

Growth of *Scytalidium* sp. in a counterfeit bevacizumab bottle

Gerardo Garcia-Aguirre, Virginia Vanzinni-Zago¹,
Hugo Quiroz-Mercado²

After drawing a dose from an closed bevacizumab (Avastin) bottle, a fungus-like foreign body was observed inside. Samples from the vial were cultured in Sabouraud Emmons media. Growth of multiple light brown colonies with dark pigment was observed after 10 days. The species was identified as

Access this article online	
Quick Response Code:	Website: www.ijo.in
	DOI: 10.4103/0301-4738.119455

Departments of Retina, ¹Microbiology Laboratory, Asociacion para Evitar la Ceguera en Mexico, Mexico, ²Ophthalmology, Denver Health Medical Center, Denver, Colorado, U.S.

Correspondence to: Dr. Gerardo Garcia-Aguirre, Department of Retina, Asociacion Para Evitar la Ceguera en Mexico. Vicente Garcia Torres 46, San Lucas Coyoacan Mexico City, Mexico 04030. E-mail: jggaretina@gmail.com

Manuscript received: 21.05.12; Revision accepted: 09.02.13

Scytalidium sp. Vial, analysis reported that the seal was lacking proper identification measures and that the label, batch number and expiry date did not correspond to a genuine product. Chemical analysis showed no protein, but 3% of polyethylene glycol, citrate and ethanol. Counterfeit bevacizumab is a real situation that poses a significant risk for ophthalmology and oncology patients. The medical community should be aware of this situation in order to enforce adequate preventive measures.

Key words: Bevacizumab, complications, intravitreal injection, *Scytalidium* sp.

Intravitreal bevacizumab has proven to be an excellent alternative for the treatment of choroidal neovascularization. It has been proven as effective as the FDA-approved treatment, ranibizumab, and with considerably less cost.^[1,2] There have been problems with its use such as, an endophthalmitis outbreak because of incorrect handling when being processed by a compounding pharmacy in the United States,^[3] or the appearance of counterfeit bevacizumab in China, which caused an outbreak of intraocular inflammation in a good number of patients.^[4,5] We would like to report the growth of fungi in a counterfeit bevacizumab bottle, out of which one patient was injected.

Case Report

On October 2010, a 64-year-old patient with active choroidal neovascularization in the left eye (best corrected visual acuity of 20/30) was receiving the second intravitreal bevacizumab injection. The bevacizumab bottle was previously closed, and the dose was drawn straight from the bottle (batch number B33928), as it is usually done in Mexico. After injecting the patient, a foreign body was observed floating inside the bottle [Fig. 1], which resembled a fungus ball. The following day, after

vigorous shaking of the bottle, under sterile conditions, three 0.5 ml samples were obtained from the bottle and cultured independently in Sabouraud Emmons media. Two of the samples were incubated at 36°C and one was incubated at 27°C. After 10 days, growth was observed in one of the 36°C cultures, which during the following two weeks grew rapidly into multiple light brown colonies that produced a dark pigment [Fig. 2], and were identical to the foreign body observed inside the bottle. After isolating the microorganism in micro-culture, it was found to have septate hyphae with arthroconidia, and was identified as belonging to *Scytalidium* sp. [Fig. 3]. After obtaining the culture samples, the bottle with its remaining contents was sent to Roche (the distributor of Bevacizumab in our country) for analysis. The analysis showed that the box that contained the vial was additionally opened and glued, that the vial seal was lacking proper identification measures and that the label, the batch number and the expiry date did not correspond to a genuine Avastin product. Chemical analysis performed by Roche showed no protein, but polyethylene glycol, citrate and ethanol. The Mexican Health Authorities were notified immediately after the report was received, which led to an investigation of the supplier of the vial. However, no other counterfeit vials were found in their stock. Also, personnel and physicians were informed of the security measures that the authentic vials have (mainly a blue logo on the vial seal).

The patient was closely observed during the following month and did not develop any intraocular inflammation or adverse events, and therefore, no treatment was initiated. She has been receiving monthly doses of intravitreal bevacizumab since then and has retained visual acuity of 20/25.

Discussion

We are reporting the case of a fungal agent growing in a counterfeit bevacizumab bottle. In our country, compounding pharmacies are not employed as a source of individual doses of bevacizumab. Therefore, the physician draws the dose directly from the bottle. Bottles are obtained from pharmaceutical distributors, which in turn buy the drug from the manufacturer. Since, the process involves the drug changing hands twice, any of the two steps is vulnerable for the introduction of the counterfeit drug.

In this case, the bottle contained not just water, but ethanol, citrate and polyethylene glycol, which could have been added to the contents in order to inhibit microbial growth that could draw attention to the bottle and elicit an investigation. Growth in this case was observed because fungi are organisms that tend to grow in very unfavorable media.

Scytalidium sp. is characterized by having septate hyphae and arthroconidia, and is known to cause onychomycosis and subcutaneous lesions in humans. A case of fungal keratitis has also been reported,^[6] but no cases of endophthalmitis have been published to date. Our patient has presented no clinical evidence of ocular or systemic infection during the 1.5 year follow up. It is difficult to say whether it is due to the fact that no fungal cells were present in the dose administered to the patient or that the human vitreous was not a favorable media for the growth of the microorganism, but the former seems more likely.

We believe that the medical and pharmaceutical community should be aware of the existence of counterfeit products that could

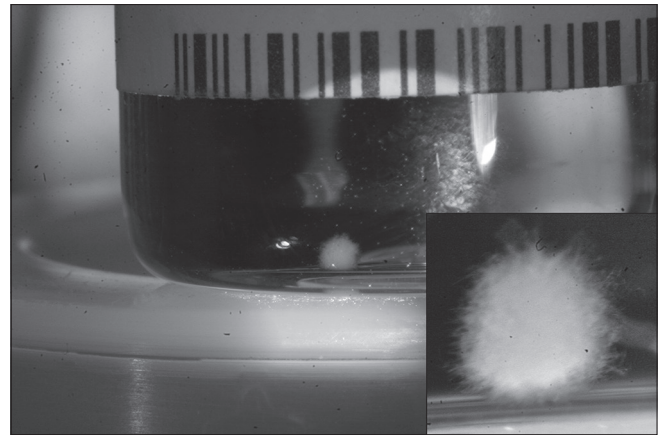


Figure 1: Foreign body observed floating within the contents of a bottle labeled as Avastin (Bevacizumab)

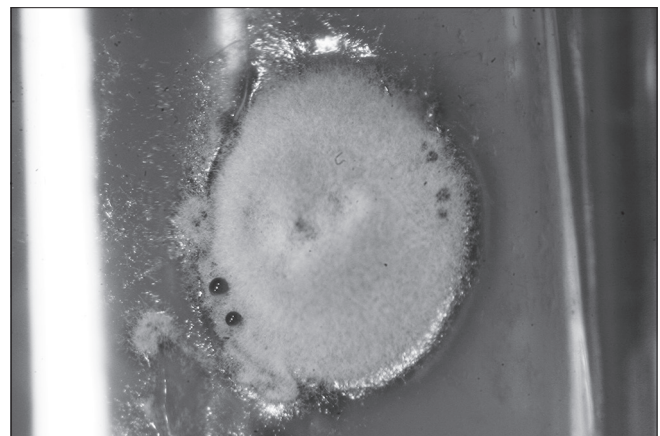


Figure 2: Culture growth at 14 days, in Sabouraud Emmons media, showing multiple light brown colonies that produced a dark pigment



Figure 3: Photomicrography of the microorganism, showing septate hyphae with arthroconidia, identified as belonging to *Scytalidium* sp.

pose a risk for the patient and that preventive measures should be enforced to avoid exposing patients to an unnecessary risk.

References

1. Arevalo JF, Sanchez JG, Fromow-Guerra J, Wu L, Berrocal MH,

- Farah ME, *et al.* Comparison of two doses of primary intravitreal bevacizumab (Avastin) for diffuse diabetic macular edema: Results from the Pan-American Collaborative Retina Study Group (PACORES) at 12-month follow-up. *Graefes Arch Clin Exp Ophthalmol* 2009;247:735-43.
2. Martin DF, Maguire MG, Ying GS, Grunwald JE, Fine SL, Jaffe GJ. Ranibizumab and bevacizumab for neovascular age-related macular degeneration. *N Engl J Med* 2011;364:1897-908.
 3. Goldberg RA, Flynn HW Jr, Isom RF, Miller D, Gonzalez S. An outbreak of streptococcus endophthalmitis after intravitreal injection of bevacizumab. *Am J Ophthalmol* 2012;153:204-8.
 4. Cheng JW, Wei RL. Ranibizumab for age-related macular degeneration. *N Engl J Med* 2011;364:582.
 5. Sun X, Xu X, Zhang X. Counterfeit bevacizumab and endophthalmitis. *N Engl J Med* 2011;365:378.
 6. Farjo QA, Farjo RS, Farjo AA. Scytalidium keratitis: case report in a human eye. *Cornea* 2006;25:1231-3.

Cite this article as: Garcia-Aguirre G, Vanzinni-Zago V, Quiroz-Mercado H. Growth of *Scytalidium* sp. in a counterfeit bevacizumab bottle. *Indian J Ophthalmol* 2013;61:523-5.

Source of Support: Nil. **Conflict of Interest:** None declared.