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Case report

Multimodal imaging of macular subretinal deposits following intravitreal ocriplasmin injection

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ABSTRACT

Purpose: Ocriplasmin is effective in closing macular holes due to vitreomacular traction. We present a case of macular subretinal material deposition observed with spectral-domain optical coherence tomography (SD-OCT) and multimodal imaging, following successful closure of a macular hole following intravitreal ocriplasmin injection.

Observations: An 81-year-old male presented with decreased vision in the left eye due to a full-thickness macular hole secondary to vitreomacular traction. Ocriplasmin (Jetrea) was injected into the vitreous and hole closure was observed after one week. Macular subretinal material deposition developed along the outer surface of the resultant serous detachment on OCT one week post-injection. Fluorescein angiography demonstrated no expanding hyperfluorescence due to retinal or choroidal leak, or staining of the lesion. The material was mildly autofluorescent. The macular subretinal material complex spontaneously decreased with no significant effect on vision over 60 weeks.

Conclusions and importance: Macular subretinal material deposition has not previously been reported following intravitreal ocriplasmin injection. This material is likely composed of photoreceptor outer segments. It is important to recognize that macular subretinal deposits can occur following intravitreal ocriplasmin injection as it may cause diagnostic confusion and potentially influence the visual and anatomical outcomes following successful hole closure.

1. Introduction

Ocriplasmin produces vitreous separation from the retina and vitreous liquefaction by enzymatically degrading laminin, fibronectin and collagen.[1] The MIVI-TRUST[2] trial showed that nonsurgical closure of macular holes were more likely in ocriplasmin-injected eyes (40.6%) than placebo-injected eyes (10.6%).[1,3] Vitrectomy surgical techniques remains the established treatment option for macular hole and symptomatic vitreomacular traction.[4]

Adverse effects associated with ocriplasmin injection include vitreous floaters, photopsia, decreased visual acuity, retinal tear/detachment and progression of the vitreomacular traction towards a macular hole.[1,3,4] Electroretinogram changes, dyschromatopsia and ellipsoid zone changes on SD-OCT following ocriplasmin injection have also been described.[5–10]

The investigation of functional effects on vision post-ocriplasmin treatment is relatively new. Full-field ERG changes post-ocriplasmin have prompted further investigations into potential diffuse effects of ocriplasmin in the retina.[11] Recently, the functional effects of ocriplasmin injection have been studied using macular perimetry.[12]

2. Case report

An 81-year-old male presented with subacute decreased vision in the left eye due to a full thickness macular hole which was confirmed on SD-OCT (Fig. 1A). The patient's visual acuity was 20/20 and 20/50 in the right and left eyes, respectively. Intraocular pressures were normal in both eyes and anterior segment examination was unremarkable. There was no previous significant ocular history or family history of retinal pathology. There were also no subretinal changes noted on OCT in the right eye.

Intravitreal ocriplasmin was injected via pars plana into the left eye. The macular hole was closed one week post-injection. Visual acuity was 20/40 in the left eye and on OCT, persisting vitreofoveal traction (Fig. 1B) was still visible. At 12 weeks post-injection, macular subretinal material deposition was observed along the posterior ellipsoid

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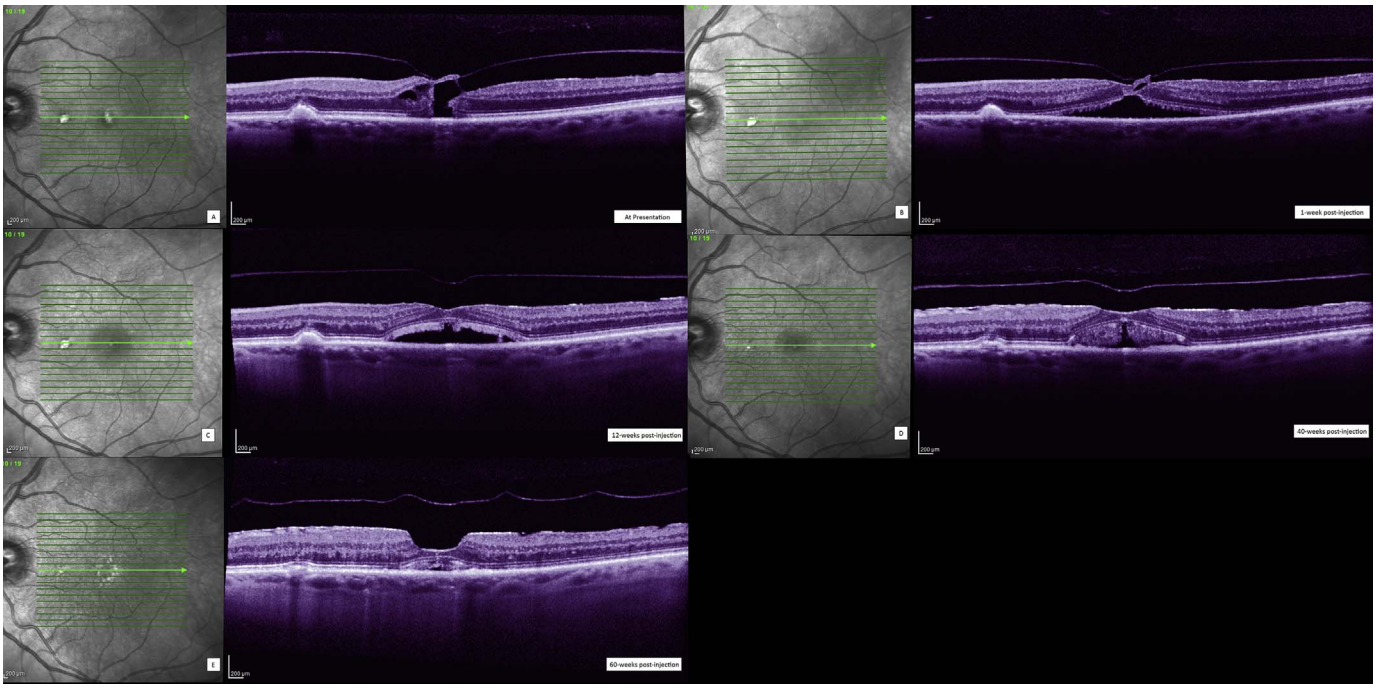

Fig. 1. Spectral Domain-Optical Coherence Tomography (SD-OCT) images with corresponding nIR photos. (A) SD-OCT images with corresponding nIR photos at presentation. **(B)** SD-OCT images with corresponding nIR photos at one week post-ocriplasmin injection. **(C)** SD-OCT images with corresponding nIR photos at 12 weeks post-ocriplasmin injection. **(D)** SD-OCT images with corresponding nIR photos at 40 weeks post-ocriplasmin injection. **(E)** SD-OCT images with corresponding nIR photos at 60 weeks post-ocriplasmin injection.

zone interface (Fig. 1C) within the serous detachment. Visual acuity remained stable (20/40) in the left eye. At 40 weeks post-injection, visual acuity remained unachanged (20/40) and there was a further increase in macular subretinal material deposition on OCT (Fig. 1D). At 60 weeks post-injection, visual acuity improved to 20/32 and the subretinal material decreased in volume as observed on OCT (Fig. 1E).

At one week post-injection, multicolour imaging showed yellow deposits at the fovea (Fig. 2A). These deposits demonstrated mild hyperautoflurescence (Fig. 2B). The yellow deposits were observed to increased in density at 40 weeks post-injection (Fig. 2C). On autofluorescence imaging, increased hyperautofluorescence with a surrounding ring at 40 weeks post-injection (Fig. 2D) was observed. At 60 weeks post-injection, the deposits were still observed to be hyperfluorescent on autofluorescence imaging (Fig. 2E) but appeared less visible on multicolour imaging at the fovea (Fig. 2F). Both imaging modalities demonstrated an overall reduction in size of the macular subretinal material complex at 60 weeks post-injection.

Due to concerns of possible subretinal exudation from choroidal or deep retina pathology, a fluorescein angiogram was performed at 12 weeks post-injection. Fluorescein angiography showed no expanding hyperfluorescence in early (Fig. 3A), mid (Fig. 3B) or late phase (Fig. 3C) to suggest choroidal neovascularization or serous leak. Furthermore, no staining of the lesion was observed.

Macular Integrity Assessment (MAIA Microperimeter Centerview, Padova Italy) was performed to assess the impact of the macular hole and the subsequent macular subretinal material complex on macular fuction. On presentation, the MAIA demonstrated normal average sensitivity threshold (25.4 dB) despite the presence of a small macular hole (Fig. 4A). The MAIA sensitivity plot displayed a signal reduction over the foveal region only. At 1 week post-injection, there was reduction in the average sensitivity threshold on the MAIA (23.3 dB) (Fig. 4B) and reduction in signal extending to the parafoveal region on the MAIA sensitivity plot. At 12 weeks post-injection, there was an improvement in the average sensitivity threshold on the MAIA (25.1 dB)(Fig. 4C) and normalization of the MAIA sensitivity plot. At 40 weeks (Fig. 4D) and 60 weeks post-injection (Fig. 4E), the average sensitivity thresholds on the MAIA remained relatively unchanged, 24.5 dB and 24.4 dB respectively. The MAIA sensitivity plots at 40 weeks and 60 weeks post-injection were normal as well.

3. Discussion

Sub-retinal fluid (SRF) following ocriplasmin intravitreal injection has been reported previously, particularly in eyes where traction has been successfully resolved.[6,8,10,13–17] Development of a serous detachment may be more common after ocriplasmin injection when compared to vitrectomy surgery.[18] Vitreomacular traction is rapidly resolved in vitrectomy surgery by peeling of the ILM with gas tamponade. Following ocriplasmin injection, vitreomacular traction is separated more gradually, thus potentially allowing more subretinal fluid to accumulate in that time.

Subretinal hyperreflective material deposition within the subretinal fluid has been described in a range of macular pathologies such as vitelliform lesion, macular haemorrhage and fibrin deposition in central serous chorioretinopathy.[19]The “shaggy” appearance of the subretinal deposits in the above case report has been observed in the context of central serous chorioretinopathy and vitreo-macular traction syndrome.[20] On multimodal imaging, these deposits appear as yellow spots and are autofluorescent and hyperreflective on OCT imaging.[20] This material is likely to comprise of opsins associated with photoreceptors, Muller cells and lipofuscin-laden macrophages.[21] Spaide et al.[21] hypothesized that an accumulation of subretinal hyperreflective deposits could indicate an abnormality of phagocytic function and a loss of polarity in the retinal pigment epithelium (RPE).

We considered that the macular subretinal material deposition in this case was due to the breakdown of photoreceptor outer segments. This would correlate with the observed macular subretinal material deposition along the outer surface of the ellipsoid zone on OCT imaging. Such orderly deposition would suggest a turn-over process rather than random precipitation. Further multimodal imaging demonstrated no enhancing hyperfluorescence or staining of the material complex on fluorescein angiography and an increased central zone of hyperautofluorescence on autofluorescence imaging. Macular subretinal material deposition may be a result of diminished RPE function leading to

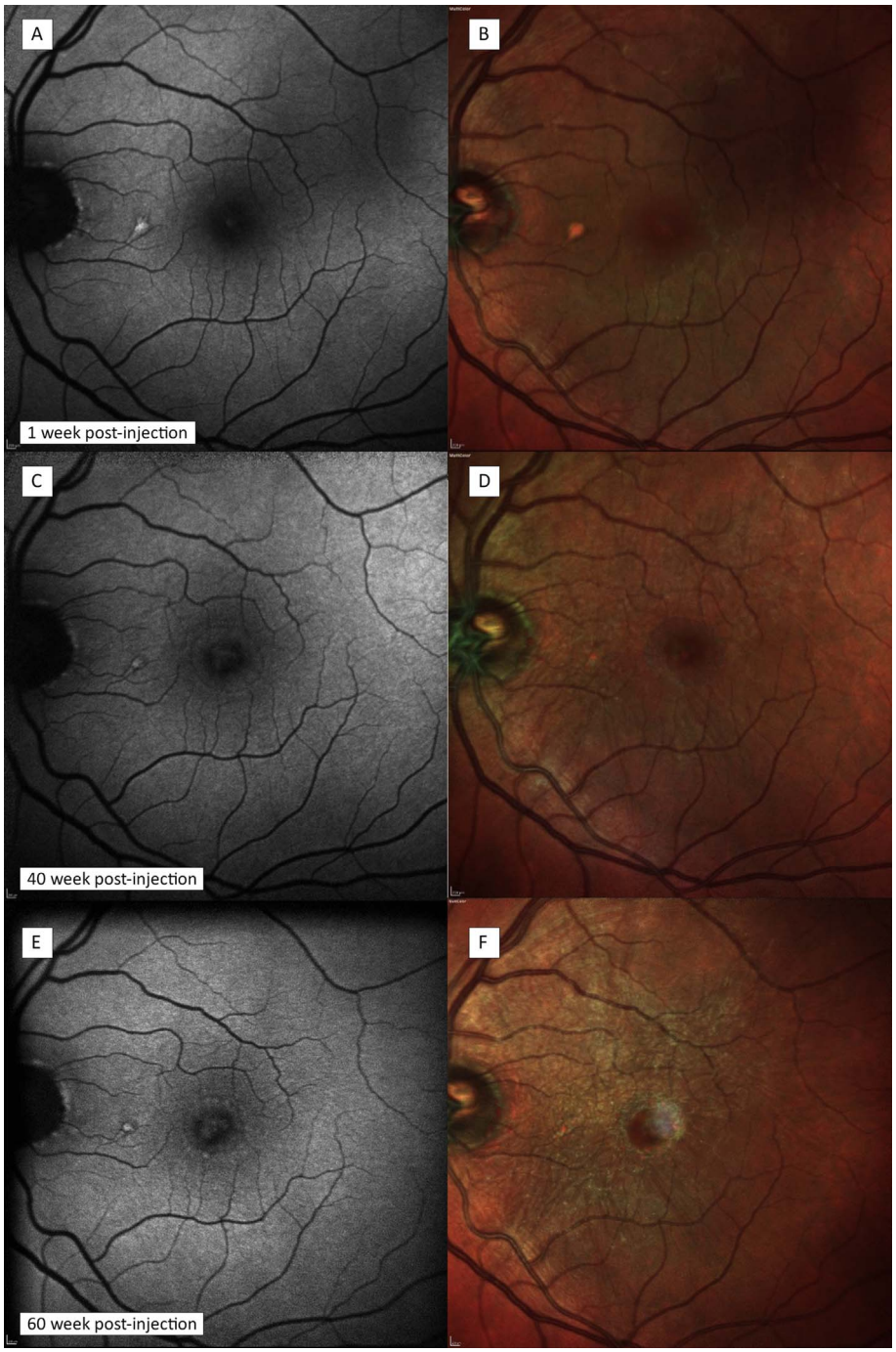

Fig. 2. Autofluorescence imaging; Multicolour imaging. **(A)** Autofluorescence image at one week post-ocriplasmin injection. **(B)** Multicolour photo taken one week post-ocriplasmin injection. **(C)** Autofluorescence image at 40 weeks post-ocriplasmin injection. **(D)** Multicolour photo taken at 40 weeks post-ocriplasmin injection. **(E)** Autofluorescence image at 60 weeks post-ocriplasmin injection. **(F)** Multicolour photo taken at 60 weeks post-ocriplasmin injection.

decreased absorption of SRF and accumulation of opsin breakdown material along the outer photoreceptor layer.

Interestingly, there was a narrow subfoveal area within the serous detachment that was devoid of this material. This area measured approximately 50 microns across and was evident in the OCT images at 12 and 40 weeks post-injection. By week 60, this area was no longer identifiable on OCT imaging. We considered this finding to potentially reflect delayed cone photoreceptor functional recovery following foveal detachment or macular hole. From week 40 post-injection, progressive resolution of the serous detachment and a decrease in the amount of subretinal material would perhaps be indicative of RPE function recovery.

In this case, the macular subretinal material did not affect vision significantly. A decrease in the average sensitivity threshold measured on the MAIA was noted one week post-orciplasmin injection. This was accompanied by a signal reduction on the MAIA sensitivity plot extending from the fovea to the parafoveal region. This transient decrease in macular function was most likely due to incomplete posterior vitreous detachment resulting in increased foveal/parafoveal traction. This observation was similar to findings reported in the OASIS MP-1 substudy[12] where perimetry sensitivity parameters initially decreased coinciding with induction of vitreous detachment but subsequently recovered.

It is unclear whether the presumed RPE dysfunction was solely due to foveal detachment. Chen et al.[22] has shown that ocriplasmin did not affect photoreceptor cells, however its effect on the RPE and adjacent structures remained unclear. Electroretinogram (ERG) changes post-ocriplasmin injection have also been reported.[5–10] These findings raise

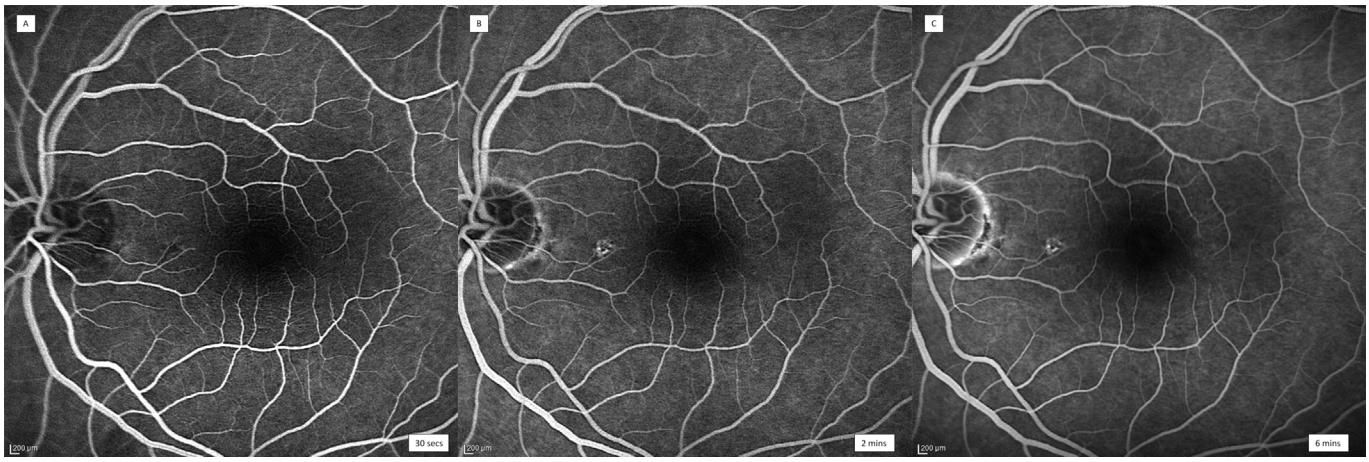

Fig. 3. Fluorescein angiography. (A) Early, **(B)** mid and **(C)** late phase fluorescein angiography image at 12 weeks post-ocriplasmin injection.

questions regarding the potential diffuse retinal effects of ocriplasmin injection. Transient and long-term effects of ocriplasmin injection require further study.

4. Conclusions

To our knowledge, macular subretinal material deposition has not been previously reported after intravitreal ocriplasmin injection. The subretinal material deposition was likely due to photoreceptor outer

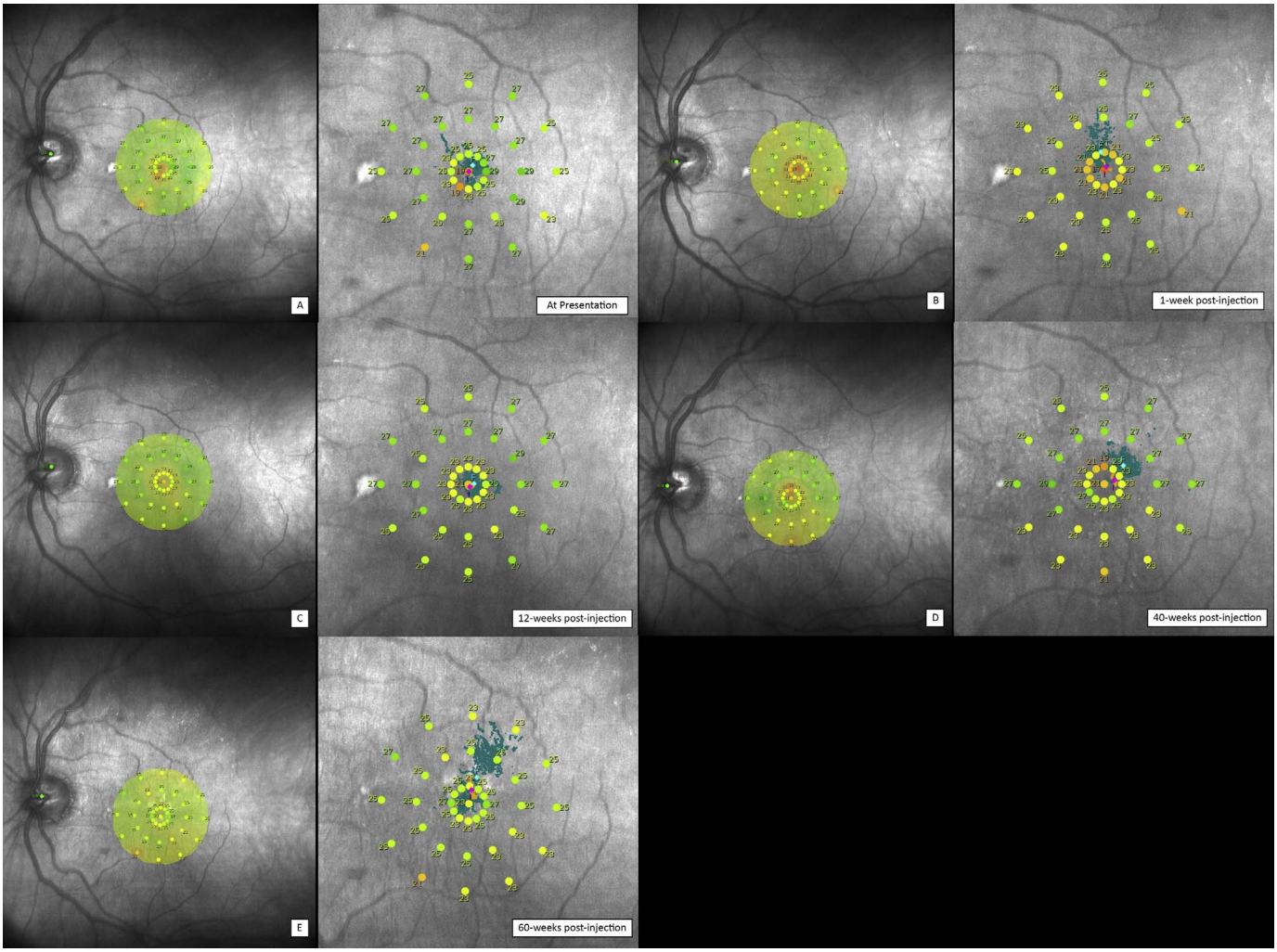

Fig. 4. Macular Integrity Assessment (MAIA) average sensitivity threshold function maps with corresponding sensitivity plots. (A) MAIA average sensitivity threshold function map and sensitivity plot at presentation. **(B)** MAIA average sensitivity threshold function map and sensitivity plot at one week post-ocriplasmin injection. **(C)** MAIA average sensitivity threshold function map and sensitivity plot at 12 weeks post-ocriplasmin injection. **(D)** MAIA average sensitivity threshold function map and sensitivity plot at 40 weeks post-ocriplasmin injection. **(E)** MAIA average sensitivity threshold function map and sensitivity plot at 60 weeks post-ocriplasmin injection.

segment accumulation secondary to RPE dysfunction. Recognition of macular subretinal material deposition as a potential effect of ocriplasmin injection is important to prevent diagnostic confusion and initiation of inappropriate therapy.

Patient consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

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Conflicts of interest

All authors have no financial disclosures.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

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