A Missed Case of Acute Macular Neuroretinopathy

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ABSTRACT

Acute macular neuroretinopathy (AMN) is a rare disease of the outer retina, most commonly presenting with a central or paracentral scotoma, wedge-shaped foveal lesions and hyper-reflective lesions, followed by thinning at the inner segment-outer segment junction. Patients report central/paracentral scotomas which correlate with visual field defects as detected by Amsler grid and automated static visual field testing. The case presented in this paper demonstrates the diagnosis of AMN in the absence of the full range of disease markers and highlights the importance of high density optical coherence tomography scanning in aiding the diagnoses of previously missed clinical conditions.

Keywords: Acute macular neuroretinopathy, spectral domain optical coherence tomography, paracentral lesion, scotoma

INTRODUCTION

Acute macular neuroretinopathy (AMN) is a rare condition which results in temporary or permanent visual loss.[1] It was first described in 1975 and at that time it was believed to be a condition which primarily affected the inner retina,[1] however further research and development in imaging techniques has shown that AMN is in fact a disease of the outer retina.[2-4] AMN is usually characterised by paracentral or central scotomas[1-4] and has been reported with the macula either unilaterally or bilaterally affected and visual acuity either normal or slightly decreased.[4] Wedge-shaped foveal/parafoveal retinal lesions of a reddish brown nature are commonly seen on retinal examination[4,5] with retinal haemorrhages occasionally seen.[6] It has been suggested that the aetiology is likely to be viral, with preceding flu-like symptoms commonly described.[1-5]

One case of suspected AMN in a young woman, who presented with paracentral scotomas, and remained undiagnosed for six years, is discussed.

CASE REPORT

A 21-year-old female presented to clinic initially in 2009, complaining of a small scotoma in the upper temporal visual field of the left eye for approximately eight days. She reported that the onset coincided with the end of a severe bout of flu. Visual acuity was 6/4 bilaterally, with fundus examination showing no defect or visible signs of maculopathy. A small superior temporal scotoma in the left visual field could be mapped on an Amsler grid, however Humphrey Visual Field Analyser (HVF) 30-2 demonstrated no abnormality in either eye. No signs of retinal lesions or haemorrhages were noted, with optical coherence tomography (OCT) and fluorescein angiography (FA) showing no apparent defect. The OCT was performed on the Zeiss Cirrus HD-OCT (Carl Zeiss Meditec, Jena, Germany), with a high definition 5-line raster completed, and FA was performed on the Topcon IMAGEnet 2000 (Topcon Medical Systems Inc, Oakland, USA). At this time no diagnosis or conclusions were able to be made by the ophthalmologists involved and the patient was not required to return for follow-up and was discharged.

Six years later the patient was re-scanned using the Heidelberg Spectralis OCT (Heidelberg Engineering, Heidelberg, Germany). The scan showed the absence of hyper-reflectivity with a residual paracentral lesion and disruption at the location of the inner and outer segment junction (ISOS), as shown in Figure 1. Amsler grid demonstrated a small superior temporal lesion in the left visual field as shown in Figure 2, however HVF 10-2 testing showed no defect. The patient reported the ongoing presence of the superior temporal scotoma, however over time a reduction in size occurred and it is no longer as pronounced.

DISCUSSION

Acute macular neuroretinopathy usually presents in young women of reproductive age,[5] as was the case with this patient. Disease markers for this condition include the presence of scotomas, foveal retinal lesions apparent on the fundus, retinal haemorrhages, and early presenting hyper-reflective retinal lesions followed by disruption or thinning of the outer nuclear layer demonstrated on OCT.[1,4,5,7] It is a condition which has been reported considerably in the literature, with the full range of disease markers aiding in diagnosis in the known cases.[1,3-12] The presenting symptom of a central or paracentral scotoma occurs in patients

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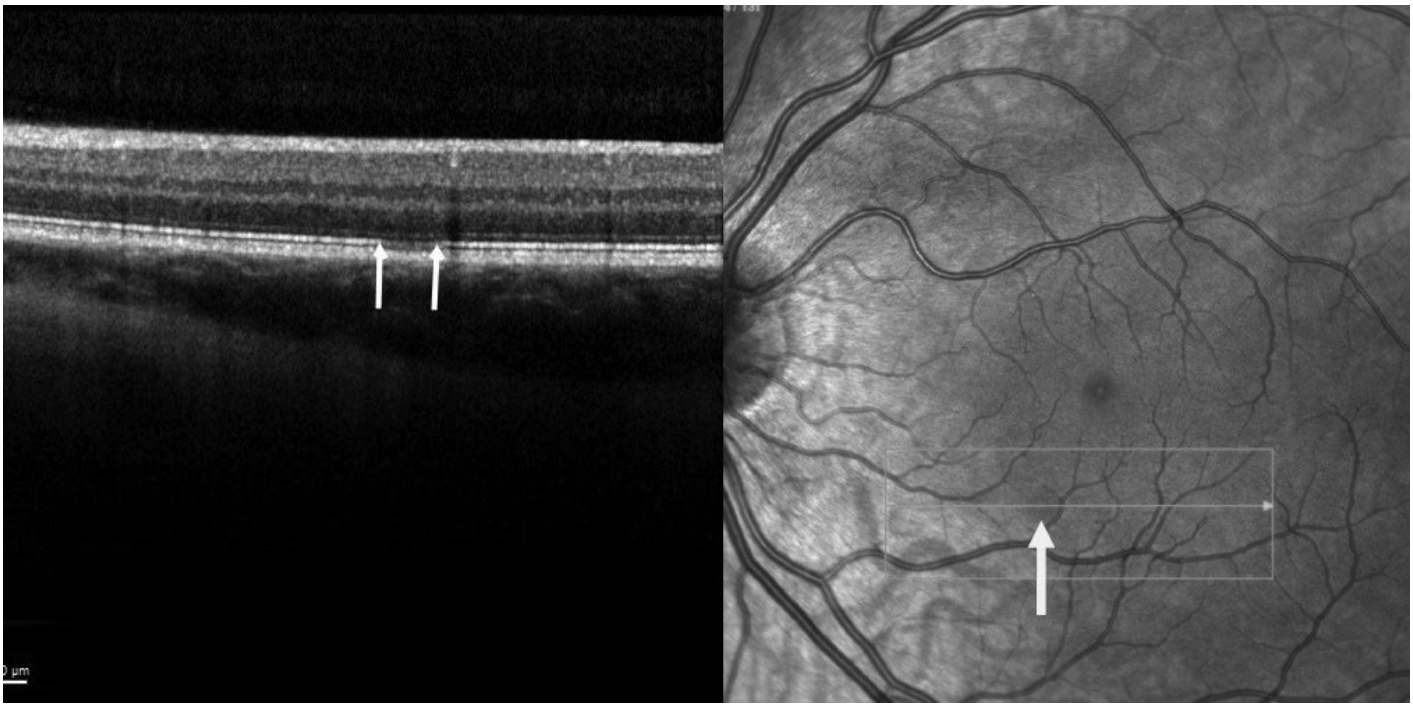

Figure 1. Residual paracentral lesion and disruption at the inner segment-outer segment junction (shown between the two arrows).

with AMN, prompting a thorough clinical examination to allow differential diagnosis.[4,12-14] Visual acuity is most commonly reported as normal, although cases have been reported where reduced vision is present.[7,12,14] Upon fundus examination reddish brown foveal or parafoveal lesions are reported in all but two of the published AMN cases,[4,5] with retinal haemorrhages also accompanying these lesions in rare circumstances.[6] In the case presented, foveal lesions as a distinct disease marker were not demonstrated, therefore the diagnosis of AMN in this case, as well as two others discussed in literature, was based purely on the presence of a scotoma and location of a lesion and disruption at the ISOS junction. The location of the discoloured foveal lesion will generally correlate with the scotoma location subjectively described and may be found on HVF 10-2.[4,13,15] The diagnosis of this rare condition can often be difficult with the signs appearing over a slow time course.[4,15] Aziz et al[5] reviewed 44 cases between 2002 and 2012, comparing them alongside 41 cases previously reviewed by Turberville et al.[4] The mean age at presentation was 30 years, 86% were female and 46% reported a preceding flu-like illness, just as in the case presented in this report.[5] Throughout the literature, pathogenesis of the lesion is described as uncertain, with immune-based aetiology agreed upon as the most likely cause.[1,5,9,16] The commonly used investigative techniques include OCT, Amsler grid, HVF 10-2, and colour and red-free retinal photographs. OCT is described as the most useful of the diagnostic tests, with its ability to show the initial hyper-reflective lesions in the outer nuclear layer which occur due to the disruption of the photoreceptor cell bodies, followed by the thinning of the outer retinal layers and the outer plexiform layer

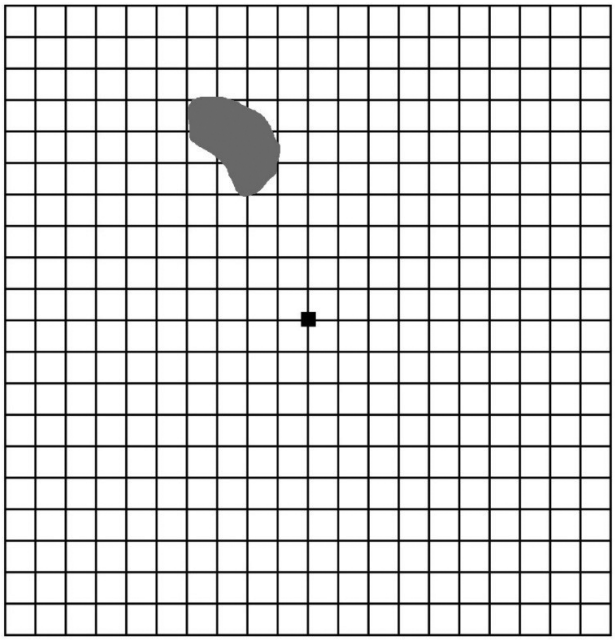

Figure 2. Small superior temporal scotoma in the left visual field.

which reveals absence of hyper-reflectivity.[2,13,16-21] Patients demonstrate retinal disease at the boundary or junction of the inner and outer segments,[5,13,19] which is able to be seen clearly on the OCT images. The case presented in this paper showed a residual lesion due to thinning and disruption of the inner and outer segment junction, however this lesion was less pronounced at the time of diagnosis due to long-term scarring, with subsequent absence of

hyper-reflectivity and a likely degree of resolution. This associated abnormality on OCT and HVF may persist for an indefinite period.[9] Electrophysiology is not routinely performed on those with AMN and typically elicits normal responses.[20,22,23] A limited number of cases in literature have shown both normal and subnormal implicit times on multifocal electroretinogram, demonstrating depressed cone photoreceptor amplitudes which would correlate to the location of the hyper-reflective lesion and abnormal photoreceptor function.[20,24] Fluorescein angiography and indocyanine green angiography (ICG) findings in AMN are reported as normal in the majority of cases where they have been performed as part of investigation, however hypofluorescence on FA corresponding to the lesion location is noted in a small number of cases.[5,13] In contrast, Sanjari et al present one case of bilateral AMN with correlating ICG changes, showing a delay in the filling of choroidal arteries and choroidal hyperpermeability.[14] This raises the question of whether more cases would show ICG changes if this level of testing was available or chosen to be performed at the time, including the case presented in this paper, where ICG testing was not performed. FA was performed in the case presented, and it was the finding of a normal result that enabled the ophthalmologist to rule out any pathological cause, and subsequently discharge the patient with no clear diagnosis.

The use of FA and ICG in patients with suspected AMN allows the differential diagnosis between other conditions which have similar presenting signs.[5,13] Common differential diagnoses include acute posterior multifocal placoid pigment epitheliopathy (APMPPE), acute retinal pigment epitheliitis, central serous chorioretinopathy (CSC), acute zonular occult outer retinopathy and idiopathic blind spot enlargement syndrome, which may also be referred to as white dot syndromes.[4,13] The similar nature of these conditions, associated subtle lesions and temporary visual loss in young to middle-aged adults presents them as important conditions to consider during investigation.[4] The lesions in AMN are distinguishable from these conditions by location and appearance, with those in AMN identified as depressed central macular lesions located in the outer retina. In comparison, CSC is identified by its serous detachment of the retina shown on OCT, and APMPPE is characterised by yellow coloured lesions located in the retinal pigment epithelium. APMPPE will also present with non-fluorescent lesions in early stages of the FA, whereas AMN commonly exhibits no abnormality in FA results.[4] Due to the rarity of AMN as an ophthalmic diagnosis, differential diagnosis is vital to avoid misdiagnosis and therefore to ensure the correct management.

Management of AMN is a debated topic within the literature. The prescription of corticosteroids as a method of treatment has been described, with Hashimoto et al reporting decreased scotoma size after four months of corticosteroid treatment.[25] Interestingly, this line of treatment does not appear to be discussed elsewhere and it is widely agreed that no treatment demonstrates benefits in assisting the resolution of AMN.[8] Scotomas which are present as a result of AMN may resolve over time,[6,9] however in many cases they remain, with approximately half of the reported cases showing no improvement.[4,5,9] Sixty-six of the 85 cases discussed by Aziz et al included follow-up results, and of these, improvement was reported in thirty-two.[5] This ongoing gradual improvement indicates that the disease process involves cell dysfunction over an extended period, rather than cell death, in which case no improvement would be expected.[9] The cause of the remaining long-term scotomas, documented present for up to nine years, is likely due to the thinning of the outer nuclear layer resulting in an irreversible attenuation of the photoreceptor body.[9,16,26] The case reported in this paper is an example of this with the scotoma remaining long-term, with only minimal improvement revealed since onset.

The technology of optical coherence tomography has improved significantly with development from the time domain Stratus, to the spectral domain Zeiss Cirrus and Heidelberg Spectralis now routinely used. The quality of scan produced and detail presented in spectral domain OCTs are superior to their predecessor the time domain, and disruption to the inner and outer segment retinal layers may only be demonstrated on spectral domain technology.[27-29] Currently there is no published literature which demonstrates superiority of the Heidelberg Spectralis to that of the Zeiss Cirrus in retinal layer examination. Given that spectral domain OCT imaging was used on the patient in both investigations, the failure to locate an initial hyper-reflective retinal lesion or subsequent residual lesion was not due to the technology used. Analysis of the two OCTs performed on the patient show the main difference being the spacing between scans. The Cirrus performed in 2009 was completed with scan spacing of 250 microns, whereas the spacing for the Spectralis scan was 11 microns. This increase in high density scans in a compact location is the most probable cause of the discovery of the lesion and disruption at the inner segment-outer segment junction which was previously missed six years prior.

CONCLUSION

The diagnosis of AMN in the presented case demonstrates the ease by which ophthalmic diagnoses can be missed. The absence of multiple disease markers, along with insufficient scan density, may have resulted in the failure to locate the lesion and the inability to provide a clear diagnosis in 2009. It is shown throughout the literature that the reddish brown foveal lesions consistently occur as a presenting sign, however it is interesting to see that along with the one presented in this paper only two other cases have been reported with scotoma and hyper-reflective lesions or

retinal layer disruption as the sole disease markers. This highlights the importance of considering the diagnosis of AMN in all patients presenting with central or paracentral scotomas. Failure of in-depth investigation using spectral domain OCT, particularly in the case of the absence of foveal lesions, may lead to a missed diagnosis. Performing a greater level of high density scans on the Cirrus OCT in the location of the scotoma, and considering the possibility of AMN as a diagnosis at the time of presentation, may have led to an earlier diagnosis of the condition for this patient. Although diagnosis of acute macular neuroretinopathy is uncommon and requires no treatment, it is an important ophthalmic condition which should not be overlooked as a possibility in the presentation of a sudden onset scotoma.

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