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Different retinopathy of prematurity severity and outcomes in triplets: A case report

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Abstract

In this case report, we discuss the presentation of retinopathy of prematurity in triplets born at 25 + 3 weeks gestational age of whom each had a different birth weight, weight gain and treatment requirements. Triplet A weighed 800 g and his retinopathy of prematurity had resolved with no intervention. Triplet B weighed 630 g at birth and he required bilateral intravitreal ranibizumab injection at 32 + 6 weeks. Triplet C weighed 520 g and required bilateral intravitreal ranibizumab injection at 36 weeks, but after 5 weeks he had recurrence which was treated with bilateral diode laser. Triplet C had the poorest weight gain. The main differences between the triplets are the birth weight and the weight gain. Furthermore, refraction was performed at 10 months; triplet A had a hyperopia of +1.25 spherical equivalent in both eyes, triplet B had mild myopia of −0.25 spherical equivalent and triplet C had a myopia of −3.00 spherical equivalent in the right eye and −2.75 spherical equivalent in the left eye.

Keywords

Ophthalmology, anti-VEGF, retinopathy of prematurity, laser, premature, triplets, weight gain

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Introduction

Retinopathy of prematurity (ROP) is an abnormal retinal vasculature development that may lead to retinal detachment.[1] Multiple risk factors have been associated with ROP development but the most significant are low birth weight and younger gestational age (GA).[1–4] Other risk factors include respiratory distress syndrome (RDS), sepsis, mechanical ventilation and intraventricular hemorrhage.[1–3] Studies are inconclusive with regard to the increased risk of ROP in multiple pregnancies versus singletons. Some studies showed no relation between multiple gestations and ROP development, while others showed an increased risk of ROP in multiple gestations.[4,5] Recent studies emphasize the importance of poor postnatal weight gain as a predictive factor of ROP which requires treatment. The calculation methods vary between studies: either absolute, relative or proportion weight gain.[2,6,7]

Case presentation

A 41-year-old mother was pregnant by in-vitro fertilization (IVF) treatment. She had no medical problems during the antenatal period. There is no consanguinity between the parents. All triplets were boys and were born at 25 + 3 weeks of GA by cesarean section.

Triplet A weighed 800 g and had patent ductus arteriosus (PDA), sepsis and RDS that progressed to chronic lung disease (CLD) and as a result was on mechanical ventilation for 61 days. He was treated with penicillin and gentamicin for presumed sepsis. At day 18, he had developed sepsis (blood culture showed *Staphylococcus capitis*) which was treated with teicoplanin and amikacin for 10 days. ROP screening at 32 + 6 weeks (weight 1.57 kg) revealed no ROP. At 34 + 6 weeks, his weight was 1.88 kg and he presented with stage 2, zone 2. At 41 weeks, there was no ROP detected on examination and his weight had increased to 3.70 kg. In the follow-up period after 10 months, his weight had increased to 7.99 kg and fundus examination showed zone 3 vascularization.

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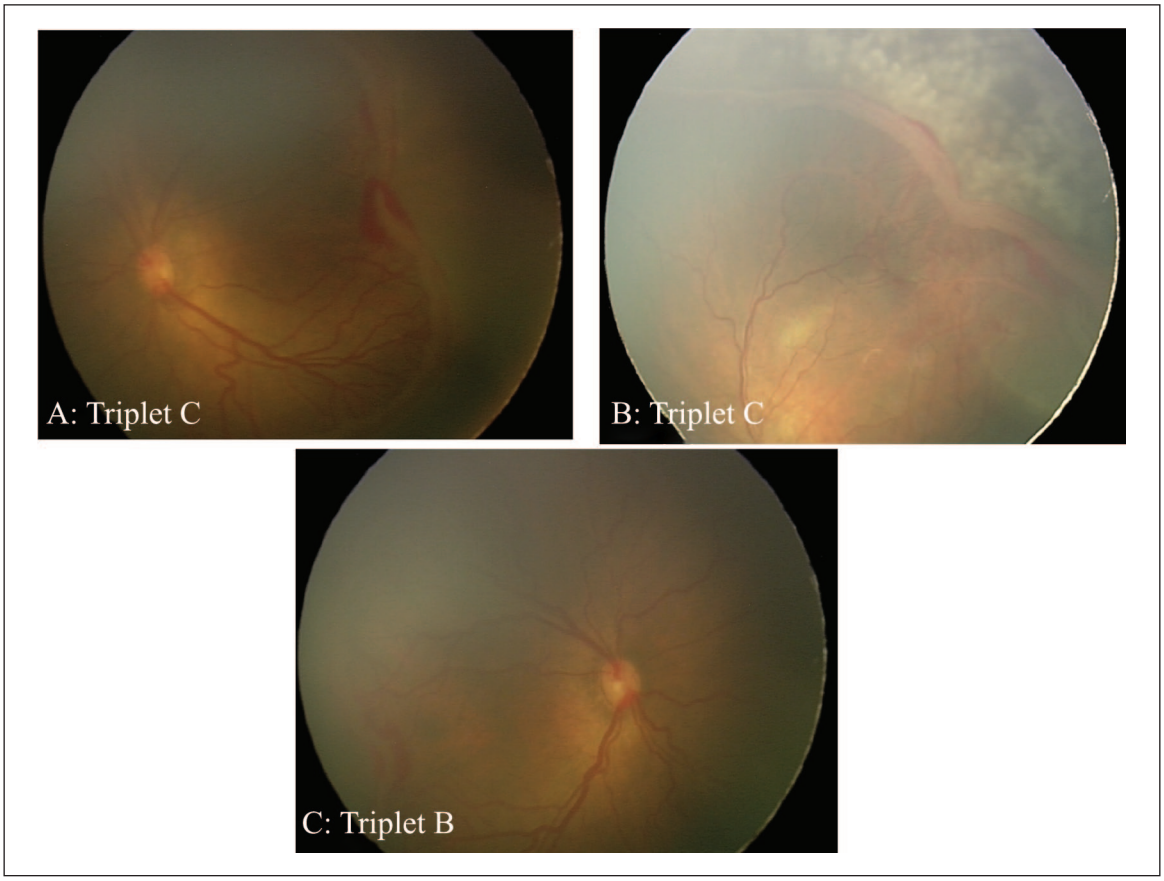

Figure 1. (A) Triplet C at 36 weeks: ROP stage 3, zone 2 with plus disease; before treatment with intravitreal ranibizumab injection. (B) Triplet C's right eye at 41 weeks: ROP stage 3, zone 2 with plus disease; treated with diode laser. (C) Triplet B at 32 + 6 weeks: ROP stage 3, zone 2 with plus disease but hazy view; before treatment with intravitreal ranibizumab injection.

Cycloplegic refraction was done revealing a mild hyperopia in both eyes (oculus dexter (OD): +1.5/−0.5 × 180, oculus sinister (OS): +1.5/−0.5 × 180).

Triplet B weighed 630 g at birth and he had PDA and RDS which progressed to CLD. He was intubated twice and was on mechanical ventilation for 85 days. He also had presumed sepsis and was treated with penicillin and gentamicin for 7 days. At 32 + 6 weeks, he weighed 1.470 kg but ROP screening showed bilateral stage 3, posterior zone 2 with plus disease (Figure 1). He was treated with intravitreal ranibizumab injection (0.03 mL) in both eyes. At 36 weeks, his weight increased to 1.91 kg and at 41 weeks his weight was 3.20 kg. At 10 months of age, the retina was vascularized to zone 3 with no plus disease. His weight was 8.30 kg and cycloplegic refraction for both eyes was done (OD: plano/−0.50 × 180, OS: plano/−0.50 × 180).

Triplet C's birth weight was 520 g with PDA, jaundice and RDS which progressed to CLD. He was intubated once and then was placed on mechanical ventilation for 63 days. At 36 weeks, he developed ROP stage 3, posterior zone 2 with plus disease while his weight was 1.65 kg. Intravitreal ranibizumab (0.03 mL) was injected in both eyes. After initial regression of ROP, it recurred again after 5 weeks with stage 3, zone 2 with plus disease in right eye (threshold disease); and stage 2, zone 2 with mild plus in left eye (Type I ROP). He was treated with diode laser photocoagulation in both eyes with 4435 shots in the right eye and 3969 shots in the left eye (Figure 1). His ROP regressed completely after laser treatment. After 10 months, his weight was 6.70 kg and he developed myopia. His cycloplegic refraction was (OD: −2.75/−0.50 × 180, OS: −2.50/−0.50 × 180). Table 1 summarizes the demographics of the triplets.

Discussion

In this case report, the triplets had similar comorbidities and risk factors, except for sepsis in triplet A and jaundice in triplet C. Furthermore, the most significant factor between the triplets was the birth weight. Triplet A with the highest birth weight (800 g) had no ROP; triplet B had lower birth weight (630 g) with bilateral threshold ROP requiring treatment with intravitreal ranibizumab injection; and triplet C had the lowest birth weight (520 g) with bilateral threshold ROP requiring treatment with intravitreal ranibizumab injection and recurrence of bilateral ROP treated with diode laser. In multiple pregnancies, the one with the lowest birth weight is at a

Table 1. Demographic data of the triplets (gestational age: 25 + 3 weeks).

	Triplet A	Triplet B	Triplet C
Birth weight	800 g	630 g	520 g
Comorbidities	PDA Presumed sepsis RDS CLD	PDA Presumed sepsis RDS CLD	PDA Jaundice RDS CLD
Ventilation and oxygen supply	Mechanical ventilation: 61 days	Intubated twice Mechanical ventilation: 85 days	Intubated once Mechanical ventilation: 63 days
ROP severity	34 + 6 GW: stage 2, zone 2	32 + 6 GW: bilateral stage 3, zone 2 with plus disease	36 GW: bilateral stage 3, zone 2 with plus disease
First treatment	None	Intravitreal ranibizumab injection	Intravitreal ranibizumab injection
Recurrence	None	None	41 GW: Right eye: stage 3, zone 2 with plus disease Left eye: stage 2, zone 2 with mild plus
Second treatment	None	None	Diode laser photocoagulation
Fenton chart (weight gain)	10th–50th percentile[a]	10th–50th percentile[a] At 34 GW: 3rd–10th percentile[b]	3rd–10th percentile[b] At 32 GW: below 3rd percentile
Cyclorefraction at 10 months	OD: +1.5/−0.5 × 180 OS: +1.5/−0.5 × 180	OD: plano/−0.50 × 180 OS: plano/0.50 × 180	OD: −2.75/−0.50 × 180 OS: −2.50/−0.50 × 180

PDA: patent ductus arteriosus; RDS: respiratory distress syndrome; CLD: chronic lung disease; ROP: retinopathy of prematurity; GW: gestational week; OD: oculus dexter; OS: oculus sinister.
[a]10th–50th percentile = appropriate for gestational age.
[b]3rd–10th percentile = small for gestational age.

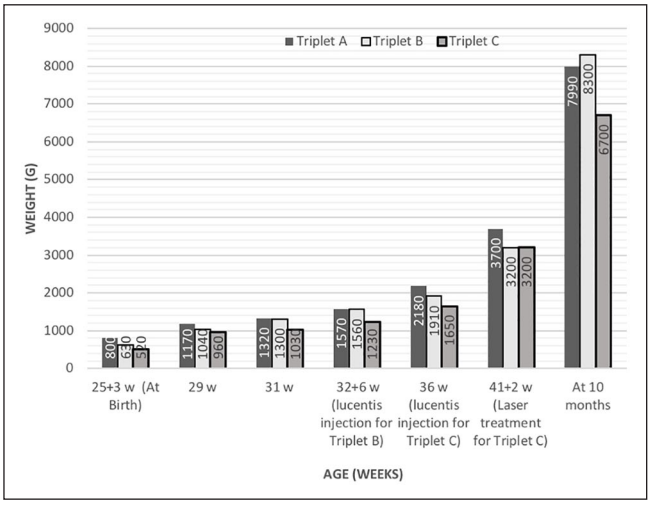

Figure 2. Weight gain differences between the triplets at different ages.

higher risk to get ROP and the order of deliveries had no correlation with increased ROP risk.[8] Infants who gain an average of 12 g/day have a decreased risk of plus disease, whereas those who gain an average of 4 g/day have an increased risk of plus disease. For every additional 100 g, risk of plus disease is reduced by 34%.[6] In our case, during the first 6 weeks, triplet A's average weight gain was 12.4 g/day, triplet B's average weight gain was 16 g/day and triplet C's average weight gain was 12.1 g/day (Figure 2). According to Fenton growth chart,[9] triplet A's weight gain was plotted within 10th to 50th percentile (appropriate for GA) and triplet B's weights were plotted within 10th to 50th percentile until 34 weeks GA when his weight gain dropped between 3rd and 10th percentile (small for gestational age (SGA)). In contrast, triplet C's birth weight was between 3rd and 10th percentile, and then he started to gain weight until 32 weeks when his weight gain was plotted below 3rd percentile until 41 weeks (Figure 3).[10] At this period, his ROP had progressed and he needed treatment with bilateral intravitreal injection and retinal ablation. Multiple studies have shown that SGA is associated with a higher risk of severe ROP which requires treatment.[11]

According to the Colorado Retinopathy of Prematurity Screening Algorithm, a net weight gain of 400 g or less within a month after birth serves as an alarm of developing high-risk ROP and a net weight gain of 650 g or less serves as an alarm for developing any ROP.[12] Although triplets B and C gained less than 650 g within 1 month and triplet A gained less than 400 g, the latter had the least risk. Ahmed and Badeeb[13] published the Alexandria retinopathy of prematurity model (Alex-ROP) which included the mean weight gain ratio 28 days after birth in addition to GA and birth weight. High-risk Alex-ROP screening model included postnatal weight gain ratio (PGWR) of less than 0.15.[13] Triplet A had PGWR of 0.46, triplet B had a ratio of 0.65 and triplet C had a ratio of 0.85. There have been different postnatal calculation methods published but none are ideal.[2,7,12,13] Triplets' weight gain pattern does not match any of the studies, in fact it was higher and incompatible.

With regard to the refractive error, triplet A (no treatment) had hyperopic eyes, triplet B (ranibizumab injection only)

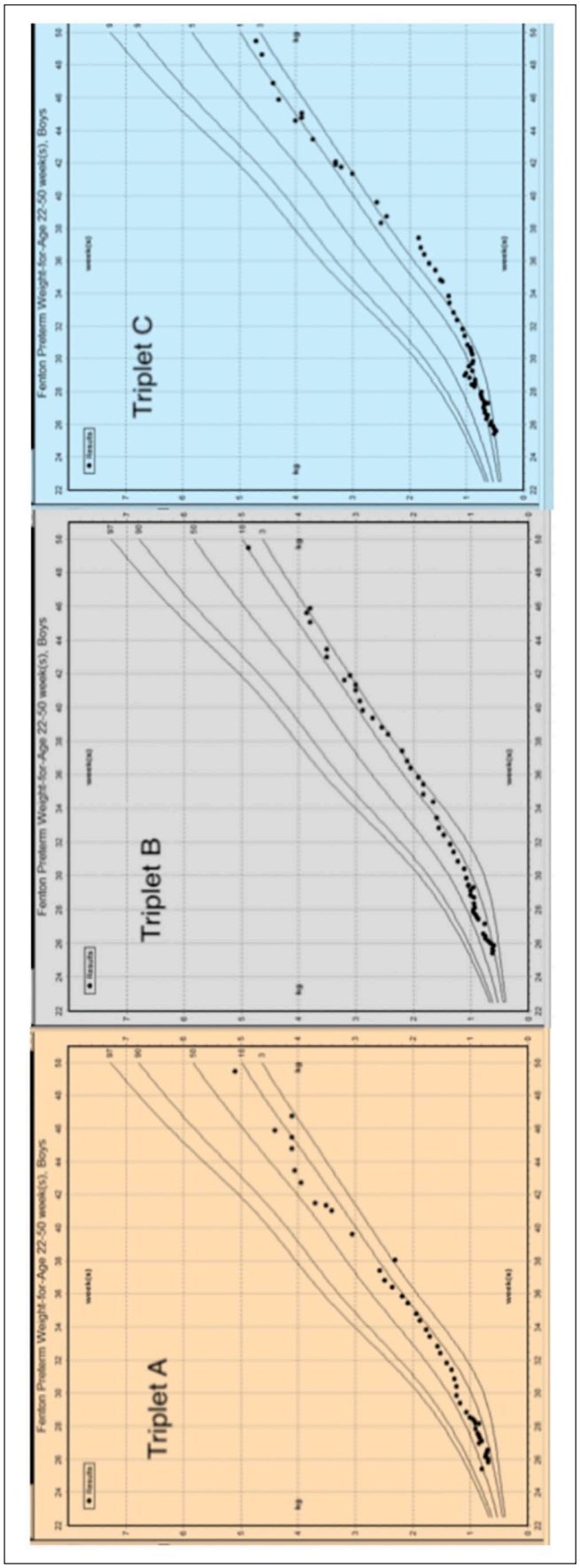

Figure 3. Fenton growth charts for the triplets (taken from their electronic file).
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had emmetropic eyes and triplet C (ranibizumab injection and laser) had myopic eyes at 10 months of age. Quinn et al.[14] reported that preterm babies with ROP requiring retinal ablation treatment were more likely to get a higher degree of myopia which correlates well with our triplets in this case report. Preterm babies with ROP treated with intravitreal anti-vascular endothelial growth factor injections showed significantly less myopia (-1.04 ± 4.24) in comparison with preterm babies treated with retinal ablation (-4.41 ± 5.50), as in triplet B.[15]

Conclusion

This report highlights that the different risk factors between the triplets are birth weight and poor weight gain. To our knowledge, this is the first case report of triplets who had developed ROP with different severity, subsequent treatment and refractive outcome.

Declaration of conflicting interests

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Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed consent

Written informed consent was obtained from the patient's parents for their anonymized information to be published in this article.

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