Diagnosis and Classification of ROP

4

Anna L. Ells

Abstract

Retinopathy of prematurity (ROP) is a vasoproliferative disease that affects those infants born of the smallest weight and lowest gestational ages. The disease is characterized by its morphology and described as the International Classification of Retinopathy of Prematurity (ICROP). Zone, stage, presence of pre-plus or plus disease and aggressive posterior disease, define the morphology possibly seen during the acute phase of ROP.

Keywords

Retinopathy of prematurity (ROP) · International classification of ROP (ICROP) · Zone · Stage · Plus disease · Aggressive posterior ROP

4.1 Introduction

Retinopathy of prematurity (ROP) is a vasoproliferative disease that affects those infants born of the smallest weight and lowest gestational ages [1]. The disease is characterized by its morphology and described in the International Classification of Retinopathy of Prematurity (ICROP) [2–4]. ICROP is used by all ophthalmologists to document the severity of the ROP seen on clinical examination.

4.2 Diagnosis

Premature infants are examined in the neonatal intensive care unit (NICU). Visualization of the premature retina is performed using an indirect ophthalmoscope and a 25 or 28 diopter condensing lens [5]. Digital imaging systems can also be used to identify, photograph, and document the ROP [6, 7]. In some tertiary centers, fluorescein angiography may be performed for additional diagnostic purposes [8].

Most countries have their own national evidence-based recommended ROP screening guidelines that are used as a protocol for screening [9, 10]. In the United States, infants with a birth weight of less than 1500 g or a gestational age of less than 31 weeks require an ROP screening examination [11]. Also, infants of less than 2000 g with an unstable clinical course may be referred for an ROP examination [11, 12]. It is important to note that premature infants requiring ROP examinations in developing countries are larger in weight and have older gestational ages [10].

The first exam is at 4 to 6 weeks after birth but this can be dramatically earlier in infants born in developing countries [10, 11, 13]. Subsequent ROP examinations intervals are determined by the examining ophthalmologist and will be every 1 or 2 weeks unless treatment is required. Treatment is recommended within 48–72 hours of diagnosis of Type I ROP, defined as: zone I, any stage ROP with plus; zone I with stage 3, with or without plus and zone II with stage 2 or 3, with plus disease [13, 14].

Ongoing retinal ROP examinations are required until the retina is vascularized into zone III and the infant is at least 37 weeks of post-menstrual age. If ROP is still present, examinations should continue until there are at least two consecutive exams without ROP and vessels are in zone III.

4.3 Classification

The classification system is based on the morphology of the vasoproliferative disease present at the time of examination.

4.4 Location of Disease

The location of ROP is defined by anteroposterior zones, in three concentric rings.

A. L. Ells (✉)
University of Calgary, Calgary, AB, Canada

W.-C. Wu, W.-C. Lam (eds.), *A Quick Guide to Pediatric Retina*, https://doi.org/10.1007/978-981-15-6552-6_4

Zone I is centered on the optic disc with a radius of twice the distance from the center of the optic disc to the center of the fovea. This zone is the most posterior and ROP located within this zone is predicted to be the most severe form of the disease [4].

Zone II defines the area of the retina from the border of zone I to the nasal ora serrata.

Zone III is the crescent of retina adjacent to the temporal border of zone II (Fig. 4.1).

4.5 Clinical Approach to Localization the Zone of ROP

If using indirect ophthalmoscopy to perform the ROP clinical examination, the extent of zone I can be defined by using a 25 or 28 diopter condensing lens and placing the nasal edge of the optic disc at one end of the physician's field of view, then the retina that is visualized will be within zone I (Fig. 4.2). [5]. If wide-field digital imaging systems are used,

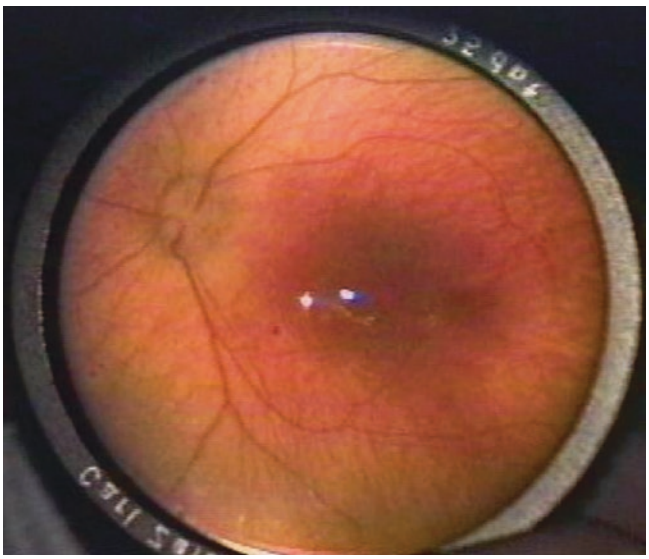

Fig. 4.2 Indirect ophthalmoscopy image through a 25 diopter condensing lens, may be used to clinically approximate the extent of zone I [4]. © International Committee for the Retinopathy of Prematurity

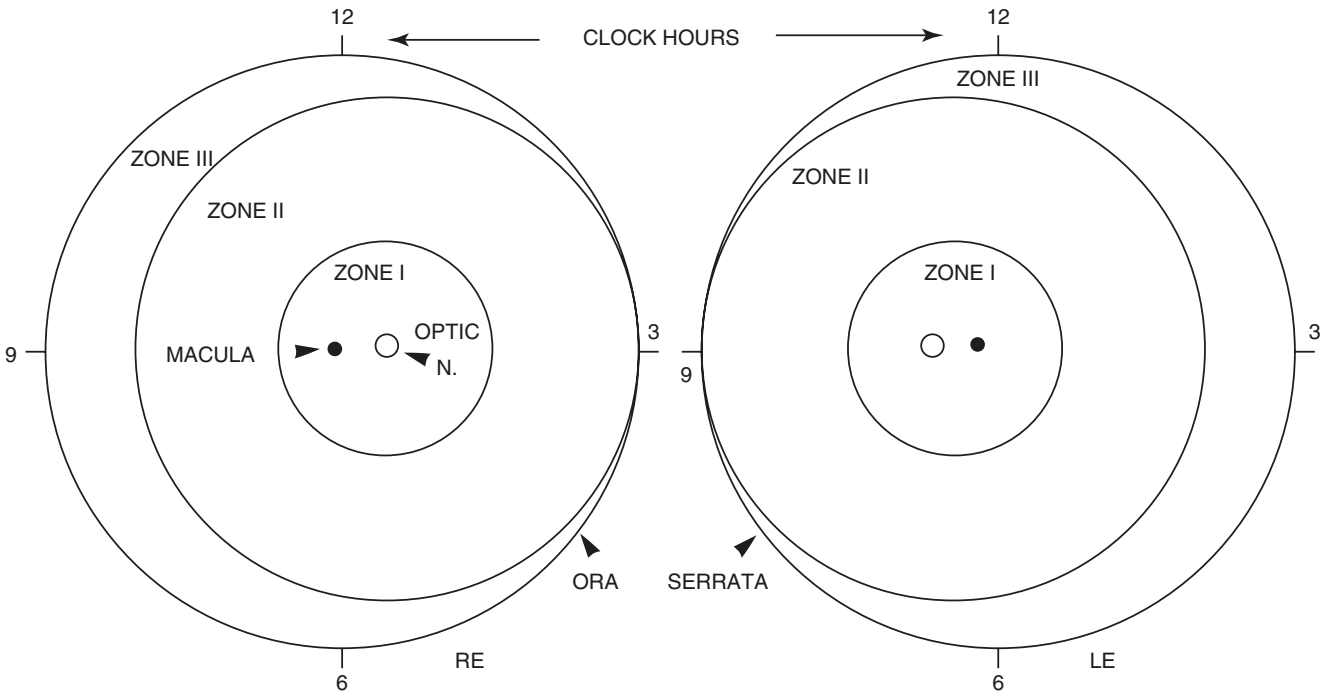

Fig. 4.1 This figure illustrates the position of the concentric zones, with zone I and II, centered around the optic disc. Clock hours are also used to localize the ROP lesions [4]. © International Committee for the Retinopathy of Prematurity

the physician must identify the fovea (which may be underdeveloped and difficult to identify), in order to define zone I limits [15–17].

4.5.1 Key Points About Zones

1. Zones define the geography and location of the ROP.
2. Zones I and II are concentric rings centered around the optic disc.
3. Zone I is most posterior and the predictor of the most severe ROP.

4.6 Staging of the Disease

The five stages of the disease describe the morphology of the ROP as seen on clinical examination or on digital imaging. One or more stages of disease can be present at any time in the eye (Fig. 4.9). The stages are documented according to how many clock hours they occupy in the retina. Retinal vascularization may initially be incomplete but no ROP is present, and this is referred to as immature retina (Fig. 4.3).

- Stage 1: defined by a demarcating intra-retinal structure or line that divides the vascularized retina from the avascularized retina (Fig. 4.4).

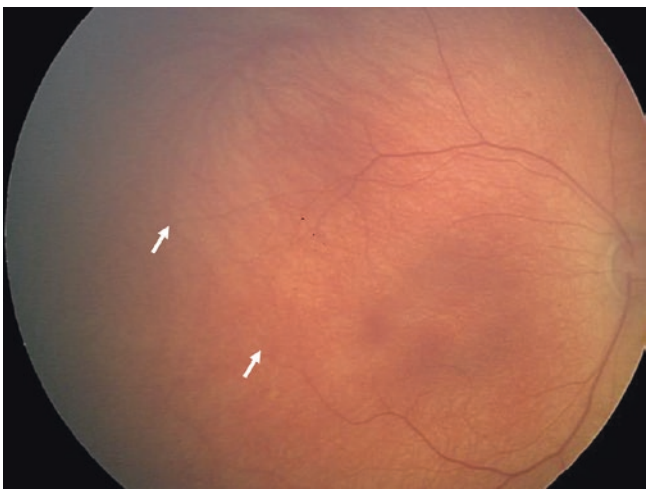

Fig. 4.3 Immature retina. This image demonstrates the immature retinal vessels (arrows) located in posterior zone II without the presence of ROP. © International Committee for the Retinopathy of Prematurity

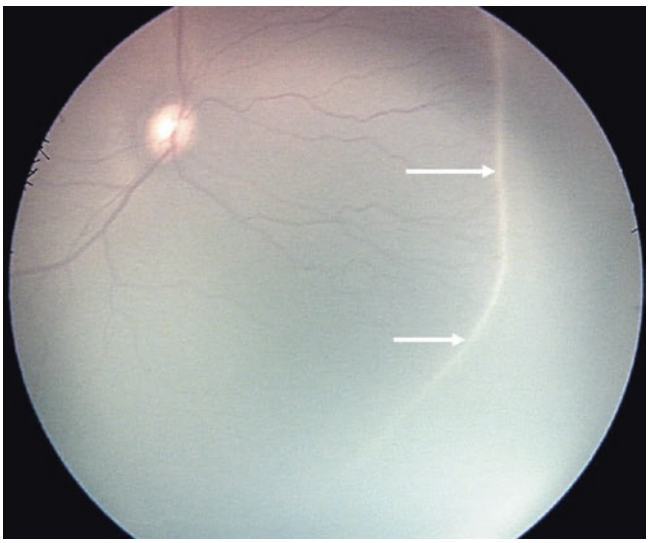

Fig. 4.4 Stage 1 ROP. Arrows are at the demarcating line between vascularized and non-vascularized retina. © International Committee for the Retinopathy of Prematurity

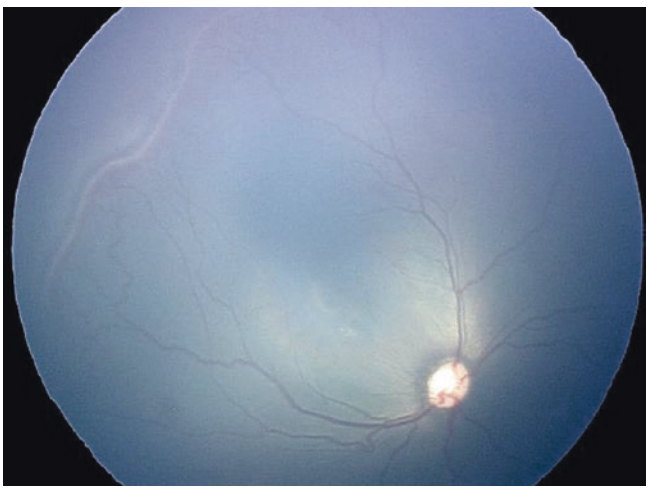

Fig. 4.5 Stage 2 ROP. The ridge can be seen between vascularized and non-vascularized retina. © International Committee for the Retinopathy of Prematurity

- Stage 2: defined by a ridge structure that has height and width and develops from the demarcating line as the disease progresses (Fig. 4.5).
- Stage 3: defined by extraretinal fibrovascular proliferation or neovascularization that extends from the ridge structure into the vitreous (Figs. 4.6, 4.7, 4.8, and 4.9).
- Stage 4A: extrafoveal retinal detachment (Fig. 4.10).

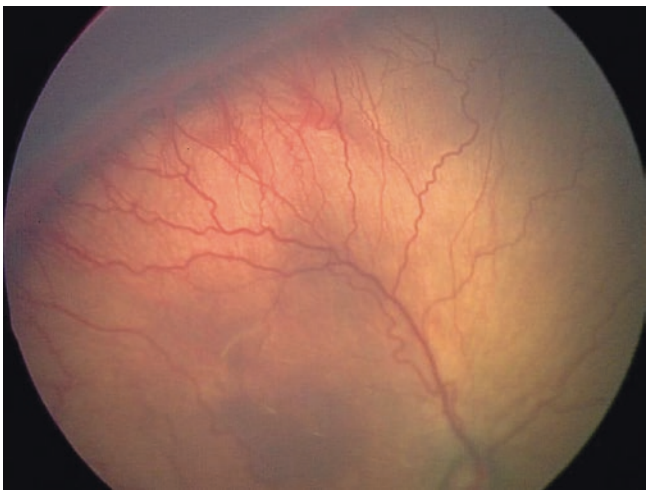

Fig. 4.6 Stage 3 ROP can be seen in the superior part of the image. The ridge is elevated and there is neovascularization on the surface of the ridge. Note the arborization of vessels just posterior to the ridge. © International Committee for the Retinopathy of Prematurity

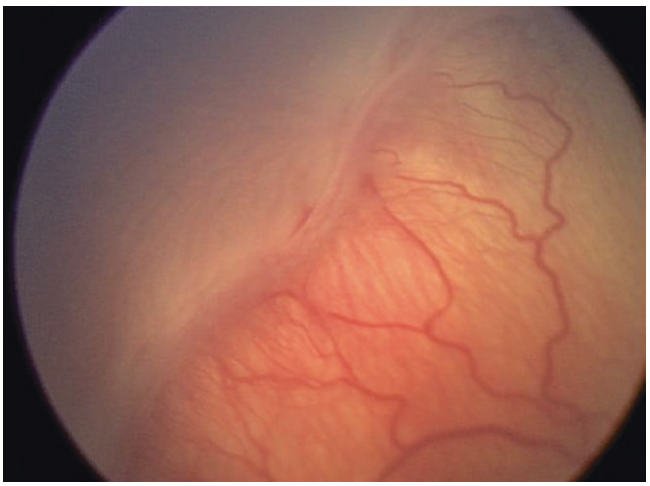

Fig. 4.7 High magnification of Stage 3. © International Committee for the Retinopathy of Prematurity

- Stage 4B: foveal retinal detachment (Fig. 4.11).
- Stage 5: total retinal detachment that is usually tractional, concave, or funnel in shape (Fig. 4.12).

4.6.1 Key Points About Stages of ROP

1. Stages describe the morphology and severity of the ROP.
2. Include stages 1–5.
3. There may be one or more stages within an eye concurrently.

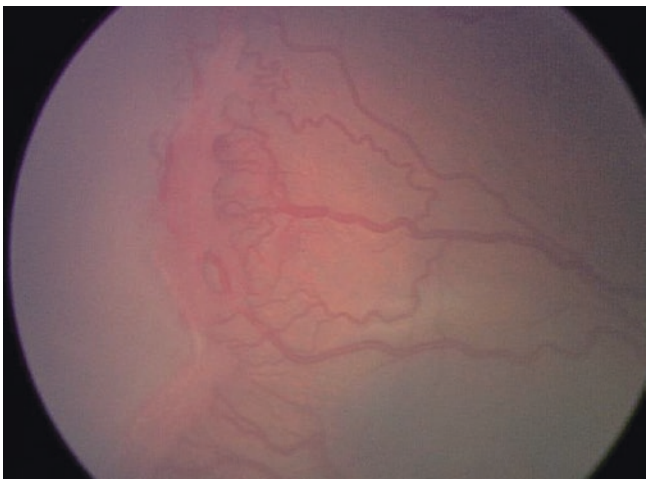

Fig. 4.8 High magnification of stage 3 fibrovascular proliferation at the junction between vascularized retina and non-vascularized retina. © International Committee for the Retinopathy of Prematurity

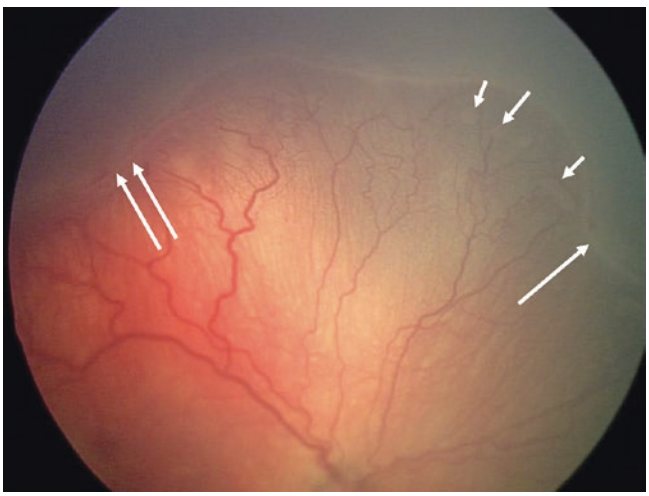

Fig. 4.9 Multiple stages of ROP may be concurrently present in the eye. Note stage 2 (long, single arrow), stage 3 (double arrows), and "popcorn" (short arrows) which are small regressing buds of neovascularization. There is also plus disease. © International Committee for the Retinopathy of Prematurity

4.7 Pre-plus and Plus Disease

In addition to the abnormal proliferation of retinal vasculature that is described in the stages of ROP, the existing arteries and veins of the retina may undergo changes as the severity of the ROP increases over time which include both dilation and tortuosity. Iris vascular engorgement may also occur. Mild dilation and tortuosity of the posterior pole vessels is called "pre-plus" disease and is defined as changes

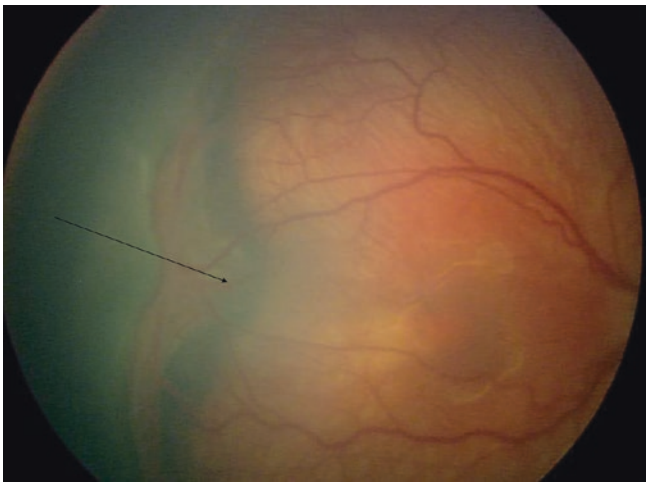

Fig. 4.10 Stage 4A. Widefield digital retinal image of 4A retinal detachment in ROP. Note the shallow temporal retinal detachment that does not involve the fovea (arrow). © International Committee for the Retinopathy of Prematurity

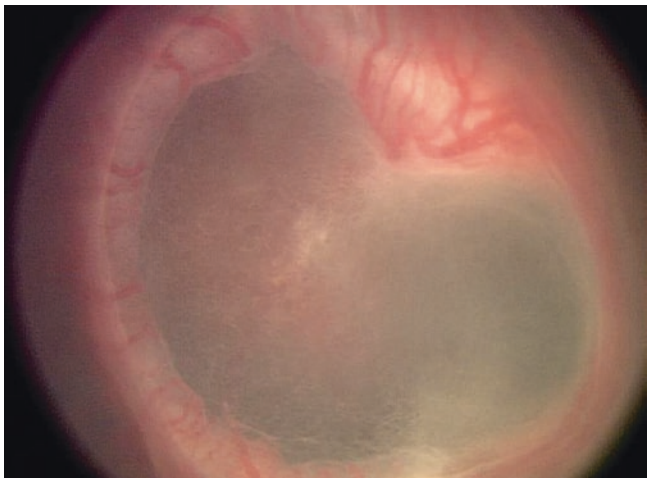

Fig. 4.12 Image of stage 5 ROP with an open funnel, total retinal detachment. © International Committee for the Retinopathy of Prematurity

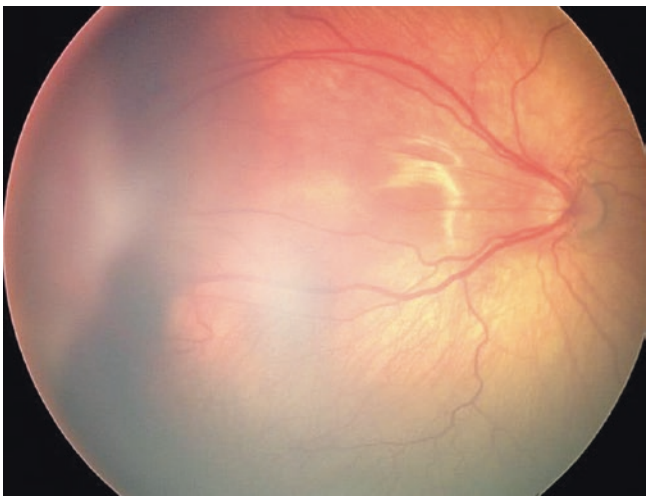

Fig. 4.11 Stage 4B. Widefield retinal image of stage 4B retinal detachment in ROP. Note the foveal involvement. © International Committee for the Retinopathy of Prematurity

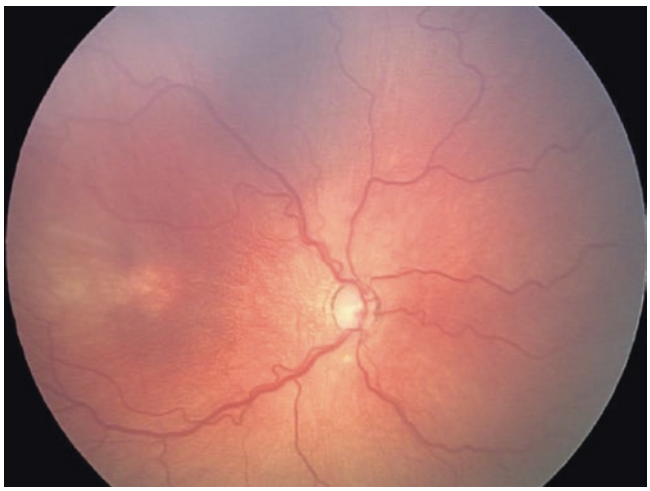

Fig. 4.13 Pre-plus disease. Image of pre-plus disease in ROP. There is a greater than normal amount of vascular dilation and tortuosity but insufficient for the diagnosis of plus disease. © International Committee for the Retinopathy of Prematurity

that are insufficient for the diagnosis of plus disease but are not normal (Fig. 4.13). These vascular changes may progress over time to become "plus disease" or they may regress to more normal caliber vessels as the ROP regresses. Plus disease is defined as venous and arterial dilation and tortuosity in at least two quadrants that met a minimum amount of abnormality that was originally defined by a photograph of the posterior pole in the original classification publication in 1984 (Fig. 4.14). [2] The clinical diagnosis of pre-plus and plus disease may vary between examiners either at the bedside during the clinical exam or in the evaluation of wide-field retinal digital images [6]. Automated retinal vessel computerized software is currently being researched and developed which may assist in the quantification of vascular changes so that the diagnosis of pre-plus and plus disease can be standardized between examiners [18–20]. The presence of plus disease almost always determines the need to treat an infant's eye with ROP therefore the standardization of this important clinical manifestation of ROP is critical [7].

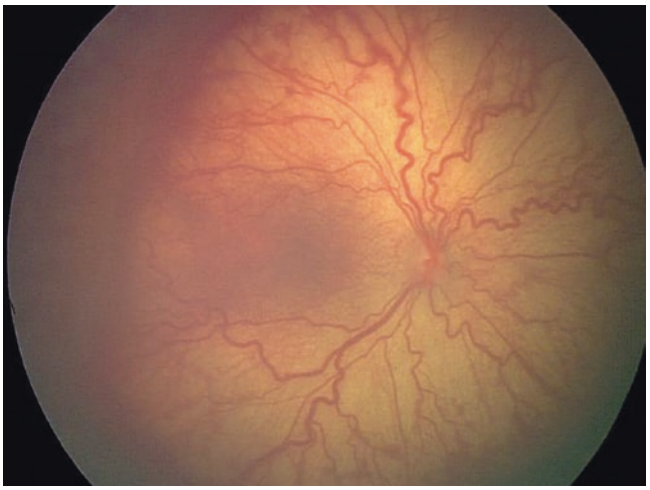

Fig. 4.14 Plus disease. Widefield digital retinal image of plus disease. Note extensive dilation and tortuosity in all four quadrants in the posterior pole. Venules are more dilated than the arterioles. It is difficult to see the temporal stage 3 present. © International Committee for the Retinopathy of Prematurity

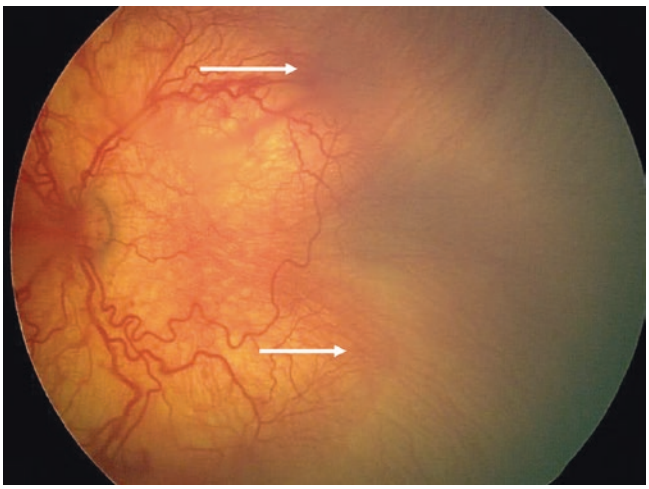

Fig. 4.15 Aggressive posterior ROP. © International Committee for the Retinopathy of Prematurity

4.7.1 Key Points About Pre-plus and Plus Disease

1. Pre-plus vascular changes are insufficient for the diagnosis of plus disease.
2. Plus disease requires at least two quadrants of abnormal dilation and tortuosity of posterior pole vessels.
3. The presence of plus disease almost always indicates the need to treat the eye.

4.8 Aggressive Posterior ROP (AP-ROP)

Aggressive posterior ROP is a rare but most severe form of ROP that is seen in extremely premature and low weight infants or in infants with prematurity and associated comorbidities of prematurity such as sepsis, pulmonary disease, and necrotizing enterocolitis [21, 22]. This virulent form of ROP is called aggressive posterior ROP and is characterized by its posterior location, usually zone I, relatively flat and extensive stage 3 neovascularization, and massive plus disease in all four quadrants (Figs. 4.15 and 4.16). An important feature of AP-ROP is that it does not usually progress through the stages of ROP but develops a flat network of neovascularization early on in the disease without the preexisting ridge.

4.8.1 Key Points About AP-ROP

1. AP-ROP is the most virulent and aggressive form of ROP.

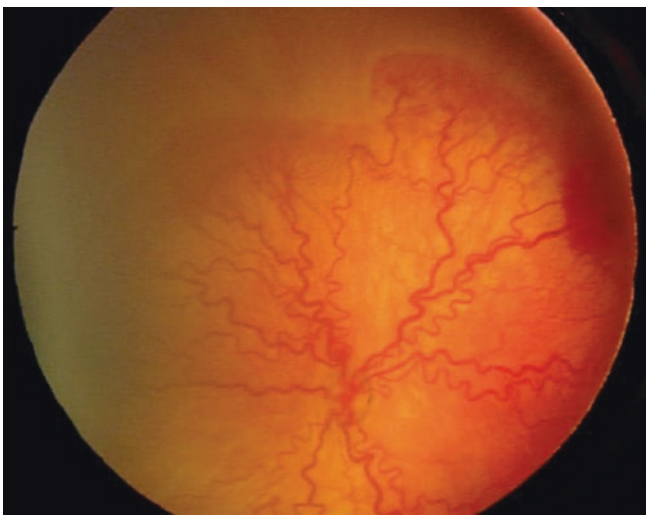

Fig. 4.16 Image of aggressive posterior ROP. Note the posterior location of zone I, the flat neovascularization (arrows), and the extensive plus disease present. © International Committee for the Retinopathy of Prematurity

2. Features massive plus disease, flat neovascularization, and usually zone I.
3. Lacks the classic stages of 1, 2, and 3. Often there is no ridge seen.

4.9 Regression of ROP

Acute ROP either progresses to a point that requires treatment, or it spontaneously regresses. Often the failure of one stage to progress to the next stage is an indication of regression. Signs of regression occur at the junction between vascularized and non-vascularized retina and retinal vessels

usually advance slowly toward the ora serrata. [23] The most peripheral retina may remain avascular as was noted in the 1987 ICROP publication on regression and retinal detachment [3]. It is extremely important to continue retinal examinations after treatment (regardless of treatment modality) or spontaneous regression to ensure adequate vascularization into zone III without reactivation of neovascularization. Failure to detect inadequately regressed ROP or significant persistent peripheral avascular retina over time may lead to cicatricial ROP causing visual loss or blindness. [24].

4.10 Summary

1. Clinical examination of the premature infant's retina is performed using an indirect ophthalmoscope or digital imaging systems to identify or photograph and document the ROP.
2. Evidence-based screening guidelines have been published for many countries and it is important to note that developing countries have very different birthweights and gestational ages of at-risk infants for Type I ROP.
3. ICROP is an international classification system, based on the morphology of the disease. The unifying principle of this classification is the more posterior the disease and the greater the amount of involved retinal vascular tissue, the more serious the disease. The presence of plus disease is critical to identify, as it almost always indicates the need for treatment.
4. Careful description, documentation, and photography may lead to more timely and accurate treatment of ROP.

Acknowledgments All figures are reprinted from the International Classification of Retinopathy of Prematurity Revisited, Arch Ophthalmol/Vol. 123, July 2005, with permission from the ICROP committee.

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