Cobb’s Tufts: A Systematic Review

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Abstract

Cobb’s tufts, also known as iris vascular tufts (IVT) and iris microhemangiomas (IMH), are coils of tightly clustered, minute blood vessels at the iris pupillary border. This study aimed to analyze previous literature and provide an update on Cobb’s tufts. A systematic literature review was carried out by interrogating PubMed, Google Scholar, Cochrane, and Embase databases. Full-text English language articles of any year were included in this study. A total of 38 articles fulfilled our inclusion criteria. A total of 115 reported cases of Cobb’s tufts were incorporated into our review. The age of the patients ranged between 36 and 86 years. No sex or racial predisposition was noted. Most patients had no history of trauma, surgery, or blood dyscrasia. The majority of cases are asymptomatic and bilateral unless a spontaneous hyphema occurs, which most commonly presents as blurred vision. The etiology of this condition remains uncertain; however, a higher incidence has been shown in systemic conditions such as myotonic dystrophy and diabetes. Fluorescein angiography can be utilized to investigate tufts. Management includes treatment of raised intraocular pressure, observation for single bleeds, laser therapy for recurrent hyphemas, and lastly, iridectomy, which is considered in cases of recurrence following laser treatment.

Categories: Emergency Medicine, Ophthalmology

Keywords: hyphema, spontaneous hyphema, iris microhaemangioma, iris vascular tufts, cobb’s tufts

Introduction And Background

Cobb’s tufts, also known as iris vascular tufts (IVT) and iris microhemangiomas (IMH), are true hamartomas of the iris stromal blood vessels [1]. The first case of a spontaneous hyphema with iris microhemangioma was reported by Tyson in 1932, according to Fechner’s article in 1958 [2]. In 1969, Cobb provided an observational study providing a detailed description of the condition [3]. This led to them being eponymously named Cobb’s tufts. Cobb noted that these lesions protruded forward from the iris in single or multiple loops, were vascularized, adjacent to pupillary ruff, and were separate from each other. In a later publication, he also associated the occurrence of vascular tufts in patients with myotonic dystrophy and diabetes [4]. They can uncommonly present as spontaneous hyphemas, which can lead to high intraocular pressure (IOP) and may potentially cause irreversible damage to the optic nerve [5]. There is a lack of good quality evidence as to the management of this condition. To our knowledge, the last review of the literature was in 2013 [6]. The purpose of this study was to analyze current literature and provide a comprehensive update on all aspects of this condition.

Review

Methods

We present a systematic review of the literature on Cobb’s tufts following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [7]. The PRISMA statement and checklist were used to critically analyze articles and structure this review [7]. Our literature search extends from 1958 to February 2020. The systematic search was conducted through PubMed, Embase, Google Scholar, Cochrane, and the reference lists of the articles. We utilized the following terms in our search: Cobb’s tufts, iris microhemangiomas, iris vascular tufts, and neovascular tufts.

Studies published from any year in the English language were included. Studies that reported spontaneous hyphemas without evidence of IVT and iris neovascularization (rubeosis iridis) were excluded. Moreover, editorials and correspondences were also included. The study identification and selection process are demonstrated in Figure 1 [7].
FIGURE 1: Flowchart outlining the systematic review process.

Full texts were obtained for articles that met inclusion criteria. Data were extracted and information was expressed according to data points as shown in Table 1.

| Author                  | Year | Sample | Age | Trauma | Blood dyscrasias | HTN | PMHs + medications | POHs + medications |
|-------------------------|------|--------|-----|--------|------------------|-----|---------------------|--------------------|
| Meades et al. [1]       | 1986 | 1      | 79  | N      | N                | N   | COPD, CCF           | Glaucoma, cataracts |
| Fechner [2]             | 1958 | 1      | 42  | N      | N                | N   | Nil                 | Nil                |
| Cobb [3]                | 1969 | 44     |     | N      | 40 > 60, 2 < 60  | NR  | Nil                 | Diabetes mellitus, cardiovascular disease, and respiratory failure |
| Cobb et al. [4]         | 1970 | 10     | 28-47| N      | N                | N   | Five patients with MD and IVT; one with T1RF, one with left internal carotid thrombosis, and one with cylinderoma of the salivary gland. Three patients were on quinine and one on steroids. The other five had bronchitis and epilepsy. Two patients were on quinine and one on steroids | Three patients had cataracts |
| Cio et al. [5]          | 2015 | 1      | 86  | Y (Warfarin) | Y | Warfarin - recurrent PE, hypothyroidism, HTN. CVA 30 years ago following 6F stent revision | Nil |
| Dhamoosins and Walla [6]| 2013 | 1      | 63  | N      | N                | Y   | HTN, Cardiac arrhythmias, Bendrofluazide and aspirin. Cholesterin-lowering through diet | Nil |
| Williams et al. [7]     | 2018 | 14 (22 eyes) | N | N      | N                | NR  | NR                 | Prev. hyphemas in 13 eyes, prev. glaucoma in seven eyes |
| Skeie and Ondrum [8]    | 2006 | 1      | 74  | N      | N                | Y   | COPO, Ischemic changes on ECG. 160 mg Acipir. Beta-blocker | Idiopathic juxtafoveolar retinal telangiectasia bilaterally |
| Mason [9]               | 1979 | 60     | 30-60| N      | N                | N   | N                  | NR |
| Blankens and Hoogmans  | 1979 | 1      | 53  | NR     | N                | N   | N                  | Vascular sclerosis |
| Blankens and Hoogmans   | 1979 | 1      | 64  | NR     | N                | N   | N                  | Vascular sclerosis |
| Author(s) | Year | Age | Gender | Diagnosis | Treatment | Findings |
|-----------|------|-----|--------|-----------|-----------|----------|
| Blanksma and Hooijmans | 1979 | 61 | NR | COPD | Vascular sclerosis |
| Nuin et al. | 2020 | 74 | NR | HTN - on antihypertensives | Nil |
| Krause | 1977 | 36 | NR | Congenital heart disease - tricuspid atresia, arterial septal defect, truncus arteriosus, and persisting ductus arteriosus | Cyanotic retina with severe venous stasis |
| Elgohary and Sheldrick | 2004 | 66 | NR | HTN | Nil |
| Perry et al. | 1977 | 69 | NR | Emphysema | Nil |
| Ah-fat and Canning | 1993 | 55 | NR | Nil | Nil |
| Francis et al. | 1982 | 70 | NR | Heart failure, COPD | Cataract and glaucoma – on pilocarpine and Timoptol |
| Francis et al. | 1982 | 59 | NR | Nephrectomy for Grawitz tumor, T2DM | Mild diabetic nephropathy |
| Francis et al. | 1982 | 83 | NR | Angina | LE – bilateral due to aphthis retinal detachment |
| Francis et al. | 1982 | 63 | NR | COPD | RE – glaucoma receiving mitic and carbonic anhydrase inhibitor therapy, otherwise normal |
| Strous et al. | 2005 | 80 | NR | PVD with claudication, hypothyroidism, colon Ca - resected, prostate Ca – radiation Tx | Nuclear sclerotic cataract |
| Blanco et al. | 2019 | 71 | NR | Nil | Nil |
| Frei and Carr | 2001 | 59 | NR | IHD, HTN | Nil |
| Somrath et al. | 2018 | 61 | NR | HTN – on antihypertensives | Nil |
| Rosen and Lyons | 1999 | 73 | Y | HTNs, chronic bronchitis | Strabismus on the opposite eye (RE) |
| Dahlmenn and Bergen | 2001 | 79 | NR | Nil | Nil |
| Coleman et al. | 1977 | 71 | NR | Nil | Nil |
| Jelazaj et al. | 2019 | 55 | NR | Nil | Family His of childhood glaucoma |
| Medine et al. | 2018 | Late 50s | NR | Prev. breast cancer, Primary biliary cirrhosis | Nil |
| Robinson et al. | 2009 | 51 | NR | OA, Naproxen, ibuprofen, calcium | Prev. spontaneous hyphemas treated conservatively |
| Robinson et al. | 2008 | 73 | NR | HTN - amiodarone-hydrochlorothiazide, AF, OA | Nil |
| Hagen and Williams | 1986 | 61 | NR | Nil | Nil |
| Walsh | 1980 | 54 | NR | T2DM | Emmetropic, presbyopia, small choroidal naevus |
| Author et al. | Year | Age | Sex | Race | HTN | PMHx | POHx | Y | T1DM | COPD | T1RF | Other Risk Factors | Treatment |
|--------------|------|-----|-----|------|-----|------|------|---|------|------|------|-------------------|-----------|
| Akram et al. [30] | 2003 | 74 | N | N | Y | HTN - atenolol | Nil | | | | | | |
| Bandello et al. [31] | 1993 | 60 | N | N | Y | HTN - amiloride and hydrochlorothiazide | Nil | | | | | | |
| Kang et al. [32] | 2017 | 75 | N | N | Y | Controlled HTN | Nil | | | | | | |
| Cota and Pecker [33] | 1998 | 69 | N | Y | Y | Hereditary hemorrhagic telangiectasia, HTN, IDA | Nil | | | | | | |
| Goyal et al. [34] | 2010 | 69 | N | N | N | Osteoporosis, hyperthyroidism | Hypermetropia | | | | | | |
| Winick et al. [35] | 2003 | 75 | N | N | N | Nil | Recurrent hyphemas LE. Multiple hemangiomas on the pupillary border bilaterally | | | | | | |
| Thomas et al. [36] | 1988 | 75 | N | N | N | Nil | Nil | | | | | | |
| Goetz and Cosgrave [37] | 2016 | 60 | N | N | N | Peptic ulcer, fibromyalgia | Nil | | | | | | |
| Goetz and Cosgrave [37] | 2016 | 72 | N | N | Y | T1DM, HTN, hyperlipidemia | Nil | | | | | | |
| Goetz and Cosgrave [37] | 2016 | 53 | N | N | N | Crohn's, vertigo | Treatment for glaucoma one week earlier | | | | | | |
| Goetz and Cosgrave [37] | 2016 | 79 | N | N | N | Hyperlipidemia | Non-neovascular age-related macular degeneration | | | | | | |
| Podolepy and Srinivasan [38] | 1979 | 73 | N | N | Y | HTN | Nil | | | | | | |
| Papastefanou et al. [39] | 2016 | 70 | NR | NR | NR | NR | NR | | | | | | |

**TABLE 1: Article data, patient demographics, and risk factors.**

HTN - hypertension; PMHx - past medical history; POHx - past ocular history; Y - yes; N - no; RE - right eye; LE - left eye; NR - not reported; MD - myotonic dystrophy; IVT - iris vascular tufts; T1RF - type 1 respiratory failure; COPD - chronic obstructive pulmonary disease; T1DM - type 1 diabetes mellitus; T2DM - type 2 diabetes mellitus; CCF - congestive cardiac failure; IDA - iron deficiency anemia; IHD - ischemic heart disease; PVD - peripheral vascular disease; Ca - cancer; ECG - electrocardiogram; Tx - therapy; OA - osteoarthritis; Prev. - previous; PE - pulmonary embolism; CVA - cerebrovascular accident; VP - ventriculoperitoneal; Hx - history; AF - atrial fibrillation.

**Results**

This review compiled 38 articles based on the selection criteria including one case-control study, two cross-sectional studies, five case series, and 30 case reports, describing a total of 115 cases of iris vascular tufts. Since the last literature review in 2013, there have been 10 new articles reporting 26 new cases of IVTs. One article was a retrospective observational case series on 14 patients [8].

**Patient Characteristics**

Patients’ ages ranged from 36 to 86 years with a mean of 65 years and median of 67 years. No sex or racial predisposition was noted. There was no case of prior intra-ocular trauma or surgery. Only one case of blood dyscrasia was reported with the patient being on warfarin [5]. Hypertension (48%), ischemic heart disease (18%), and diabetes (12%) were common among those with co-morbidities. Previous medical and ocular history is summarized in Table 1. The lesions appear as very small and nodular hemangioma on the iris and range from 15 to 150 microns in size [2,3]. They can be single or multiple and are most commonly bilateral [2,3]. The onset is usually in the sixth decade or older [3,4]. Meades et al. provided an electron microscopic
description of IVT, indicating the nature of a true hamartoma of the iris stromal blood vessels [1].

Etiology and Other Associations

The exact cause of IVT remains unclear. Initially, these lesions were assumed to be congenital [2]. However, as there are no reported cases in children, these lesions are believed to be acquired [9]. Literature suggests a higher incidence of this lesion in those with systemic and other ocular conditions. Mason (1979) and Cobb et al. (1970) provided evidence that IVT can be associated with myotonic dystrophy and diabetes mellitus [5,4,10]. Mason’s investigation demonstrates an incidence of tufts in 6.7% of adult-onset diabetics and in 12.5% of patients with myotonic dystrophy. Tufts were not seen in 14 patients with juvenile-onset diabetes [10]. There appeared to be increased pancreatic B cell responsiveness in patients with myotonic dystrophy in response to glucose, thus causing high endogenous insulin levels. This study hypothesized that the higher levels of serum insulin might participate in the development of iris neovascularization by immunologic or other unknown mechanisms [10]. Cobb et al. (1969) hypothesized that tufts may proliferate in response to biochemical changes in the aqueous as in cataracts, diabetes, respiratory failure, and ocular hypotony [4]. Blanksma and Hooijmans (1979) also suggested that there seems to be a connection between the development of IVT and cardiovascular and pulmonary disease [11]. Systemically, they could also be associated with hypertension [12], congenital cyanotic heart disease [13], and congenital hemangiomas [6]. Nuova et al. (2020) presented a study of a patient with poorly controlled hypertension who presented with a spontaneous hyphema and hypertensive crisis [12]. Krarup (1977) reported a case of two years of bilateral IVT and recurrent microhyphema with the background of congenital cyanotic heart disease. The study summarized that a prolonged stasis with subsequent hypoxia of the iris tissue is a common factor in those conditions where a local or systemic disease is known to be present [13].

Cobb’s tufts have also presented simultaneously with other ocular manifestations. Elgohary and Sheldrick (2004) presented a case of spontaneous hyphema from IVT in the context of acute branch retinal vein occlusion. The authors concluded that hyphema from IVT may indicate a recent retinal vein occlusion and that their presence can be a risk factor for the development of hyphema during the acute stage of an ischemic retinal vein occlusion [14]. There has been a report of idiopathic juxtapfoveal retinal telangiectasis presenting concurrently with IVT, although no association could be identified [9]. Acute glaucoma has presented simultaneously with spontaneous hyphema secondary to IVT; however, their association cannot be accurately determined based on the lack of reports. Perry et al. (1977) felt the attack of glaucoma could be precipitated by the occurrence of the hyphema [15]. IVT may also present similar to amaurosis fugax as the tufts bleed occasionally and resolve rapidly. Care must be taken to avoid this misdiagnosis [16].

Signs and Symptoms

Cobb’s tufts usually remain asymptomatic [3,17]. They can rarely cause spontaneous hyphemas, for which the most common presenting complaint is a sudden blurring of vision [2,6,13,14,18-28]. Less common symptoms are eye pain, discomfort, and sudden loss of vision [5,12,29-31]. The symptoms usually resolve within 48 hours [2,5,23]. They may resolve as quickly as a few hours thus presenting with transient visual loss and mimicking amaurosis fugax [16]. The extent of visual disturbance is usually related to the degree of hyphema and patients may have a normal visual acuity (VA) [9] or deterioration to “light perception” [30]. In addition to hyphemias, patients will usually present with elevated IOP [11,30]. Persistently raised IOP risks damage to the optic nerve, thus requiring aggressive medical therapy. This usually settles down as the hyphema resolves [30]. Patients can even present with the only positive finding being raised IOP, leading to possible misdiagnosis of ocular hypertension or glaucoma [6]. In Ah-fat and Canning’s study (1994), a patient was misdiagnosed with “mild iritis” on two occasions. However, the patient noticed “blood in the eye,” ultimately leading to a diagnosis of hyphema [16].

Investigations

The external ocular examination is usually normal. VA ranges from normal to light perception based on the degree of hyphema. Tonometry commonly reveals raised IOP when there is an observable hyphema [9]. If there was a hyphema, gonioscopy can reveal a trace of blood, otherwise, this part of the examination is usually normal [16]. There has been a case where the patient presented with acute angle-closure on gonioscopy, as well as a spontaneous hyphema secondary to IVT [15]. Fundoscopy is also largely unremarkable; however, Akram et al. provide a case demonstrating a hyperemic disc with a splinter hemorrhage and venous congestion. These changes did resolve within six weeks of topical therapy [30]. Similar retinal nerve fiber changes can also be seen if there is a simultaneous branch retinal vein occlusion [14]. A slit-lamp examination can demonstrate vascular abnormalities at the pupillary border and may reveal active bleeding or a blood clot; only a third of IVT were revealed by slit-lamp microscopy that was later demonstrated on iris fluorescein angiography (IFA) [22]. These changes can be subtle and further assessment with IFA is recommended to delineate the full extent of these lesions [22]. IIVT appears as coils of tightly clustered, minute blood vessels at the pupillary margin and demonstrate early hyperfluorescence with late staining [22]. Photographic/videographic documentation is recommended to assess changes over time [19,29]. The fellow eye should also be imaged as IVT is most commonly bilateral [3,22]. Meades et al. (1986)
provided the first electron microscopic description of an iris microhemangioma, indicating it to be a true hamartoma of the iris stromal blood vessels [1]. Histopathology illustrates endothelial cells surrounded by pericytes and loose connective tissue and electron microscopic evidence of normal cell thickness with no fenestrations [1]. Another valuable tool that has recently been reported is the anterior segment optical coherence tomography (OCT) of IVT. Its advantages include shorter acquisition time, no need for intravenous dye injection, and three-dimensional visualization of ocular tissue permitting segmental analysis of microvascular anatomy [32]. However, IFA remains the more commonly used mode of investigation supplements clinical examination. In addition to all the above, a full blood count, clotting screen, and urine analysis should be carried out, which are normal in the vast majority of cases. A fasting blood glucose and oral glucose tolerance test is also recommended due to the incidence of IVT in diabetics [5,10].

**Differential Diagnosis**

When trauma is excluded, clinicians should be vigilant of the following conditions. Uveal melanoma is the most vital differential diagnosis to exclude and this can be detected by IFA and serial examinations with photographic surveillance [1,6]. Hereditary hemorrhagic telangiectasia (HHT) is another differential that is a rare autosomal dominant disorder. It is characterized by multiple dilatations of capillaries and venules of skin, mucous membranes, and viscera that may cause bleeding. Conjunctival and eyelid involvement is common, which is not present in IVT [53]. Gonioscopy can be valuable in differentiating IVT from iris neovascularization [25]. Rubeosis can appear similar to IVT; however, the major morphological difference is IVT are elevated, not flat, and they are confined to the pupillary border [10]. Other differentials include inflamed iris vessels and iris hemangiomas [6].

**Management**

**Conservative**

Cobb’s tufts do not produce symptoms unless the patients develop a hyphema [17]. Most patients with IVT rarely develop bleeding and rarely re-bleed [21,27]. Studies have shown that most hyphemas resolve without requiring intervention, thus they are initially treated with time and bed rest [2,15,26,29,30]. There has been a case of spontaneous hyphema from IVT secondary to over-anti-coagulation with warfarin and intravenous vitamin K was part of the management plan [5].

Raised IOP commonly presents with hyphemas and is a vital part of acute management. Prolonged elevation in IOP may lead to optic nerve damage. There have been many studies showing successful responses to acetazolamide and/or topical beta-blockers such as Timoptol [5,6,15,16,20,27,30,34]. Topical steroids and mydriatics/cycloplegics should also be considered and help to decrease light sensitivity and intraocular inflammation [5,8,20,26,27,29,34,35]. Conservative management is sufficient even if there is active bleeding or hyphema is recurrent or pronounced [34].

**Laser Photocoagulation**

There have been numerous studies documenting the treatment of hyphema caused by IVT with serial argon laser photocoagulation (ALP) [6,8,14,18,20,21,24,27,31,34-36]. Variable laser parameters are shown in literature, in terms of spot size, laser power, duration, and the number of spots targeted (Table 2). IFA prior to ALP or surgical treatment is necessary [6]. Dharmasena and Wallis (2015) employed a laser with neodymium-doped yttrium aluminum garnet (Nd:YAG) with YAG Pi settings with a good outcome and no recurrence within six months. The laser was aimed at an angle to reduce the risk of inadvertent macular burn. The parameters used were 500 um spot size, 100 mW power, 0.5 seconds, and eight confluent burns [6]. ALP was utilized for a single episode of active bleeding in four studies [21,27,28,36]; Williams et al. (2018) recently published a retrospective observational case series reporting a good outcome from the use of ALP in two cases of active bleeding despite medical therapy with topical steroids and atropine [8]. There have also been three reports of its use in single episodes of hyphema [20,24,31]. Only one of these five studies suffered a recurrence years later, which was managed conservatively [27]. Bandello et al.’s (1995) study demonstrated no further bleeding but showed angiographic evidence of new IVT, leading to two further treatments with ALP [31]. The rationale behind the use of ALP in single episodes of hyphema is unclear, especially since these have shown good outcomes with conservative management alone. Two cases have been documented of ALP use in recurrent hyphema prior to cataract surgery and have shown good outcomes [18,35]. The risk of bleeding from cataract surgery is unknown. Winnick et al. (2005) utilized parameters of 200 mW power for the 0.1-second duration on 50 spots of 200 um size [55]. It was theorized that closure of IVT would reduce the intra-operative risk of bleeding during surgery. Only minimal bleeding from the iris was observed and no further hyphema was documented in the postoperative period [35]. Interestingly, Goetz and Cosgrave (2015) report a case of cataract surgery without prior laser photo coagulation three months after a hyphema occurred in a patient with IVT. The procedure was carried out successfully without intra- or postoperative bleeding [57]. The follow-up periods post-procedure were variable and ranged from two to 228 months, with a mean of 42 and a median of 16 months (Table 2). Corneal complications include burns, persistent focal edema, and generalized edema with significant endothelial dysfunction. Strauss et al. (2005) employ clinicians to consider multiple treatment sessions at sufficient intervals to facilitate increased total laser
energy requirements without promoting potential corneal complications [18]. Robinson et al. and Goyal et al. recommend that ALP is reserved for cases of hyphema recurrence or failure of medical therapy [27,34].

| Author | Year | Raised IOP | Raised IOP | Duration of symptoms | Management of condition | Recurrence | Suggestion from author |
|--------|------|-------------|-------------|-----------------------|-------------------------|------------|-----------------------|
| Fechner [2] | 1958 | N | Y (micro) | Seven hours | blurred vision and eye pain | Placebo, observation. Hyphema resolved within 24 hours | N | The iris vascular pattern with micro-aneurysms at pupillary margin is presumed to be congenital |
| Rosen and Lyons [22] | 1969 | NR | Y (micro) | 24 hours | blurred vision | Bed rest | N | IFA showed more extensive vascular lesions at the pupillary border of both eyes than clinical findings indicated. These are most likely congenital |
| Cobb [2] | 1969 | N | N | Asymptomatic | Nil | N/A | N/A | The first paper to provide a detailed description of tufts and how it differs from tubular iris. It also provides evidence of f/TV's possible association with systemic conditions like diabetes, vascular, or respiratory disease |
| Cobb et al. [6] | 1970 | N | N | Asymptomatic | Nil | N/A | N/A | IVT can be associated with MD. Hypothesized that tufts may proliferate in response to biochemical changes in the aqueous such as in cataracts, diabetes, respiratory failure, and ocular hypotony |
| Perry et al. [15] | 1977 | Y | Y (macro) | 24-36 hours | Topical pilocarpine, oral acetazolamide and glycerol | N | Usually bilateral, male predominance, 6th-7th decade, associated with MD, respiratory disease, and diabetes |
| Coleman et al. [24] | 1977 | N | Y (micro) | Simulated vision, No duration | ALP | N - within two months follow up | IFA delineated the IVT. ALP eradicated the tufts that bled. Most of the patients with IVT have no systemic disease but they have been seen in diabetes and MD |
| Krupin [13] | 1977 | N | Y (micro - bilaterally) | Few days of “dizzy” vision | Nil | Y - in both eyes, multiple times over two years | A prolonged stasis with subsequent hypoxia of the iris tissue is a common factor in these conditions where a local or systemic disease is known to be present |
| Mason [11] | 1979 | N | N | Asymptomatic | Nil | N | IVT was associated with systemic conditions like MD and diabetes |
| Blankens and Hoogimans [11] | 1979 | N | Y (macro) | Diminished vision for “short period” | Observation, Resolved within two days | N - within one year | These vascular lesions can be caused by cardiovascular diseases and by elevated venous pressure caused by intrathoracic processes |
| Blankens and Hoogimans [11] | 1979 | Y | Y (macro) | Few weeks | temporary decrease in VA | Bed rest. Oclofenamid. Resolved within two days | N - within four years | |
| Blankens and Hoogimans [11] | 1979 | N | Y (macro) | Sudden decrease in vision after getting out of bed | Observation, Resolved within three days | N - within 18 months | |
| Podolsky and Srinivasan [34] | 1979 | N | Y (macro) | Sudden painless onset of “red spot” | Topical homatropine and dexamethasone. Hyphema cleared within three days | N - within four years | IVT is usually asymptomatic. They can give rise to spontaneous hyphemas. ALP can be reserved for recurrent hyphema |
| Welch [29] | 1980 | N | Y (macro) | One day. Unilateral eye pain | Homatropine, bed rest, and eye padding. Resolved after one day | N | Nil |
| Francia et al. [17] | 1982 | N | N | Asymptomatic | Nil | N | |
| Francia et al. [17] | 1982 | N | N | Asymptomatic | Nil | N | |
| Francia et al. [17] | 1982 | N | N | Asymptomatic | Nil | N | |
| Francia et al. [17] | 1982 | Y | Y (macro) | Sudden clouding of vision | Bed rest and acetazolamide | N - within 12 months follow up | IVT are not uncommon lesions, and although they are usually asymptomatic, they now form an important part of the differential diagnosis of spontaneous hyphema, whether unilateral or bilateral. The vast majority will probably never need any intervention |
| Meades et al. [1] | 1986 | N/A | N/A | N/A | N/A | N/A | N/A | The first electron microscopic description of an IVT, indicating it to be a true hamartoma of the iris stromal blood vessels |
| Name and Year | Year | Sex | Duration of Blurred Vision | Initial Treatment | Recurrence | Outcome |
|---------------|------|-----|---------------------------|------------------|------------|---------|
| Hagen and Williams [28] | 1986 | Y | Y (macro) | Topical prednisolone and Timoptic | No - within two months follow up | Case of efficient and successful use of ALP to treat bleeding IVT without complications |
| Thomas et al. [36] | 1988 | Y | Y (micro) | Topical prednisolone and Timoptic | No | The discovery of an IVT per se is not an indication for treatment, but treatment in the case of active bleeding is probably justified |
| Bakke and Drolsum | | | | | | |
| Straus et al. | 1988 | Y | Y (micro) | Topical prednisolone and Timoptic | No | |
| Elgohary and Sheldrick | 1998 | Y | Y (macro) | Topical prednisolone and Timoptic | No | |
| Akram et al. | 1993 | Y | Y (micro) | Topical prednisolone and Timoptic | No | |
| Winnick et al. | 2003 | Y | Y (micro) | Topical prednisolone and Timoptic | No | |
| Dahlmann and Benson | 2001 | Y | Y (macro) | Topical prednisolone and Timoptic | No | |
| Puri and Chan | 2001 | Y | Y (macro) | Topical prednisolone and Timoptic | No | |
| Cota and Pecker | 2003 | Y | Y (macro, RE-macro) | Topical prednisolone and Timoptic | No | |
| Dahlmann and Benson | 2003 | N | Y (Micro) | Topical prednisolone and Timoptic | No | |
| Witrok et al. | 2003 | N | Y (macro) | Topical prednisolone and Timoptic | No | |
| Aksar et al. | 2003 | Y | Y (macro) | Topical prednisolone and Timoptic | No | |
| Elghaemy and Shieldsrick | 2004 | N | Y (macro) | Topical prednisolone and Timoptic | No | |
| Strasz et al. | 2005 | N | N | Topical prednisolone and Timoptic | No | |
| Baake and Dietiker | 2006 | N | Y (macro) | Topical prednisolone and Timoptic | No | |
| Robinson et al. | 2008 | Y | Y (micro) | Topical prednisolone and Timoptic | No | |
| Robinson et al. | 2008 | N | Y (micro) | Topical prednisolone and Timoptic | No | |
| Study | Year | Follow-up | Duration | Treatment | Vision Improvement | Comments |
|-------|------|-----------|----------|------------|-------------------|----------|
| Gopal et al. [34] | 2010 | Y (macro) | One day | Scleral, cycloplegic and hypertensive drops, and oral acetazolamide | N | Conservative management is sufficient even if there is active bleeding or hydrops is recurrent or pronounced. Although none of the reports noted any adverse effects with ALP, IVT rarely needs intervention |
| Dharmaas et al. [9] | 2013 | Y (micro - bilaterally) | One to two days | ALP with Nd:YAG with YAG P line settings, aimed at an angle to reduce the risk of inadvertent vascular burn. 500 μm spot size, 100 mW power, 0.5 s, eight confluent burns. Acetazolamide and antiglaucoma medication | N - within six months follow up | YAG P line settings, angled laser beam. Worthy bearing in mind with intermittent secondary OA glaucoma |
| Cioi et al. [9] | 2015 | Y (macro) | Eight hours | Combination of prednisolone, atropine, brimonidine, timolol, betaxolol, and timolol. Vitamins K IV to normalize INR. | N | The possibility of over-anticoagulation should always be considered. |
| Papasterfanou et al. [34] | 2016 | N - NR | Observation | | NR | Topical and systemic steroids can be used to induce IVT regression or hasten spontaneous shrinkage. Conservative management of IVT in the initial instance is more than appropriate. |
| Goetz and Cosgrave [37] | 2016 | Y (macro) | Four hours | Topical desmopressine and IOP lowering agents. Full recovery | N | Important to carefully examine all eyes. IVT is more numerous than clinically apparent. IFA can prove invaluable. The majority of hyphemas can be treated conservatively. |
| Goetz and Cosgrave [37] | 2016 | N (macro) | Blurred vision on awakening | Topical steroid and cycloplegic. Full recovery | N | Reports case of phacovascularization on the background of IVT. |
| Goetz and Cosgrave [37] | 2016 | Y (macro) | 24 hours | Sudden, paralytic vision loss | Topical brimonidine, timolol, acetazolamide, and desmopressine. Full recovery | N | This is the first report of OCTA of IVT. Although FA has traditionally been effective in highlighting iris vascular lesions, the non-invasive nature and depth-localizing strengths of OCTA are appealing. |
| Goetz and Cosgrave [37] | 2016 | Y (macro) | Five hours | Topical desmopressine, cyclogypid and apraclonidine. Full recovery | Y - once a month later | Reports case of phacovascularization on the background of IVT. |
| Kang et al. [32] | 2017 | N | Asymptomatic | Observation | N | This is the first report of OCTA of IVT. Although FA has traditionally been effective in highlighting iris vascular lesions, the non-invasive nature and depth-localizing strengths of OCTA are appealing. |
| Samad et al. [31] | 2018 | Y (macro) | One day | ALP, ARB 532nm, two burns, 50 μm spot size, 0.1 s, 400 mW. Dorzolamide, timolol, and prednisolone | N - within five years of follow up | Important to carefully examine all eyes. IVT is more numerous than clinically apparent. IFA can prove invaluable. The majority of hyphemas can be treated conservatively. |
| Williams et al. [9] | 2018 | Y (two patients - macro) | Blurred vision in 13 eyes | Observation in 14 cases. In seven patients and treated topical anti-HTN. Topical steroids or atropine in four cases. ALP in two cases resulting in complete hemostasis | Y - (one case which was followed up for 56 months) | Observation in those without ongoing signs or symptoms. Topical steroids and atropine could be beneficial if hyphema persists. Topical anti-HTN for raised IOP. ALP for persisting bleeding or recurrence |
| Jabejat et al. [35] | 2018 | N (macro) | Blurred vision | Best need. Topical prednisolone and cyclopentolate | Y | Gonioscopy to differentiate IVT from iris neovascularization. Topical steroids and mydriatics for hemostasis can be used. IOP monitoring and treatment is an important component |
| Idale et al. [36] | 2018 | Y (macro) | Blurred vision | Topical corticosteroid, cycloplegic, and aqueous suppressant | N - within four months follow up | Observe the patient in the first instance. Reserve ALP for hyphema recurrence |
| Blanco et al. [16] | 2018 | N (macro) | Two days | Repeated digital compression over the superior eyelid. The bleeding stopped the next day | N - within nine months follow up | Performing digital compression repeatedly could help achieve hemostasis |
| Nuova et al. [12] | 2020 | Y (macro) | Acute visual deterioration | Topical prednisolone and cyclopentolate. Resolved within 15 days | N - within 24 months follow up | Hypertensive crisis in the patient presented here triggered the occurrence of the hyphema. Ultrasound microscopy could be utilized in order to rule out neoplasms of the iris and ciliary body. Blood pressure control is important to avoid complications |

### Table 2: Presentation, management, and suggestions from authors.

IOP - intraocular pressure; N - no; Y - yes; NR - not reported; IFA - iris fluorescein angiography; FA - fluorescein angiography; IVT - iris vascular tufts; N/A - not applicable; ALP - argon laser photocoagulation; MD - myotonic dystrophy; LE - left eye; RE - right eye; B-blockers - beta-blockers; HHT - hereditary hemorrhagic telangectasia; OA - open angle; IV - intravenous; OCTA - optical coherence tomography angiography; Anti-HTN - antihypertensives; Nd:YAG - neodymium-doped yttrium aluminium garnet; μ - micrometer; nm - nanometer.

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**Discussion**

Cobb's tufts are coils of tightly clustered, minute blood vessels at the iris pupillary margin [22]. The etiology and pathogenesis of this condition are largely unknown. To date, there is no literature based on these aspects. As there are no reported cases in children, these tufts are believed to be acquired [9]. Moreover, there is a higher incidence of Cobb's tufts in patients with systemic conditions such as myotonic dystrophy and diabetes mellitus [3,4,10]. IVT also seems to occur more in patients with cardiovascular, respiratory disease, and hypertension [11,12]. There are also single reports of IVT presenting as spontaneous hyphemas in patients with congenital heart disease, congenital hemangiomatosis, and hereditary hemorrhagic telangiectasia, respectively [6,13,33]. Clinicians should also be aware of possible ocular associations. Interestingly, these lesions have presented as hyphemas in the context of acute branch retinal vein occlusion, idiopathic juxtapfoveal retinal telangiectasis, and acute glaucoma [9,14,15]. The authors would recommend considering the possibility of the aforementioned systemic and ocular associations when assessing patients with spontaneous hyphemas and/or IVT.

Spontaneous hyphema can be a rare sequela of IVT. The most common presenting complaint is sudden blurring of vision [2,6,8,13,14,18-28,38]. However, they can also present as eye pain, discomfort, sudden loss/deterioration of vision, or "blood in the eye" [5,12,29-31]. Symptoms usually resolve within 48 hours [2,5,23]. Hyphemas are commonly associated with raised IOP and this can be transient leading to a misdiagnosis of ocular hypertension or glaucoma [6]. Examination generally consists of external ocular examination, VA assessment, tonometry, gonioscopy, fundoscopy, and slit-lamp examination. IVT can be easily missed on clinical examination alone and the authors would recommend supplementing the aforementioned modes of examination with IFA.

IFA is helpful to investigate the full extent of these lesions. They are commonly found to be bilateral, more numerous, and demonstrate early hyperfluorescence with late staining [22]. IFA can be combined with serial examinations to exclude iris melanoma. The authors would recommend considering differential diagnoses such as rubeosis, iris neovascularization, iris hemangiomas, HHT, and inflamed iris vessels [6,10,25,33]. However, there is a weak level of evidence surrounding differential diagnosis for IVT.

Prior to treatment, it is commonly reported that IFA is performed [6]. The majority of spontaneous hyphemas secondary to Cobb's tufts can be treated conservatively. Conservative modalities include bed rest and topical therapy including IOP-reducing drugs such as beta-blockers, steroids, and mydriatics/cycloplegics [2,15,26,29,30]. Literature has shown the successful use of ALP in active bleeding, single episodes of bleeding, and recurrent hyphemas [6,8,14,18,20,21,24,27,31,54-56]. The indication for laser treatment in single episodes of bleeding remains unclear due to the very good outcomes of conservative management. Therefore, we would recommend that ALP is reserved for cases of hyphema recurrence or failure of medical therapy.

The benefit of ALP prior to intraocular surgery is unknown. There have been two studies of ALP prior to cataract surgery, one of which resulted in minimal bleeding intra-operatively [18,35]. On the other hand, Goetz and Cosgrave (2016) reported a case of cataract surgery in a patient with IVT and reported no complications or bleeding [37]. Iridectomy can be considered in patients who are still symptomatic despite ALP or if there is suspicion of malignancy.

Dharmasena and Wallis provided us with the last literature review on this topic in 2013, there have been 10 new articles reporting 26 new cases of IVT. One issue is the majority of these studies are case reports and consist of a very small sample size (one to four). Some studies also add further evidence of known knowledge regarding Cobb’s tufts but lack any new breakthroughs [12,21,25,26,39]. These articles reiterate that conservative management is recommended initially, the importance of controlling IOP and blood pressure and that ALP should be reserved for recurrent hyphemas. Blanco et al. (2019) provided rare video documentation of the course of this condition. They utilized repeat digital compression of the superior eyelid as part of conservative management [19]. The authors feel this is unlikely to be of many benefits since the majority of such hyphemas settle with bed rest and time. Another study highlighted the risk of anticoagulation therapy as a predisposing factor for spontaneous hyphema and this should factor into management considerations [5].

Recent updates in literature, such as Williams et al.’s (2018) observational study of 14 patients (22 eyes), further confirm that IFA is a diagnostic modality and that ALP should be reserved for recurrence [8]. This was the second recent article to mention optical coherence tomography angiography (OCTA) as an alternative to IFA [32]. The non-invasive nature and depth-localizing strengths of this new development are appealing but require further studies before it would surpass IFA. Another recent study by Goetz and
Cosgrave makes us rethink the use of ALP prior to intraocular surgery in eyes containing IVT [37]. The authors feel that further studies are required surrounding ALP prior to intraocular surgery in the context of IVT as conflicting results have been shown in the very few studies available.

Limitations
The sum of this systematic review is limited by the published literature due to the relative scarcity of the condition. Most papers are case discussions or small number case series. There has been limited research into etiology and much remains to be investigated.

Conclusions
Cobb’s tufts are benign true hamartomas of the iris stromal vessels at the pupillary border. They cause no symptoms unless a hyphema develops, which most commonly presents as blurred vision. A single episode of bleeding is rare and re-bleeding is also a rare occurrence. Recent literature provides further evidence to support conservative treatment of a spontaneous hyphema in the first instance, given the reports of great resolution rates and low recurrence. Laser photocoagulation has a role in cases of hyphema recurrence despite medical therapy. A large array of settings is employed resulting in uncertainty regarding the optimal settings for laser photocoagulation. Current literature largely consists of case reports/series making for weak evidence regarding etiology, laser photocoagulation, and surgical treatment. OCTA has recently emerged as an alternative imaging modality for these lesions and demonstrates favorable initial advantages over IFA. However, larger prospective studies are needed to research this imaging modality, in addition to the optimal management strategy to use with laser photocoagulation and iridectomy for these lesions.

Additional Information
Disclosures
Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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