse (disseminated) form* – scattered tumour cells are present in the vitreous humour, often with a flat infiltrate in the retina. The absence of distinct nodular lesions can cause the image to resemble endophthalmitis. This form usually occurs in older children, around 5 years of age, and poses a diagnostic challenge.

It is worth emphasizing the importance of the red reflex test (also known as the Brückner test) in the prevention and early detection of retinoblastoma. This test can be performed using an ophthalmoscope, a standard camera with a flash, or mobile apps such as CRADLE or MDEyeCare. An image taken using the latter method is shown in Fig. 1.

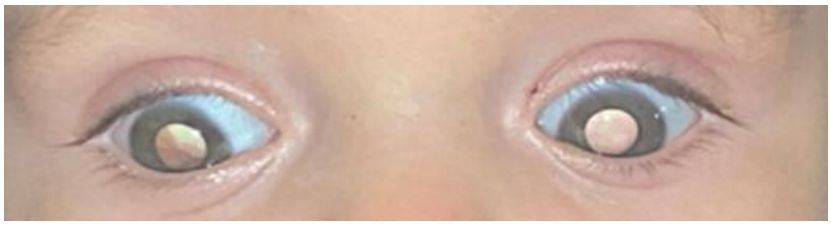

Figure 1: Image from the Brückner test in a patient with binocular retinoblastoma

Photo: own archive.

Diagnosis of retinoblastoma is based on a combination of imaging, laboratory, and genetic tests. Ultrasonography (US) allows for the visualization of calcifications and assessment of tumour size, while magnetic resonance imaging (MRI) is the method of choice for assessing the extent of intra- and extraocular disease and for differentiating from other tumours. Unlike computed tomography, MRI does not involve exposure to ionizing radiation [1]. MRI is also crucial in qualifying and assessing extraocular invasion according to current diagnostic criteria [19]. Fundus autofluorescence (FAF) is used as a supplementary method, in which calcifications within the tumour produce an image of hyperautofluorescence, facilitating the diagnosis of small lesions and differentiating them from vascular pathologies. Optical coherence tomography (OCT) is also used to determine the location of the tumour relative to the retinal layers, assess pigment epithelial invasion, and monitor treatment response, especially in the case of subretinal and intravitreal lesions.

Ultrasound biomicroscopy (UBM) is also used to assess infiltration within the anterior segment of the eye [9]. Diagnosing the spread of the disease also involves PET-CT if extraocular metastases are suspected, bone imaging studies, sometimes electroencephalograms (EEG), complete blood counts, fine-needle aspiration biopsy (FNAB), and histopathological analyses. Genetic testing of the RB1 gene is also an important element of the management, enabling the identification of hereditary forms, early diagnosis of bilateral cases, and monitoring of families affected by the disease [2].

CONTEMPORARY RETINOBLASTOMA CLASSIFICATION SYSTEMS

Several classification systems for retinoblastoma have been described in the literature. Previously, the Reese-Ellsworth Classification, ABC Classification, International Retinoblastoma Staging System (IRSS), and International Intraocular Retinoblastoma Classification (IIRC) were used, as presented in Table 1.

Table 1: Modified International Intraocular Retinoblastoma Classification

Group	Clinical presentation	Clinical characteristics	Estimated risk
A – small	Small tumour (<3 mm), not threatening vision	Tumour(s) ≤3 mm, located ≥3 mm from the fovea and ≥1.5 mm from the optic disc, limited to the retina	No significant risk
B – bigger	Larger or vision-threatening tumour	Tumour(s) >3 mm or any tumour located in the macula, or with subretinal fluid <3 mm from the tumour, without any debris	Low risk
C – containing seeds	Tumour(s) with local debris	Tumour(s) with debris into the vitreous humour or subretinal space ≤3 mm from the tumour	Moderate risk
D – diffuse	Tumour(s) with extensive debris	Diffuse infiltration into the vitreous humour or subretinal space >3 mm from the tumour	High risk
E – extensive	Eyeball not salvageable, life-threatening	Tumour(s): occupying >50% of the vitreous chamber, affecting the lens, invading the anterior vitreous base, optic nerve, or orbit, causing secondary glaucoma, iris rubeosis, or haemorrhages leading to opacity of the optical media	Very high risk

Source: own archive.

In the literature, in addition to the IIRC classification, which is still used in many centres, the currently applicable standard for assessing the stage of retinoblastoma is the AJCC system. In 2017, the American Joint Committee on Cancer (AJCC) proposed a new system in the 8th edition of the Tumour–Node–Metastasis–Heritable Trait (TNMH) classification based on the results of international multicentre studies involving 1,728 eyes [2, 20, 21].

For the first time, this system allows for the assessment of disease severity and prognosis for eye preservation. In 2018, the AJCC was recognized as the gold standard for retinoblastoma classification [2, 20]. The AJCC system includes both clinical (cTNM) and pathological (pTNM) classifications, taking into account tumour size, degree of intraocular invasion, lymph node involvement, and the presence of distant metastases. The latest edition clarifies the definitions of the T1–T4 and M1 categories in clinical assessment, modifies the pT2–pT4 and pM1 criteria in pathological assessment, and introduces a distinction between focal and massive choroidal invasion. T (*tumour*) categories describe the size and location of the tumour, the presence of tumour cell dissemination into the vitreous humour or subretinal space, and possible complications. N (*nodes*) categories refer to regional lymph node involvement, while M (*metastases*) categories indicate the presence and location of distant metastases.

The AJCC system places particular emphasis on precisely determining the stage of disease progression, which facilitates comparison of treatment outcomes between centres, improves prognosis, and promotes individualized therapeutic management. A summary of the main AJCC categories is presented in Table 2.

Table 2: AJCC System (8th Edition) – Abbreviated TNMH Classification of Retinoblastoma

Category	Description
T – Primary Tumour	
TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
T1	Tumour ≤ 2/3 of the eyeball volume, without vitreous or subretinal seeding
T1a	Tumour ≤ 3 mm, ≥ 1.5 mm from the optic nerve/macula
T1b	Tumour ≤ 3 mm, < 1.5 mm from the optic nerve/macula, without exudation > 5 mm
T1c	Tumour > 3 mm, ≥ 1.5 mm from the optic nerve/macula, with exudation ≤ 5 mm
T2	Tumour ≤ 2/3 of the eyeball, with vitreous/subretinal seeding
T2a	Focal seeding (small aggregates)
T2b	Massive seeding (diffuse clusters)
T3	Tumour > 2/3 of the eyeball or optic nerve/choroid involvement
T4	Extraocular disease (orbit, brain)
N – Lymph nodes	
NX	Lymph nodes cannot be assessed
N0	No lymph node involvement
N1	Regional node involvement (parotid, cervical)
N2	Distant node involvement
M – Distant metastases	
M0	No metastases
M1a	Single extra-CNS metastases
M1b	Multiple extra-CNS metastases
M1c	CNS metastasis (presellar)
M1d	CNS metastasis (retrosellar)
M1e	CNS metastasis with meningeal/CNS involvement

Source: own archive based on [2,20].

It is worth emphasizing that many diseases can clinically imitate various forms of retinoblastoma. Conditions that cause the white pupil sign include congenital cataracts, retinopathy of prematurity (ROP) stage 5, persistent Persistent Fetal Vasculature (PFV), Coats' disease, and hereditary retinopathies such as Familial Exudative Vitreoretinopathy (FEVR). Congenital disorders such as coloboma, certain tumours, and non-cancerous lesions, such as medulloblastoma, astrocytoma (or astrocytic hamartoma), tuberous sclerosis, toxocariasis, or endophthalmitis, can also produce a similar appearance. For this reason, a thorough differential diagnosis is particularly important, as it forms the basis for an accurate diagnosis and proper treatment planning.

TREATMENT

Retinoblastoma treatment should be individualized and conducted within an interdisciplinary team. The choice of strategy depends on the stage of the disease, the location and number of tumours, the patient's age, and the possibility of preserving visual

function. Specialists from many fields participate in the treatment process: ophthalmologists, oncologists, paediatric haematologists, radiologists, radiotherapists, geneticists, pathologists, paediatricians, family doctors, anaesthesiologists and psychologists.

The team is complemented by appropriately trained nurses and typhlopedagogues, and, if necessary, a gynaecologist, due to the care of patients of reproductive age and potential genetic predispositions [2].

Chemotherapy

Currently, the primary treatment method for retinoblastoma is chemotherapy, aimed at reducing the tumour mass (*chemoreduction*), which creates conditions for the use of less invasive local therapies and increases the chances of eyeball preservation. Intravenous carboplatin, etoposide, and vincristine (CEV regimen) are typically administered in 3–6 cycles, administered every 2–4 weeks. Some clinical centres, however, implement simplified regimens. Local treatment usually begins after the second cycle, once significant tumour regression has been achieved and the subretinal fluid has been absorbed. In advanced cases, in order to increase the drug concentration within the tumour while limiting systemic toxicity, intraarterial chemotherapy (*IAC*), is used, which involves the selective administration of cytostatics, most often melphalan or topotecan, through a catheter in the ophthalmic artery. This method is highly effective and, in many cases, allows for the preservation of the eyeball. Alternatively, in cases of vitreous and subretinal seeding, intravitreal chemotherapy (*IVitC*), is used, most often with melphalan [22,2]. Chemoreduction allows for eyeball preservation in approximately 85% of cases in groups I–IV and in 47% in group V according to the Reese-Ellsworth classification. However, the greatest problem remains recurrence in the form of tumour cell dissemination into the vitreous humour or subretinal fluid, usually within two years of completing therapy. Treatment for recurrence depends on the extent of the lesion and also includes cryotherapy, brachytherapy, external beam radiation therapy (EBRT), or enucleation. Tumour consolidation after chemotherapy using transpupillary thermotherapy (TTT) or cryotherapy plays a key role, significantly reducing the risk of recurrence.

In selected cases, especially in children with advanced disease in both eyes or in a single eye, subconjunctival administration of carboplatin is used in combination with systemic chemotherapy. This strategy increases drug penetration into the vitreous humour, but carries a risk of local complications. An alternative for small tumours with minimal tumour cell count in the vitreous is chemothermotherapy, which involves intravenous administration of carboplatin with the simultaneous use of a diode laser. This method reduces the toxicity of systemic treatment [23].

Local Treatment

Treatment aims to destroy remaining tumour foci after chemoreduction or to treat small tumours in their initial stages. The following section presents local treatment methods that play a key role in this process.

Transpupillary thermotherapy (TTT) involves heating tumour tissue using a diode laser (810 nm) to a temperature of 45–60°C, which leads to tumour necrosis while preserving retinal vessels [24]. It is used to treat tumours measuring <3 mm in diameter without vitreous or subretinal seeding, most often in combination with chemoreduction or intravenous carboplatin (chemotherapeutic therapy), allowing for the synergistic effect of both methods. The procedure is particularly useful for lesions located near the macula or optic nerve, where other local methods, such as photocoagulation or radiotherapy, could cause more severe visual impairment. Three sessions are typically performed at monthly intervals, aiming to achieve the characteristic gray-white discolouration of the tumour tissue. In appropriately selected cases, complete disease control is achieved in 86% of patients [23]. Possible complications include localized iris atrophy, off-axis lens opacity, retinal traction, transient serous retinal detachment, and transient papilledema.

Cryotherapy is an effective treatment for small retinoblastoma tumours with a base diameter of ≤3.5 mm and a thickness of ≤3.0 mm, located near the equator or in the periphery of the retina. The procedure involves a triple freeze-thaw cycle, usually in one or two sessions performed approximately one month apart. However, this method is not effective in the presence of retinoblastoma seeding in the vitreous humour. In such cases, brachytherapy remains the preferred treatment option. Cryotherapy plays an important role as a consolidation method after chemoreduction, particularly in the treatment of seeding in the subretinal fluid near the ora serrata. It can also be used to improve the permeability of cytostatics to the vitreous humour at the early stage of chemoreduction, which is important in patients with multiple retinoblastoma seeds in the vitreous humour. Possible complications include transient serous retinal detachment, localized preretinal fibrosis, retinal tear, and rhegmatogenous retinal detachment [23, 25].

Brachytherapy (Ru-106, I-125, Pd-103) involves surgical placement of a radioactive applicator in the form of a plate on the sclera directly above the base of the tumour. It is used both as a primary and secondary treatment, most often in chemotherapy-resistant or recurrent lesions [8]. This method is indicated for tumours with a base diameter of less than 16 mm and a thickness of up to 8 mm.

The standard irradiation duration is 2–4 days, delivering a dose of 45 Gy to the tumour apex. In practice, brachytherapy can be used as a first-line treatment or after failure of other methods, such as radiotherapy or chemotherapy. The effectiveness of this method is very high. Local control is achieved in over 90% of cases when it is used as a primary treatment method [23]. The choice of radiation source depends on the size of the lesion – for tumours measuring ≤5–6 mm in diameter, ruthenium-106 (Ru-106) applicators are preferred, while for larger lesions (up to 8 mm, rarely up to 10 mm), iodine-125 (I-125) is used, which helps reduce the risk of complications.

Laser photocoagulation is a method rarely used today, involving the destruction of vessels feeding the tumour, primarily for small lesions in the posterior retina [21, 26].

External Beam Radiation Therapy (EBRT)

External Beam Radiation Therapy (EBRT) remains a treatment method primarily used for advanced forms of retinoblastoma, especially in cases of diffuse vitreous seeding.

The tumour is radiosensitive, and irradiation of the entire eyeball may allow for the preservation of vision, especially when other treatments prove ineffective or are contraindicated [23]. Compared to previous treatment methods, the introduction of modern techniques, including lens-sparing methods, has contributed to an increased rate of eyeball preservation. The highest risk of relapse after EBRT occurs within 1–4 years of completing therapy and depends on the stage and size of the tumour at the time of treatment initiation. The limitations of this method include complications such as cataracts, radiation retinopathy, optic neuropathy, and secondary cancers, the risk of which is particularly high in patients with the RB1 mutation, especially when radiotherapy was administered before 12 months of age.

In selected cases, an alternative to classical EBRT may be proton beam therapy, which – thanks to the Bragg peak phenomenon – allows for more precise dose delivery to the tumour while limiting damage to healthy tissues. Therefore, this method is particularly useful in cases where maximum preservation of ocular function and structure is crucial [2, 23, 27].

Enucleation

Enucleation remains a treatment method used when vision preservation is not possible – in cases of extensive intraocular involvement or a high risk of tumour spread. This procedure is most often performed in patients with unilateral retinoblastoma, although in exceptional cases it may also be necessary in cases of bilateral involvement when the primary goal is to save the patient's life. Enucleation involves the removal of the eyeball along with a section of the optic nerve at least 1 cm long, which is crucial for assessing potential tumour infiltration [27].

Thanks to advances in the development of orbital implants (such as hydroxyapatite or porous polymers) and modern cosmetic prostheses and epiprostheses, it is possible to achieve good aesthetic results and significantly improve patients' quality of life [2]. In exceptionally advanced cases, when the cancer has spread to the orbital tissues, orbital exenteration (*exenteratio orbitae*) surgery may also be necessary, as a life-saving procedure.

Experimental Therapies

Currently, research is being conducted on innovative targeted treatment methods, including the experimental use of SYK (*Spleen Tyrosine Kinase*) inhibitors, immunotherapy (including monoclonal antibodies), and approaches in gene and epigenetic therapy. Modern controlled drug release systems, such as biodegradable implants and micro needles, are also being developed, enabling precise administration of therapeutic substances via the supra-arachnoid or intravenous route [28].

Metastases

Despite the use of modern treatment methods, in some cases – especially those untreated or refractory to therapy – metastases from retinoblastoma may develop. In developed countries, these metastases are rare and usually appear within the first 12 months of tumour

diagnosis [19]. Cancer spread occurs primarily through infiltration of the choroid, optic nerve, and sclera, resulting in involvement of the orbit, central nervous system, and haematogenous metastases.

They most often occur in the skull bones, long bones of the limbs, internal organs (especially the liver), lymph nodes, brain, and spinal cord [18]. Metastases, especially bone metastases, can cause significant pain and discomfort, while involvement of the central nervous system and increased intracranial pressure often lead to headaches. In such situations, treatment is based primarily on systemic chemotherapy, supplemented with local treatment and, in selected cases, also megachemotherapy with haematopoietic cell transplantation [5,11].

Prognosis and Efficacy of Retinoblastoma Treatment

Spontaneous resolution of the disease is observed in approximately 3% of patients, primarily in the neonatal period and infancy [1]. Regression of retinoblastoma can vary depending on the size and stage of the tumour. It is usually an asymptomatic process, leading to the development of an inactive lesion within the retina, often with presence of calcifications. After reductive chemotherapy, small tumours (up to 3 mm) usually regress, forming flat scars. Medium-sized lesions (3–8 mm) leave flat or partially calcified remnants, while large lesions (> 8 mm) usually develop into clearly visible masses with a calcified structure [5]. In recent years, significant progress has been made in the treatment of retinoblastoma [26, 27]. Ophthalmic artery chemosurgery and intravitreous chemotherapy have almost completely replaced external beam radiation therapy (EBRT) and significantly reduced the use of systemic chemotherapy. As a result, the number of enucleations performed has also significantly decreased.

The use of sparing therapies, combining selective chemoreduction with local treatment, has significantly improved prognosis and reduced morbidity and mortality rates. Genetic testing, particularly analysis of RB1 gene mutations, is becoming increasingly important in treatment planning. This allows for a more accurate prognosis and the selection of an individual treatment strategy. In bilateral forms, particular attention is paid to preserving the eyeballs by combining systemic and local chemotherapy with focal treatment. In brachytherapy, the use of Ru-106 applicators is preferred for treating tumours ≤ 5–6 mm thick, while I-125 applicators are used for larger lesions, which allows for high efficacy while reducing the risk of complications. Early diagnosis, monitoring of treatment effects, and detection of recurrence are possible thanks to modern imaging techniques [29]. Thanks to modern treatment methods, a child's life can be saved in over 90% of cases, and in many cases, it is also possible to preserve useful vision in at least one eye [18]. These advances have translated not only into better treatment outcomes but also into a significant improvement in the quality of life of patients [22]. Prognosis depends on factors such as tumour location and advancement, response to treatment, and the risk of secondary tumours. A significantly more favourable outcome is observed in the monocular form.

However, a poorer prognosis is observed in patients with extraocular (trilateral) retinoblastoma, although the use of combination chemotherapy has also significantly improved treatment outcomes in this group [29]. The degree of differentiation and the presence of high-risk factors, such as choroidal or optic nerve invasion, are crucial for prognostic significance [1].

Figure 2 shows the fundus image of the right eye after treatment for retinoblastoma in a 7-year-old female patient. Intra-arterial chemotherapy guided by cerebral angiography was administered, resulting in regression of the calcified, inactive tumour in the posterior retina.

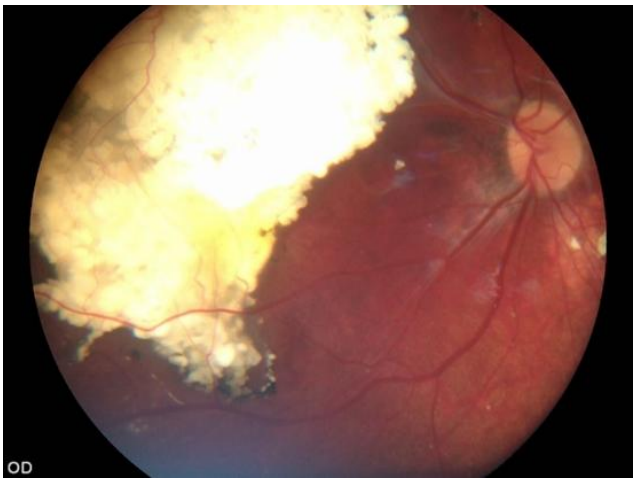

Figure 2: Image of the right eye fundus of a 7-year-old patient after completion of treatment for retinoblastoma

Photo: own archive.

SIDE EFFECTS AFTER TREATMENT

According to Furdova and Sekac [30], young adults treated for retinoblastoma in childhood may experience numerous late complications of treatment. Their nature depends on the type of therapy used and the extent of the neoplastic lesions, and the consequences encompass both the patient's physical and mental functioning. Based on the literature, they can be divided into four groups described below.

Ophthalmological Complications

The most common complications include visual disturbances, including amblyopia, visual field defects, disturbances in depth and contrast perception, strabismus, and nystagmus. Fabian et al. [11] showed that the mean visual acuity in patients after multimodal therapy was 0.07, and strabismus occurred in 60% of patients [31].

Loss of an eyeball and associated cosmetic defects, such as orbital collapse or facial asymmetry, also pose a significant clinical and aesthetic problem.

Systemic Complications

Long-term systemic consequences include growth retardation, somatic development disorders, and organ damage. Batra et al. [32] report that up to one-third of patients with retinoblastoma have short stature, which may be a consequence of prior chemotherapy or radiotherapy. Additionally, some patients develop renal dysfunction, heart disease resulting from the cardiotoxicity of the treatment, and fertility problems. Patients with a hereditary form of the disease also face an increased risk of subsequent malignant neoplasms (SMN).

Cognitive and Emotional Complications

As Dimaras [33] notes, such children may experience difficulties in cognitive and emotional development. The severity of these difficulties is related, among other things, to the need for frequent diagnostic procedures under general anaesthesia, which may adversely affect the maturation of the nervous system and neurocognitive development.

As a result of these experiences and the limitations resulting from reduced visual functions, these children may be shy, have difficulty establishing and maintaining relationships with peers, and their assimilation in preschool or school settings may be slowed. In addition, visual deficits can translate into learning difficulties, particularly in reading, writing, and spatial orientation, which requires individualized educational support.

Psychosocial Challenges and the Importance of Multidisciplinary Care

Effective treatment of retinoblastoma requires not only modern medical methods but also comprehensive support for patients and their families. In adulthood, many patients experience emotional and social problems. Banerjee et al. [34] describe difficulties in adaptation, reduced self-esteem, fear of disease recurrence, and limitations in professional and social activity. In response to these needs, support and intervention programs are being developed to improve quality of life and teach effective strategies for coping with the long-term effects of childhood cancer. In children after retinoblastoma treatment who have preserved their eyes but have significant vision limitations, visual rehabilitation conducted by typhlopedagogues in specialized centres is recommended. Its goal is to maximize the use of residual visual functions in daily life through functional training, compensatory techniques, the use of optical aids, and environmental adaptation [2].

The best therapeutic and psychosocial results are achieved in centres with a multidisciplinary team, including ophthalmologists, orthoptists, oncologists, geneticists, nurses, psychologists, and occupational therapists. An important element of the care system is the inclusion of patient organizations and support groups that provide psychosocial and non-medical support to families. This approach, used in the United Kingdom with the participation of The Childhood Eye Cancer Trust, is an integral part of the comprehensive treatment of a child with retinoblastoma [26].

CONCLUSIONS

Retinoblastoma is a malignant eye tumour, often with a hereditary basis. Symptoms such as strabismus or a white pupil may indicate its presence or other serious intraocular pathologies. Therefore, they should not be ignored – regardless of the child's age, their occurrence should prompt immediate ophthalmological evaluation [35]. Although the RB1 gene responsible for the development of the disease has been identified, the mechanisms underlying its development have not yet been fully understood [36]. The basic and commonly used diagnostic test for retinoblastoma remains fundoscopy. Although treatment requires highly specialized care, every ophthalmologist should be able to recognize its symptoms and know when to refer the patient to a reference centre. Prenatal molecular diagnosis is also extremely important, as early detection of changes increases the chances of giving birth to a child without detectable tumours, enables the use of less invasive

therapies, and improves the prognosis for vision preservation [37]. Thanks to advances in oncological treatment, children with retinoblastoma now have a very high chance of complete recovery. In many cases, it is possible not only to preserve the eyeball but also to maintain visual function. In high-income countries, including Poland, the survival rate is as high as 98% [2, 38].

Currently, all modern retinoblastoma treatment methods are available in Poland, eliminating the need for patients to travel abroad, for example, to the United States. Visual rehabilitation plays a key role and should be initiated as soon as possible after tumour control is achieved [39]. Its goal is to prevent the negative impact of the disease on the child's motor, linguistic, social, and cognitive development. It is also recommended to wear constant eye protection, preferably in the form of glasses with polycarbonate lenses.

Optical and non-optical aids for visually impaired people, such as magnifying glasses or illuminated magnifying devices, are also helpful in everyday functioning. In the treatment of retinoblastoma, the most important goal is to save the child's life. Only then is an attempt made to preserve the eyeball [23]. Thanks to medical advances, particularly the development of diagnostic and therapeutic methods, this cancer has become one of the most promising among children in high-income countries. However, the widespread use of preventive measures, such as the routine performance of the red reflex test in all newborns, early diagnosis of the disease, and the implementation of increasingly effective treatment strategies that consider not only ophthalmological aspects but also systemic, emotional, and psychosocial ones, remain a challenge.

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