·Clinical Research·

Application of Prussian blue staining in the diagnosis of ocular siderosis

Zhen Yang, Xiao-Li Yang, Li-Shuai Xu, Le Dai, Mei-Chao Yi

Department of Ophthalmology, the Affiliated Hospital of North Sichuan Medical College, Nanchong 637000, Sichuan Province, China

Correspondence to: Xiao-Li Yang. Department of Ophthalmology, the Affiliated Hospital of North Sichuan Medical College, Nanchong 637000, Sichuan Province, China. fundusyz@163.com

Received: 2014-02-19 Accepted: 2014-05-05

Abstract

• AIM: To explore the value of Prussian blue staining in the diagnosis of ocular siderosis.

• METHODS: Between January 2012 and January 2013, the Prussian blue stain used in anterior lens capsule and vitreous liquid after centrifugation from patients with definitive diagnosis and suspicious diagnosed of ocular siderosis. At the same time, give a negative control.

• RESULTS: Anterior lens capsule membrane and liquid of vitreous cavity from patients with definitive diagnosis and suspicious diagnosed of ocular siderosis revealed ferric ions that stained positively with Prussian blue. In the control group, there is no positive reaction.

• CONCLUSION: Prussian blue staining in the diagnosis of ocular siderosis has a very significant worth, suspected cases can be definitive diagnosed.

• KEYWORDS: intraocular foreign bodies; ocular siderosis; Prussian blue staining

DOI:10.3980/j.issn.2222-3959.2014.05.09

Yang Z, Yang XL, Xu LS, Dai L, Yi MC. Application of Prussian blue staining in the diagnosis of ocular siderosis. *Int J Ophthalmol* 2014;7(5):790-794

INTRODUCTION

Intraocular foreign bodies (IOFBs) accompany 18%-41% of open globe injuries[1]. Ocular siderosis is an uncommon but potentially devastating complication of penetrating ocular injuries with retained IOFBs. It is a complication induced by a chemical reaction to an iron IOFB residues, which commonly leading to a series of characteristic alterations and severe disorder of visual function [2,3]. The heavy metals iron may lead to both acute and chronic inflammatory processes resulting in severe endophthalmitis, retinal degeneration, and resultant ocular siderosis. It can cause irreversible retinal injuries and visual function damage and can even lose the eyeball of the patients [4]. Early diagnosis and removal of IOFBs is very important to determine further management and the final result of treatment. Remove the foreign body as soon as possible in order to save the patients visual function.

Currently, there are many tools available to aid in diagnosis for IOFBs, including plain X-ray, B-scan ultrasound, optical coherence tomography, orbital computerized tomography (CT) scan, electroretinography testing, and high resolution angiography [1,5,6]. Sometimes, we combined with several inspection methods, to better understand ocular siderosis pathophysiology.

The performance of intraocular foreign body after trauma may not obvious [7]. Patients often treatment with a serious decline in visual acuity. It has been reported CT scan was the most reliable method for identifying IOFBs in patients presenting with open globe injuries [8]. However, in some patients in whom the intraocular foreign body is too small to be found with B-scan ultrasound or orbital CT. Therefore, some suspected cases lack of effective diagnosis evidence.

Acidic potassium ferrocyanide with extracellular and intracellular iron can occur Prussian blue reaction, forming a blue precipitate of ferric ferrocyanide, to locate in the parts of iron. Cell Stained at our hospital are routinely stained by the Prussian blue technique to detect ferric ions. We report here the finding of anterior lens capsule membrane and liquid of vitreous cavity from patients with ocular siderosis which stain positively with Prussian blue stain.

SUBJECTS AND METHODS

Subjects We retrospectively reviewed the medical records of patients with ocular siderosis between January 2012 to January 2013 (Table 1), five definitive diagnosis cases of ocular siderosis after ocular trauma treated in our hospital, orbital CT examination (Figure 1) suggested that the foreign body was metallic, and revealed high-density foreign body in the retina. B-scan ultrasound also shows an IOFB with shadowing behind the IOFB in the retinochoroidal tissue (Figure 2). Foreign body residence times for seven days to

Table 1 Demographic and clinical profile of the patients

Age	Sex	Times	Entry site	Location of the IOFB	Preoperative visual acuity	IOP	Complication	Postoperative visual acuity
34	M	7d	Corneal	Subretinal	0.2	20	Cataract	0.1
25	M	1mo	Corneal	Retinal	HM	30	Cataract+VO	FC
55	F	Unclear	Corneoscleral	Not found	FC	24	Cataract+VO	FC
48	M	5d	Scleral	Retinal	0.05	18	Cataract+VO	0.2
39	M	2y	Corneal	Not found	LP	32	Cataract+RD	HM
42	M	1mo	Scleral	Not found	HM	16	Cataract+RD	FC
59	M	6mo	Corneal	Paramacular	HM	21	Cataract	FC
64	F	15d	Corneoscleral	Not found	FC	13	Cataract+VO	FC
67	M	20d	Scleral	Retinal	FC	19	Cataract	0.05

IOFB: Intraocular foreign body; IOP: Intraocular pressure; CF: Counting finger; HM: Hand movement; RD: Retinal detachment; VO: Vitreous opacity.

Figure 1 Orbital CT shows a retained metallic IOFBs in the wall of the right eye.

two years. Four suspected diagnosis cases of no explicitly found foreign bodies: three patients had a history of ocular trauma and complicated cataract, but there was no evidence of IOFB on neither B-scan ultrasound nor orbital CT. They could not reveal any evidence of high-density foreign body in the eyeball. One of their electroretinography showed normal waveforms in injured eyes. A patient insisted she did not have history of ocular trauma. B-scan ultrasound and orbital CT did not prompt foreign bodies. Preoperative visual acuity was ranging from light perception to 0.2. Control group: two simple retinal detachment patients who underwent cataract phacoemulsification combined pars plana vitrectomy (PPV), excluded patients with vitreous hemorrhage. Ethics statement: ethical approval was granted by the Affiliated Hospital of North Sichuan Medical College of Medical Research Ethics. The study followed the tenets of the Declaration of Helsinki. Written or verbal informed consent was obtained from all participants.

Methods All patients underwent a complete general ophthalmologic examination prior to the surgical procedure. Preoperative visual acuity, site of entry of foreign body, intraocular pressure (IOP) was assessed. B-scan ultrasound, X-ray and/or orbital CT were performed in all patients to locate and evaluate the IOFBs. Preoperative examination also included slit-lamp photograph (Figure 3), gonioscopic

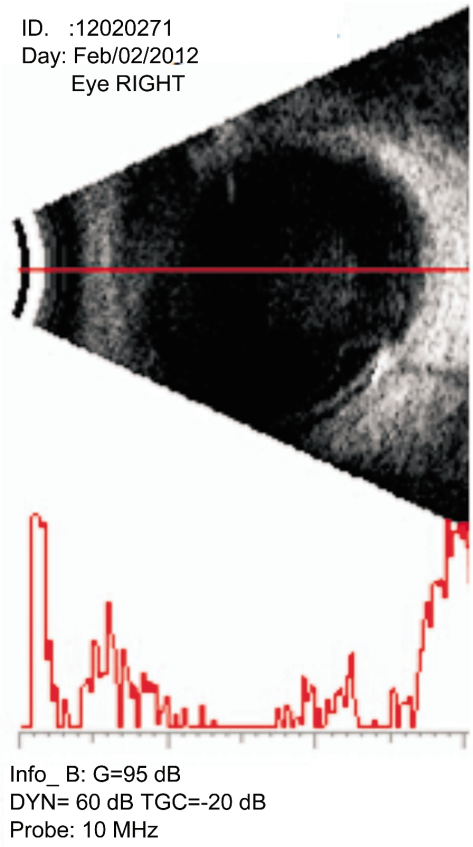

Figure 2 B-scan ultrasound of the right eye shows a retained IOFB in the retinochoroidal tissue.

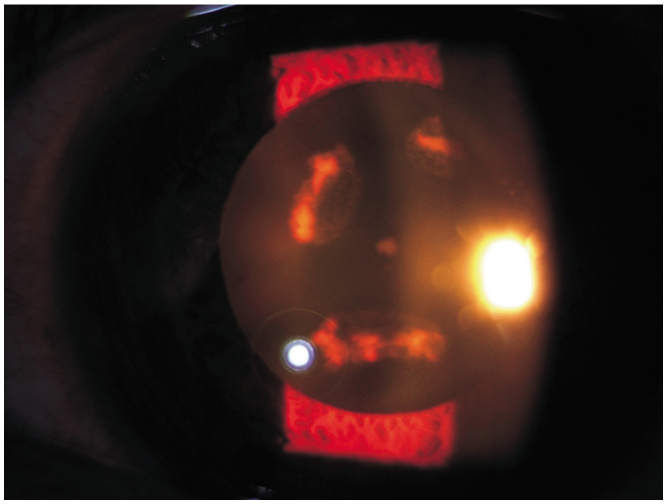

Figure 3 Slit -lamp photographs revealed rusty spots depositions in the lens capsule.

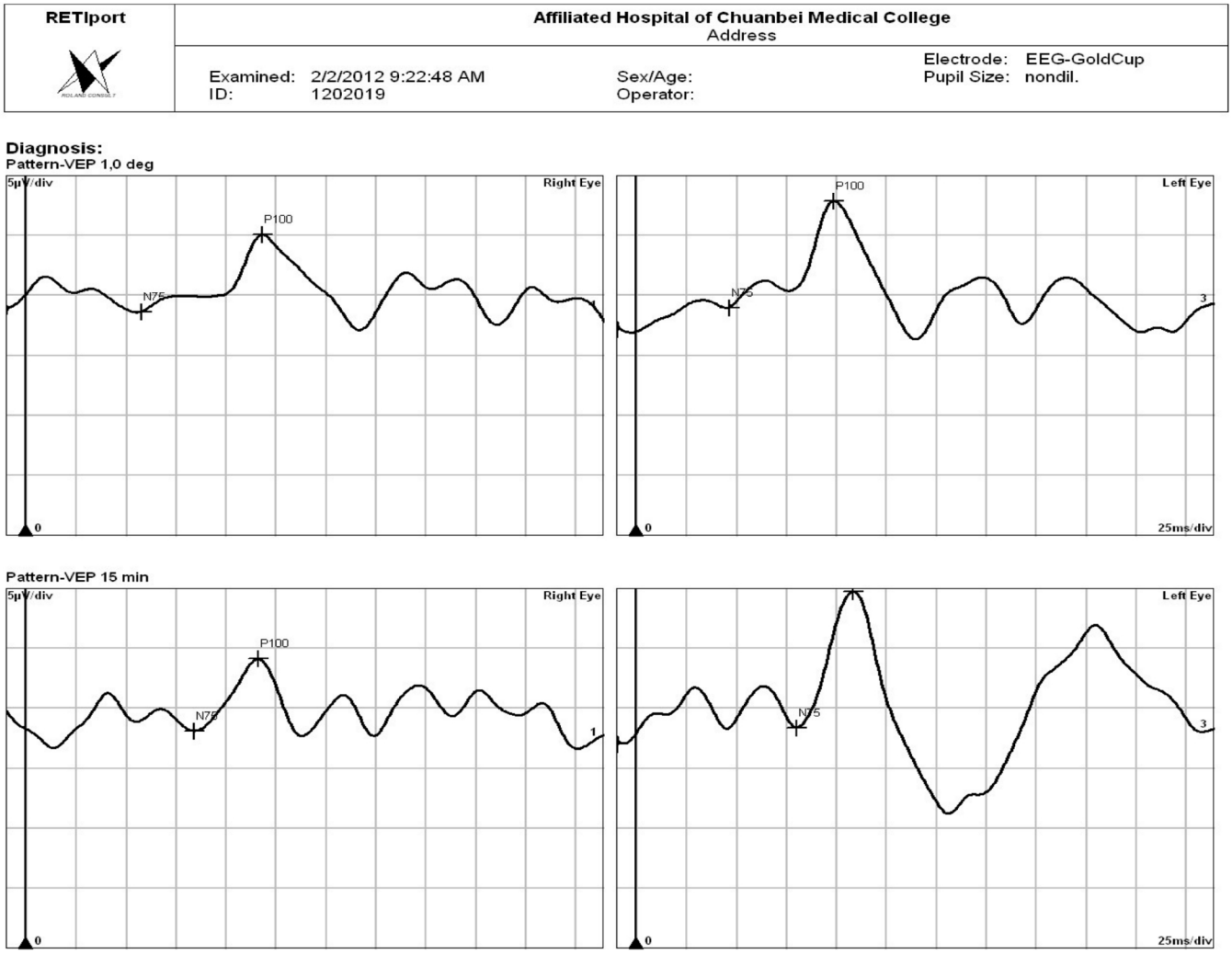

Figure 4 Electroretinography showed normal waveforms in injured eyes.

examination, electroretinography testing (Figure 4).

Surgical record After preoperative examination and preparation, surgery was given as quickly as possible. In response, cataract phacoemulsification, PPV, foreign body removal, anterior chamber and vitreous cavity irrigation were performed. All patients were given opacity lens and vitrectomy removal surgery. In cataract phacoemulsification, under the operating microscope with capsulorhexis tweezers carefully tear anterior lens capsule which diameter of more than siderosis area, and intraocular lens were not implanted at the first surgery. A standard three-port 20-gauge PPV was performed, after removing the foreign body, reserved the removed vitreous in centrifuge tubes. According to the retinal damages, the corresponding treatments such as resetting retina, closing retinal tear by retinal cryocoagulation or retinal laser photocoagulation. Then choose an appropriate endotamponades filling in the vitreous cavity after the gas-liquid exchange processing.

Specimens production Removed anterior lens capsule were fixed on rectangle glass slides with 4% glutaraldehyde immediately at room temperature, fixed 24h. Removed vitreous and fluid placed in a centrifuge tubes and centrifuged (rotational speed 1000 rpm, centrifuged for 10min, after the precipitate was dried in air, fixed the same as above anterior lens capsule. Place well fixed specimens of anterior capsule membrane vitreous on a glass slide.

Prussian blue staining procedure Stain preparation: in test tubes added in a ratio of 1:1 with potassium ferrocyanide solution and hydrochloric acid solution (BASO diagnostics, Inc. Zhuhai), dropping the prepared staining solution at the fixed anterior lens capsule and vitreous precipitation to observe iron ions (37℃, stain 60min), then well washed with distilled water 5min. Microscopic examination after absorbed by filter paper; using nuclear fast red solution restrained 2min, rinsed with distilled water, confocal microscopic examination after fluid evaporation.

RESULTS

Two suspected diagnosis cases of metallic foreign body was found by surgery. But the other two suspected diagnosis cases found no foreign body by surgery. Confirmed and suspected

diagnosed cases in the stained specimens of anterior lens capsule and vitreous were seen piles of blue granules (Figures 5, 6). In the staining control group, no positive reaction, iron ions were not detected in intracellular and extracellular (Figure 7).

DISCUSSION

Penetrating globe injuries with retained IOFBs are a relatively infrequent occurrence [9]. Typically, a small, high-speed projectile penetrates the eye and, possibly, finally lodges in the eye [10]. Metal-on-metal activities, particularly with various tools, are often associated with metallic IOFBs[11]. Occult intraocular foreign body masquerading as high IOP, anterior subcapsular cataract, iris discoloration, mydriasis, panuveitis, intraocular inflammation, retinal detachment, siderosis and so on, and reduction in electroretinography amplitude [12-15]. Iron, released from the IOFB, is toxic to the ocular tissues including the trabecular meshwork and retina. If the IOFB is not removed, iron-contaminated intraocular tissues have a characteristic clinical picture termed siderosis, and resultant visual loss [16]. Post-traumatic siderosis with retained IOFBs should attract great attention because of its poor prognosis. Early diagnosis and removal of metallic IOFBs is very important to determine the final visual acuity of treatment. Vitrectomy, which may reduce the incidence and the severity of siderosis is suggested for the treatment of IOFBs and its complications and should be performed as soon as possible. Above all, a detailed penetrating ocular trauma history and meticulous ophthalmic examination are useful to early diagnosis. Ultrasound is a safe, noninvasive imaging tool, which can be useful to detect the presence, location, and composition of IOFBs with high sensitivity, specificity, and accuracy, especially if it is in the anterior chamber angle[9,17]. The electroretinogram (ERG) is one of the most common means of detecting ocular siderosis, ERG changes have characteristics of siderosis associated with IOFB injuries [12,18]. Neuroimaging, preferably with non-contrast computed tomography, provides excellent information about IOFB size, shape, and location [19]. Recently, plain X-ray has been replace by CT because of high false-negative results, the gold standard for early detection of IOFB is CT, but CT also may be failed to detect the metallic IOFBs, these failures may be explained by the small size of the IOFBs[20]. Therefore, diagnosis by CT has its limitations. However, iron ions flow within the eyeball, which may composure the surface of the lens, and suspended in the vitreous cavity. Most of the cases with siderosis have a definite history of trauma, but some of our patients denied any history of trauma even if specifically asked. In our study, we emphasize the importance of Prussian blue staining of such patients in the absence of definite trauma to prevent delayed or missed diagnosis of siderosis. Therefore, some suspicious siderosis patients without history of ocular trauma, but has unexplained uveitis, small pigmentation on lens surface or retinal pigmentation, Prussian blue staining has a crucial significance for definitive diagnosis of ocular siderosis.

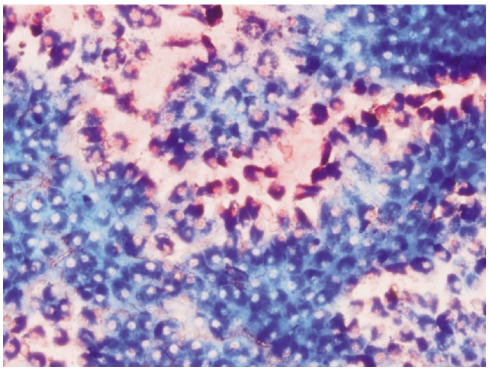

Figure 5 Iron was identified in the lens capsule using Prussian blue staining (200×).

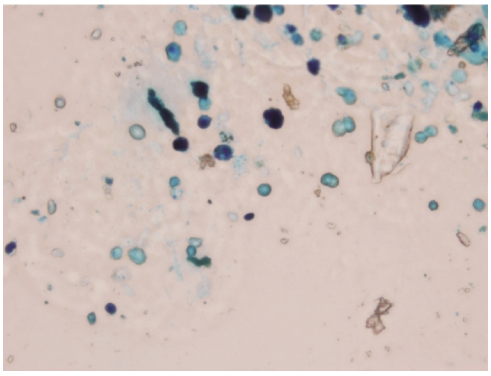

Figure 6 Iron was identified in vitreous using Prussian blue stain (200×).

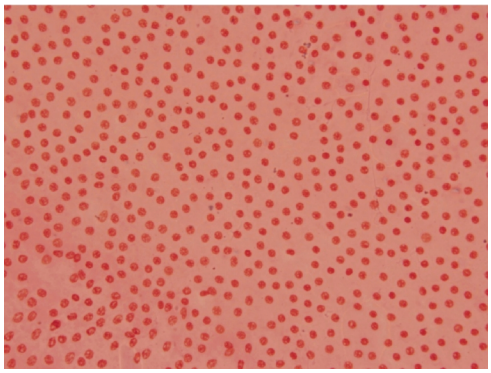

Figure 7 The lens capsule of control groups using Prussian blue stain (100×).

ACKNOWLEDGMENTS

Foundation: Supported by Education Department Funding of Sichuan Province, China (No.2005B020)

Conflicts of Interest: Yang Z, None; **Yang XL,** None; **Xu LS,** None; **Dai L,** None; **Yi MC,** None.

REFERENCES

1 Mete G, Turgut Y, Osman A, Gulsen U, Hakan A. Anterior segment intraocular metallic foreign body causing chronic hypopyon uveitis. *J Ophthalmic Inflamm Infect* 2011;1(2):85-87

2 Xie H, Chen S. Ocular siderosis. *Eye Sci* 2013;28(2):108-112

3 Bai HQ, Yao L, Meng XX, Wang YX, Wang DB. Visual outcome following intraocular foreign bodies: a retrospective review of 5-year clinical experience. *Eur J Ophthalmol* 2011;21(1):98-103

4 Wang R, Wang XL, Wang Y, Chen SJ, Huang XY, Wu N, Ying X. Endotamponades in pars plana vitrectomy for metallic intraocular foreign body associated with endophthalmitis. *Int J Ophthalmol* 2011;4(1):95-99

5 Costa MA, Garcia PN, Barroso LF, Ferreira MA, Okuda EA, Allemann N. Composition of intraocular foreign bodies: experimental study of ultrasonographic presentation. *Arq Bras Oftalmol* 2013;76(1):13-17

6 Faure C, Gocho K, Le Mer Y, Sahel JA, Paques M, Audo I. Functional and high resolution retinal imaging assessment in a case of ocular siderosis. *Doc Ophthalmol* 2014;128(1):69-75

7 Guler M, Yilmaz T, Yigit M, Ulku G, Arslan S. A case of a retained intralenticular foreign body for two years. *Clin Ophthalmol* 2010;4:955-957

8 Patel SN, Langer PD, Zarbin MA, Bhagat N. Diagnostic value of clinical examination and radiographic imaging in identification of intraocular foreign bodies in open globe injury. *Eur J Ophthalmol* 2012;22(2):259-268

9 Kaushik S, Ichhpujani P, Ramasubramanian A, Pandav SS. Occult intraocular foreign body: ultrasound biomicroscopy holds the key. *Int Ophthalmol* 2008;28(1):71-73

10 Woodcock MG, Scott RA, Huntbach J, Kirkby GR. Mass and shape as factors in intraocular foreign body injuries. *Ophthalmology* 2006;113(12):2262-2269

11 Ehlers JP, Kunimoto DY, Ittoop S, Maguire JI, Ho AC, Regillo CD. Metallic intraocular foreign bodies: characteristics, interventions, and prognostic factors for visual outcome and globe survival. *Am J Ophthalmol* 2008;146(3):427-433

12 Yeh S, Ralle M, Phan IT, Francis PJ, Rosenbaum JT, Flaxel CJ. Occult intraocular foreign body masquerading as panuveitis: inductively coupled mass spectrometry and electrophysiologic analysis. *J Ophthalmic Inflamm Infect* 2012;2(2):99-103

13 Stangos AN, Pournaras CJ, Petropoulos IK. Occult anterior-chamber metallic fragment post-phacoemulsification masquerading as chronic recalcitrant postoperative inflammation. *Am J Ophthalmol* 2005;139(3):541-542

14 Yeniad B, Beginoglu M, Ozgun C. Missed intraocular foreign body masquerading as intraocular inflammation: two cases. *Int Ophthalmol* 2010;30(6):713-716

15 Elgin U, Eranil S, Simsek T, Batman A, Ozdamar Y, Ozkan SS. Siderosis bulbi resulting from an unknown intraocular foreign body. *J Trauma* 2008;65(4):942-943

16 Wu TT, Kung YH, Sheu SJ, Yang CA. Lens siderosis resulting from a tiny missed intralenticular foreign body. *J Chin Med Assoc* 2009;72(1):42-44

17 Sargsyan AE, Dulchavsky AG, Adams J, Melton S, Hamilton DR, Dulchavsky SA. Ultrasound detection of simulated intra-ocular foreign bodies by minimally trained personnel. *Aviat Space Environ Med* 2008;79(1):58-61

18 Imaizumi M, Matsumoto CS, Yamada K, Nanba Y, Takaki Y, Nakatsuka K. Electroretinographic assessment of early changes in ocular siderosis. *Ophthalmologica* 2000;214(5):354-359

19 Lee NE, Chung IY, Park JM. A case of Pantoea endophthalmitis. *Korean J Ophthalmol* 2010;24(5):318-321

20 Omoti AE, Dawodu OA, Ogbeide OU. An unusual case of marble intraocular foreign body . *Middle East Afr J Ophthalmol* 2008;15(1):39-42