Polypoidal choroidal vasculopathy (PCV) is a disease characterized by abnormal branching vascular channels with terminal dilatations.\(^1,2\) Although this disease often presents with features similar to neovascular age-related macular degeneration (AMD), they may also manifest with serous retinal detachments mimicking central serous chorioretinopathy or asymptomatic orange-red subretinal nodules (Figure 1).\(^2,4\) Although PCV occurs more commonly among certain populations, such as Asians,\(^5\) recent evidence suggests that its prevalence may be higher among Caucasian populations than previously believed.\(^6,8\)

The visual outcome of PCV described in the literature is highly variable, with the proportion of patients attaining good visual acuity (VA ≥ 20/40) ranging from 0% to 62%.\(^9,10\) In general, patients with PCV have a better visual prognosis than those with typical neovascular AMD.\(^11\) There are cases, however, of patients with PCV suffering severe visual loss, often as a result of submacular scarring (Figure 2).\(^12,13\)
At present, the evidence for the efficacy of PCV treatment in the literature consists of a few randomized, controlled trials, whereas the rest consist of interventional case series. In this article, we will review the benefits and risks associated with the various management options. These include:

- photodynamic therapy (PDT) with verteporfin (Visudyne; Novartis International AG, Basel, Switzerland), combined with intravitreal anti-vascular endothelial growth factor (VEGF) agents;
- PDT monotherapy;
- anti-VEGF monotherapy;
- focal laser photocoagulation; and
- conservative management.

Outcome Measures in Assessing the Efficacy of PCV Treatment

It is important when interpreting the results reported in the literature to distinguish between the various outcome measures utilized. Many studies commonly assess mean VA, change in VA, or reduction of retinal thickness on optical coherence tomography (OCT). Although these are undoubtedly relevant clinically, another important consideration is the rate of polyp closure or polyp regression. Although uncommon, some patients with PCV may present with massive submacular hemorrhage, which may result in fibrotic subretinal scarring, breakthrough vitreous hemorrhage, or suprachoroidal hemorrhage resulting in angle closure glaucoma. As a result, we believe it is important to consider polyp closure rates when evaluating outcomes of PCV treatment.

PDT Combined With Anti-VEGF Injections

The EVEREST study was the first randomized, controlled clinical trial on PCV and demonstrated that PDT with verteporfin combined with intravitreal injection of ranibizumab (Lucentis; Genentech, South San Francisco, CA) or PDT monotherapy both achieved greater rates of polyp closure compared to ranibizumab monotherapy (77.8% and 71.4% compared to 28.6% respectively, \( P < .01 \)). The EVEREST study also reported that mean VA and reduction in OCT thickness was greatest in the group that received combination therapy, followed by the ranibizumab monotherapy group and the PDT monotherapy group. The differences in VA and OCT thickness between the three groups, however, were not statistically significant. It is important to note that this study was of a relatively short duration (6 months) and was not powered to detect differences in VA or OCT thickness, emphasizing the need for follow-up studies with larger sample sizes and of longer duration. These unresolved questions are currently being investigated in the ongoing EVEREST II study.
PDT Monotherapy

PDT monotherapy has been evaluated in many case series. Although most report improvement or stabilization of VA, with regression of the polyps, it is important to note that visual loss has been reported in up to 41.5% of treated eyes. Recurrences of PCV lesions are often reported. It is also essential to consider the potential side-effects of PDT, which include up-regulation of VEGF, as well as damage to normal retinal and choroidal tissue, resulting in choroidal ischemia.

Anti-VEGF Monotherapy

Treatment of PCV with anti-VEGF agents alone has been reported to improve both VA and OCT thickness. In some of these studies, however, the authors did not investigate the rates of polyp closure. Of those that did, studies using ranibizumab or bevacizumab (Avastin; Genentech, South San Francisco, CA) monotherapy have reported polyp closure rates ranging from 13.3% to 28.6%. More recently, a series of reports of treatment of PCV using aflibercept (Eylea; Regeneron, Tarrytown, NY) have shown promising results. In addition to significant improvements in best-corrected VA, as well as retinal and choroidal thicknesses, polyp regression was reported in between 47.8% to 77.7% of eyes. Many of these reports evaluated clinical outcomes between 3 to 6 months of initiating treatment, and it will be interesting to assess whether long-term closure of the polyps can be maintained, and also to ascertain the rate of polyp recurrences. Another limitation of the current studies is that they were mainly non-randomized case series. These limitations are being addressed in the current PLANET study.

Focal Laser Photocoagulation

Focal laser photocoagulation to the polyps was more frequently employed before anti-VEGF agents and PDT became widely available. Although polyp closure rates can be relatively high (71.4% in one series), recurrences have been reported and may be as high as 67%. In addition, laser photocoagulation may be complicated by formation of scars and are therefore not recommended for subfoveal or juxtafoveal lesions. However, laser photocoagulation...
may still play a role in patients with extrafoveal PCV lesions, especially if these are located well away from the fovea. This is especially so if anti-VEGF agents are contraindicated in some patients or due to financial considerations.

Conservative Management

Is there a role for conservative management of PCV? This remains somewhat controversial, and some clinicians may elect to observe patients with asymptomatic polyps, especially if these do not show evidence of activity on OCT or fluorescein angiography. In a series of 14 patients treated conservatively, 50% maintained a favorable VA (better than 20/30), whereas in six of 14 (42.9%), the VA deteriorated to worse than 20/100. Good VA on initial presentation was a predictor of a favorable outcome, with patients maintaining their vision.\textsuperscript{11,38}

Classification of PCV

Although there remains debate whether PCV is a subtype of AMD or a separate entity, it seems clear that PCV lesions have different clinical courses, and attempts have been made to classify PCV using clinical or angiographic features or genetic characteristics.\textsuperscript{9} Many of the earlier papers, however, did not explore differences in clinical outcomes among the various categories described.

A recent paper\textsuperscript{9} proposed a novel classification for PCV, using angiographic features on indocyanine green angiography (ICGA) and fluorescein angiography to distinguish PCV into three subtypes. Types A and B had good visual outcomes during a 5-year period (proportion of patients attaining VA ≥ 20/40 at 5 years: 80% and 66.7%, respectively), whereas only 7.7% of Type C PCV maintained good VA (\(P < .001\)). In contrast, patients with Type C PCV had poorer VA, with 57.7% experiencing the loss of at least 3 lines of vision. It is possible that this classification may be useful in prognosticating patients who present with PCV, and it is also of interest to explore whether the various subtypes respond differently to the currently available treatment options.\textsuperscript{9}

In another paper studying 2-year outcomes of PDT combined with intravitreal ranibizumab injections, patients with the T risk allele, A69S, were reported to

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Figure 3. Optical coherence tomography (OCT) angiography of polypoidal choroidal vasculopathy (A) Indocyanine green angiogram (ICGA) demonstrating hyperfluorescent nodules (polyps) supplied by a branching vascular network (BVN). (B) OCT angiogram of the deep capillary network, which does not reveal obvious abnormalities. (C) OCT angiogram of the outer retina, showing vessels that correspond to the BVN seen on ICGA. (D) OCT angiogram of the choriocapillaris clearly demonstrating the BVN. Some smaller vessels of the BVN are more clearly defined than in the corresponding ICGA.
have a higher rate of recurrence and were more likely to experience loss of VA during the second year.39

The Role of Imaging in PCV Management

Ophthalmic imaging modalities are crucial in the diagnosis and management of many retinal diseases, including PCV (Figure 1). Currently, ICGA is the gold standard for the diagnosis of PCV. OCT provides complementary information on the structures seen on ICGA (Figure 1) and is useful in monitoring the disease progress following treatment. In particular, recent studies using enhanced-depth imaging OCT or swept-source OCT have allowed accurate measurements of choroidal thickness. Changes in choroidal thickness may have potential prognostic significance in various retinal diseases, including PCV. In the future, the use of OCT angiography (Figure 3) a noninvasive method of imaging the retinal vessels and choriocapillaris, promises to contribute to the diagnosis and management of PCV and other retinal diseases.

Conclusion

The management of PCV will continue to evolve, with the discovery of new therapeutic options, as well as a greater understanding of the underlying pathophysiology of the disease and how the different subtypes of PCV respond to treatment. This will result in better individualized management of PCV patients, with a goal of optimizing their long-term clinical outcomes.

REFERENCES


