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Case Report

# The management of ophthalmic involvement in blue rubber bleb nevus syndrome

## Abstract

**Objective:** Blue rubber bleb nevus syndrome is a rare vascular disease most commonly associated with venous malformations of the skin and the gastrointestinal tract. Few ophthalmic cases have been reported to date, and no clear treatment regimen exists. We describe the case of a 59-year-old man, along with a review of literature, to help in the future diagnosis and treatment of patients with the disease.
**Methods:** This paper is an observational case report and a review of medical literature on the syndrome from 1981 to present.
**Results:** Our patient developed a dural arteriovenous fistula in his orbit after being diagnosed with a familial form of blue rubber bleb nevus syndrome. Multiple endovascular embolization procedures eliminated all of his ocular symptoms. Surgical procedures were also successful in other cases reviewed, and similar symptoms were seen across cases.
**Conclusions:** Comparing our case with other ophthalamic reports in literature, surgical intervention appears to be a plausible long-term treatment for optic manifestations of blue rubber bleb nevus syndrome. Systemic therapies, including sirolimus and corticosteroids, have had limited success in the long-term treatment of other forms of blue rubber bleb nevus syndrome, and therefore are not recommended in the treatment of ocular symptoms.

**Keywords:** blue rubber bleb nevus syndrome, DAVF, ophthalmic, treatment

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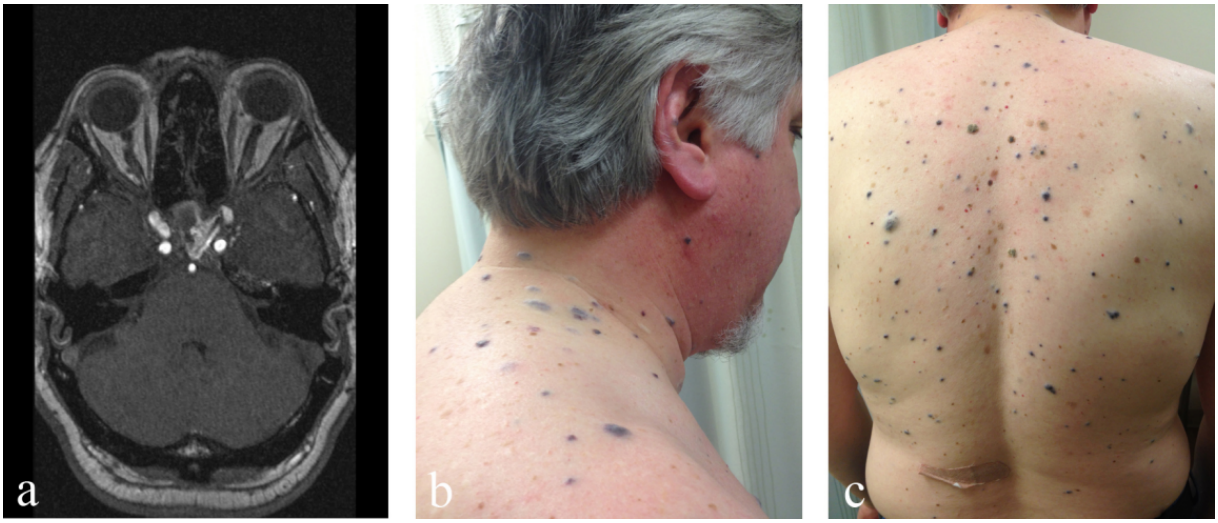


**Figure 1:** (a) **Preoperative MRA WO contrast.** (b, c) **Cutaneous lesions from vascular malformations associated with BRBNS**

## Introduction

Blue rubber bleb nevus syndrome (BRBNS) is a rare disorder characterized by venous malformations of the skin, gastrointestinal (GI) tract, and less commonly of other tissues in the body. We present the case of a 59-year-old man and a review of current literature to illuminate the diversity of ophthalmic symptoms, as well as potential treatment options for patients with blue rubber bleb nevus syndrome.

## Case report

The patient was initially diagnosed with a familial case of blue rubber bleb nevus syndrome as a child after developing multiple cutaneous lesions on his back, chest, face, and extremities. No major complications from the disease were apparent until July, 2012 (apart from mild anemia), when he presented to his local hospital with loss of vision in his right eye, and chronic pain in the left eye. Preliminary ophthalmic examination revealed significant proptosis and elevated intraocular pressure of the left eye. Magnetic resonance angiography (MRA) revealed a dural arteriovenous fistula (DAVF) in the left skull base (Figure 1).

A total of three endovascular embolization procedures were used to treat the patient's ophthalmic symptoms. Partial occlusion of the DAVF after the first procedure failed to alleviate all of his optic symptoms, as the patient developed morning blurriness and diplopia. After two further operations, the patient is now stable and reports improved symptoms. He appears to have slight pallor of the optic nerves, as well as imbalance and vertigo, but his overall health has greatly improved.

## Discussion

Blue rubber bleb nevus syndrome is a very unusual disease with multiple manifestations. Approximately 200 reports of the syndrome have been documented to date [1]. Although some forms appear to have an autosomal dominant inheritance pattern linked to chromosome 9p, the majority of cases are sporadic [2]. Patients often present with small, compressible lesions of the skin and chronic anemia from gastrointestinal bleeding [3]. Diagnosis of the disease usually occurs from these common presentations as well as histological analysis. Radical resection has had positive results in patients with gastrointestinal hemorrhage, and laser therapy has shown promise for cutaneous lesions [4], [5]. However, no pharmaceutical intervention has been proven universally successful in combating BRBNS.

We present here some of the few cases of ophthalmic symptoms associated with this disorder (Table 1). Past reports of orbital involvement of blue rubber bleb nevus syndrome have presented with a myriad of symptoms including: proptosis, enophthalmos, ptosis, vision loss, imbalance, occipital headaches, ecchymosis, and intraocular pressure. Ophthalmic symptoms can be chronic or acute in nature, as with the case of a sudden intraorbital hemorrhage [6]. Cutaneous lesions were also present in most patients (10/11 cases), and gastrointestinal lesions in a subset of reports (5/11 cases). It can be difficult to differentiate BRBNS from Mafucci's syndrome, Klippel-Trenaunay syndrome, diffuse neonatal angiomatosis, and Rendu-Osler-Weber syndrome [3]. Based on our analysis, the common orbital symptoms of blue rubber bleb nevus syndrome may include: the presence of cutaneous venous malformations, chronic anemia, decreased visual acuity, and proptosis or enopthalmos of the eye.

Systemic therapy has not yet successfully treated optic cases of BRBNS, but has achieved varied outcomes in other forms of the disease. Multiple reports have shown interferon-α and corticosteroids to be unsuccessful in long-term treatment of multi focal, large GI lesions [4],

**Table 1: Diagnostic symptoms and treatments for patients presenting with ophthalmic forms of BRBNS**

| Report | Age | Associated symptoms | Imaging findings | Treatment | Outcome |
|---|---|---|---|---|---|
| Current patient | 59M | Left eye proptosis with intraocular pressure, right eye visual impairment, headaches, imbalance, fatigue, cutaneous lesions, anemia (GI lesions) | DAVF | Multiple endovascular embolizations | *Positive:* reduced proptosis, improved visual acuity (6 months) |
| Tuncer et al. (2006) | 27F | Right eye enopthalmos, intraocular pressure | Intraconal and nasal masses | None | Symptoms unchanged (12 months) |
| Carvalho et al. (2003) | 45F | Right eye enopthalmos and ptosis, occipital headaches, bilateral retroauricular bruit, GI and cutaneous lesions | DAVF | Multiple endovascular embolizations | *Positive:* no further headaches or cranial bruit |
| Chang et al. (2002) | 32F | Bilateral eye proptosis, visual impairment, cutaneous lesions | Bilateral orbital lesions | Excision of lesions (lateral orbitotomy) | *Positive:* reduced proptosis, improved vision (6 months) |
| Sobottka Ventura et al. (2001) | 70F | Left eye enopthalmos with intraocular pressure, visual impairment, cutaneous lesions | Intraconal lesion of upper left orbit | None | Symptoms unchanged (12 months) |
| Chen et al. (1996) | 9F | Headaches, GI and cutaneous lesions | Bilateral intraconal lesions | None | Symptoms unchanged (6 months) |
| McCannel et al. (1996) | 28F, 7F | 28F– right eye lid ecchymosis and orbital pain, cutaneous lesions, GI lesions<br>7F– right eye proptosis, visual impairment, cutaneous lesions | 28F– right intraconal lesion<br>7F– right orbital apex lesion | None | N/A |
| Mojon et al. (1996) | 47F | Left eye ptosis, proptosis, miosis, spontaneous ecchymosis, cutaneous lesions | Orbital intraconal mass | None | Symptoms unchanged (14 months) |
| Rennie et al. (1982) | 71F | Acute left eye proptosis, ptosis, visual impairment and pain, cutaneous lesions | Orbital bleeding of intraconal lesion | Analgesics | *Positive:* rapid decline in acute symptoms |
| Crompton et al. (1981) | 48 hrs | Left eye lesions of the conjunctiva, iris, and retina, GI and cutaneous lesions | N/A | None | *Negative:* progressive cutaneous and GI lesions, retinal pigment defects (7 months) |

[7]. However, recent publications have suggested that sirolimus may be beneficial in the treatment of gastrointestinal bleeds and anemia [7], [8]. Therapy with sirolimus can cause many side effects including hypertension, immunosuppression, renal failure, anemia and hyperlipidemia. In these cases no significant adverse symptoms were recorded except for a slight elevation in cholesterol in one patient. Sirolimus was used in combination with propranolol to reduce adverse effects, but cutaneous lesions and melena were noted 10 days after the physicians attempted to wean the patient off the medication [7]. This agent may, therefore, be considered for short-term treatment of ophthalmic forms of BRBNS, but prolonged use of the drug may be needed to successfully reduce symptoms. Unfortunately, long-term use of sirolimus will likely expose patients to the potential adverse side effects of the drug.

Surgical treatment of chronic ophthalmic manifestations has been successful in our case as well as the other patients in our literature review [3], [9]. Endovascular embolization has been used to alleviate symptoms in patients presenting with dural arteriovenous fistulas, and surgical excision with other venous malformations in the orbit. Embolization procedures have reduced symptoms in all the cases presented, but multiple procedures were often required [9]. Understanding the critical symptoms and potential treatment options will optimize the management of patients with this extremely rare disease and hopefully lead to improved outcomes.

# Notes

## Disclosure of patient

The patient in the case report gave consent to the authors to write up this publication and gave permission to use the images.

## Competing interests

The authors declare that they have no competing interests.

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***Please cite as***
*Petek B, Jones RL. The management of ophthalmic involvement in blue rubber bleb nevus syndrome. GMS Ophthalmol Cases. 2014;4:Doc04. DOI: 10.3205/oc000017, URN: urn:nbn:de:0183-oc0000173*

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***Published:*** *2014-07-08*