Antiretinal antibody- proven autoimmune retinopathy

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A young female presented with bilateral subacute onset of progressive decrease in night vision and reduced peripheral field of vision. The short duration and rapid progression of symptoms along with the lack of family history of night blindness prompted a diagnosis of autoimmune retinopathy (AIR). Fundus fluorescein angiography, optical coherence tomography, visual fields, and electroretinogram were suggestive of AIR. A differential diagnosis of retinitis pigmentosa (RP) was also made. Antiretinal autoantibodies were detected in the blood sample. Treatment was with oral steroids and subsequently oral immunosuppressive agents. Visual acuity was maintained, fundus examination reverted to normal, and investigations repeated at every visit were stable with improvement in visual fields. Our case suggests that AIR, if diagnosed early and treated appropriately, may have a good outcome and should be considered in patients with an atypical presentation of RP.

Key words: Antiretinal antibodies, autoimmune retinopathy, immunosuppressive agents, steroids, visual fields

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Autoimmune retinopathy (AIR) is an immunologic process that involves aberrant recognition of retinal antigens as autoantigens, leading to retinal degeneration. It includes a spectrum of rare autoimmune diseases including "paraneoplastic AIR," such as cancer-associated retinopathy, melanoma-associated retinopathy, and bilateral diffuse uveal melanocytic proliferation; and a larger group of AIRs that share similar clinical and immunologic features without an underlying malignancy termed "presumed nonparaneoplastic AIR" (npAIR).[1] There is rapidly progressive, bilateral, painless visual deterioration. The clinical challenge lies in their rare incidence, dissociation between symptoms and signs, difficult access to investigations that support diagnosis, and the absence of an evidence-based treatment. Onset is acute or subacute,

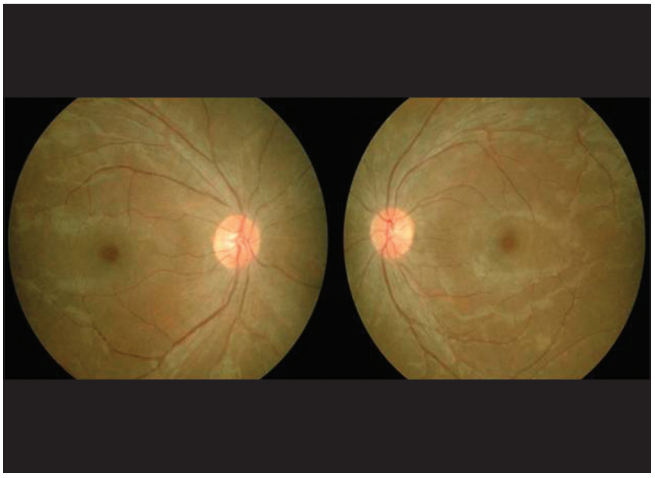

Figure 1: Color fundus photograph showing normal discs, attenuated vessels, retinal pigment epithelial mottling, and suspicion of cystoid macular edema

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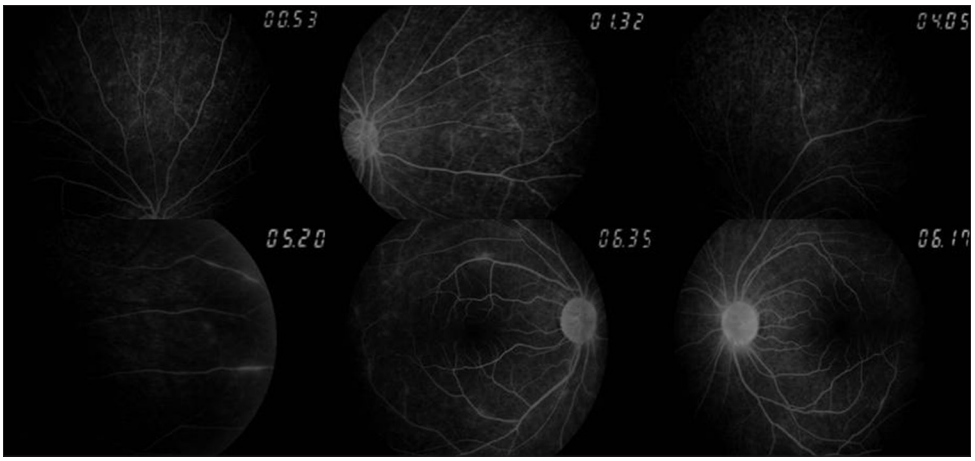

Figure 2: Fundus fluorescein angiogram showing perivenous patchy staining, retinal pigment epithelial defects, and disc staining

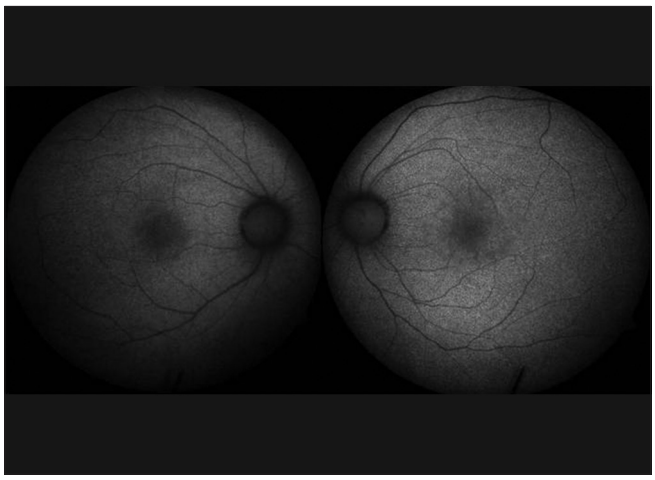

Figure 3: Normal fundus autofluorescence

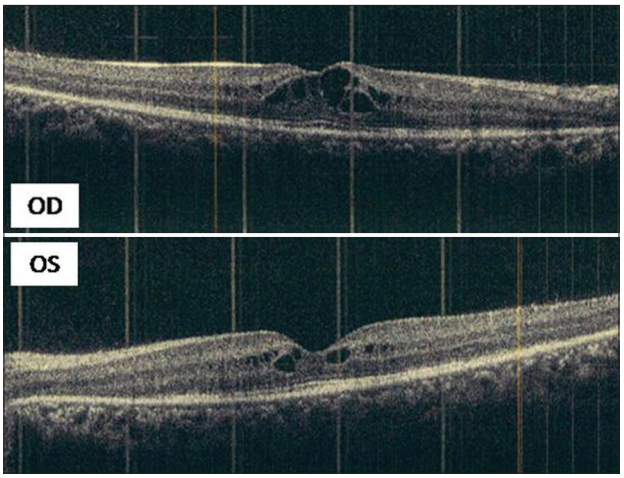

Figure 4: Optical coherence tomography showing cystic spaces

and rarely delayed.[2] Fundus can be normal or may have retinal degeneration with attenuated retinal vessels, waxy disc pallor, and retinal pigment epithelial (RPE) mottling or atrophy, and classically absent inflammatory signs. Full-field and multifocal electroretinogram (ERG)[2] are helpful and optical coherence tomography (OCT) may show cystoid macular edema (CME).[3] Diagnosis of AIR involves detection of antiretinal autoantibodies (AR-Abs) which target retinal antigens with concurrent clinical and electrophysiological evidence of retinal degeneration.

Case Report

A 25-year-old female presented with bilateral progressive decrease in night vision and reduced peripheral field of vision for 7 months, 3 months post full-term normal delivery of her first child. She had received a blood transfusion in the postpartum period. She was earlier treated with topical steroids and subsequently topical nonsteroidal anti-inflammatory drugs for acute zonal occult outer retinopathy (AZOOR) with CME. Best-corrected visual acuity (BCVA) was 6/6, N6 in both eyes. Anterior segment was unremarkable and fundus showed normal discs, attenuated vessels, RPE mottling, and suspicion of CME [Fig. 1].

Fundus fluorescein angiogram (FFA) showed perivenous patchy staining, RPE defects, and disc staining [Fig. 2], with normal fundus autofluorescence (AF) [Fig. 3]. OCT showed cystic spaces [Fig. 4] and ERG was extinguished with nonrecordable scotopic and photopic responses [Fig. 5]. Color vision and contrast sensitivity were normal. Humphrey visual fields 30-2 and full-field 120 screening showed constriction [Fig. 6a and b].

A provisional diagnosis of AIR was made with a differential diagnosis of a retinitis pigmentosa (RP) variant. She was started on systemic steroids (1 mg/kg body weight) with a tapering dose and advised AR-Ab testing.

One month later, her BCVA was maintained at 6/6, N6. OCT showed reduced cystic spaces with thinning of the inner segment-outer segment (IS-OS) junction at the macula, sparing the fovea [Fig. 7]. AR-Ab testing (Oregon Health and Science University) was positive against 23 kDa (anti-recoverin) (HSP27), 30 kDa (carbonic anhydrase II [CAII]), 33 kDa, and 136 kDa proteins by Western blot (WB).

Mycophenolate mofetil (500 mg twice daily) was then added and she was regularly followed up at each visit with BCVA, OCT [Fig. 7], and ERG. Eighteen months later, she was symptomatically better with maintained visual acuity. Fundus showed fewer peripheral areas of RPE mottling with the absence of CME and an improved retinal sensitivity on the visual field [Fig. 8], while other investigations remained stable.

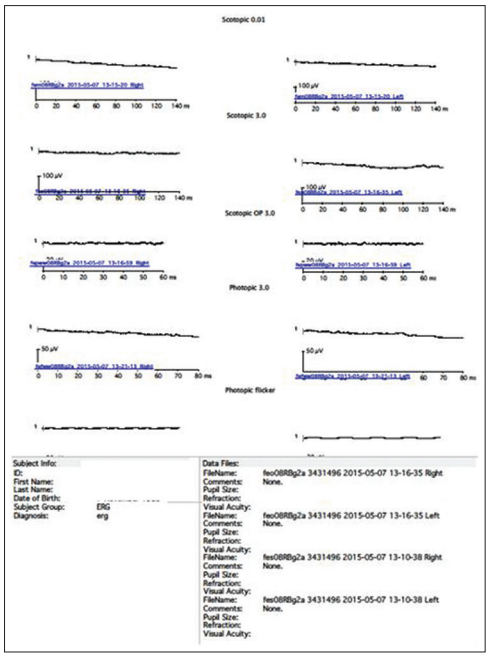

Figure 5: Electroretinogram showing nonrecordable scotopic and photopic responses

Discussion

Although the presence of autoantibodies in suspected AIR has been reported from other countries,[4] there are no proven reports from India, probably due to high costs in testing, logistic difficulties, and similarity to RP. Cases reported with similar presentations have had a longer duration of symptoms.[5]

Typical AIR presents without history of prior visual symptoms and no family history of RP. Female predominance (63%–66%) is seen in npAIR.[1,3] Our patient presented in the third decade without known malignancy.

Ancillary investigations such as perimetry, OCT, ERG, AF, and FFA aid in excluding other causes. Loss of photoreceptor layer or disruption of photoreceptor IS-OS junction has been described in AIR.[6]

Immunohistochemistry, enzyme-linked immunosorbent assay, and WB techniques have been described to detect AR-Abs.[1,7] Anti-recoverin (23 kDa), the most recognized among them, was detected in our patient by WB. While antibodies against CAII (30 kDa) are found in patients of AIR with visual symptoms, anti-arrestin autoantibodies are seen in patients with intraocular inflammation.[7] Progression of AIR

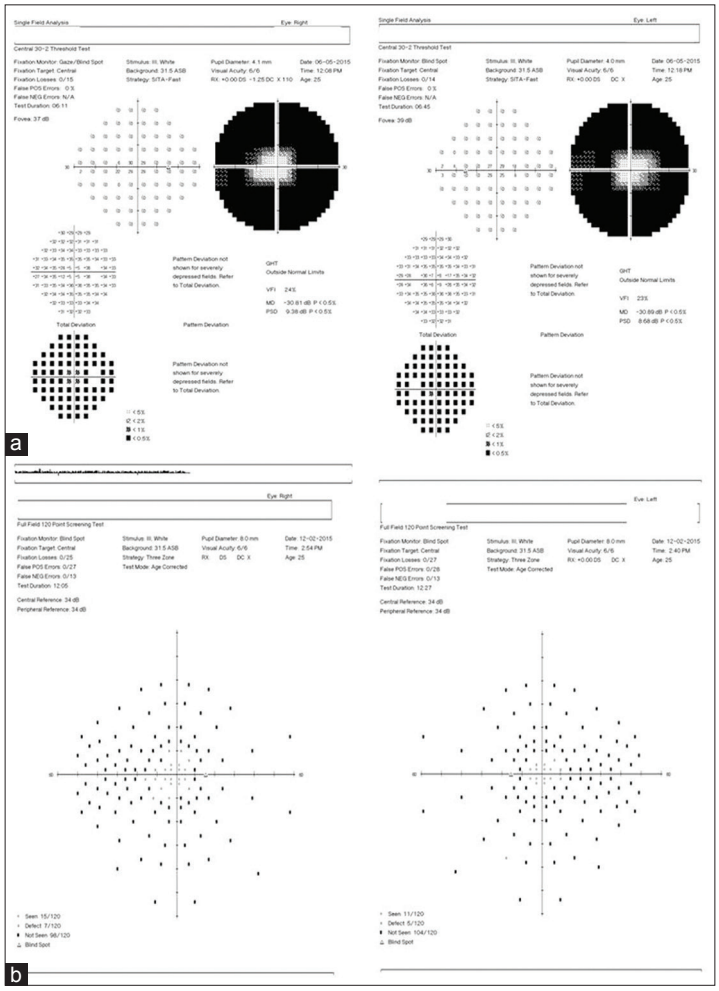

Figure 6: (a) Humphrey visual fields 30-2 showing visual field constriction (b) Full-field 120 screening three-zone strategy showing visual field constriction

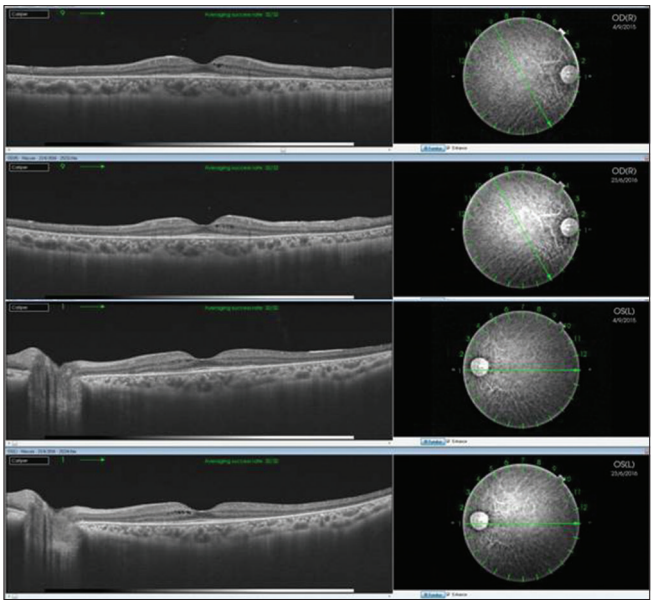

Figure 7: Serial optical coherence tomography showing reduced cystic spaces with thinning of the inner segment-outer segment junction at the macula, sparing the fovea

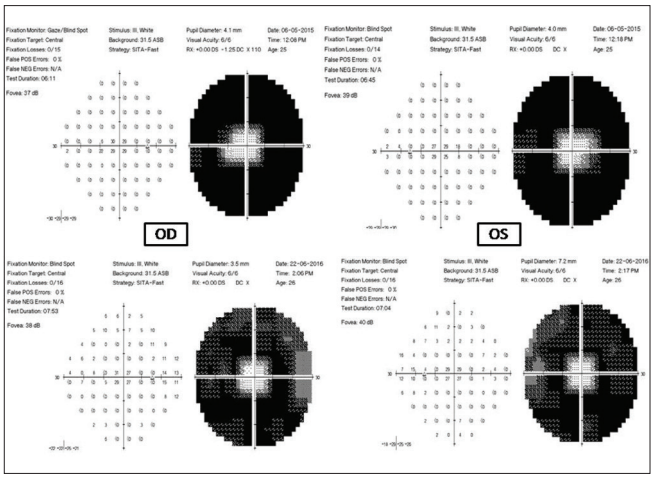

Figure 8: Humphrey visual fields 30-2 showing improved retinal sensitivity

associated with anti-alpha-enolase antibody is typically slower than that with anti-recoverin antibody.[1,2]

Although associations exist between different ERG patterns and different clinical entities of AIR, there is no definite pathognomonic feature of each type. In npAIR, extinguished full-field ERG and selective b-wave loss with reduced oscillatory potentials have been documented.[1,2]

Both cell-mediated and humoral immunity to photoreceptor antigens have been demonstrated in RP and many other uveitic conditions. They can also be found in retinal detachment, post argon laser photocoagulation,[8] and in age-related macular degeneration.[9] Hence, retinal autoimmunity can represent an epiphenomenon which develops following retinal damage caused by physical, microorganismal, or immunological insult. Although autoimmunity does not initiate ocular inflammation, it perpetuates and maintains the inflammatory state and produces further damage to ocular tissues.[8]

Common differential diagnoses of AIR include white dot syndromes (particularly AZOOR), RP, cone-rod dystrophy, and other uveitic syndromes. Enlarged blind spot and well-demarcated areas of hypoautofluorescence are typical of AZOOR. Although visual field defects and response to steroids can sometimes be similar, the absence of pain, good central visual acuity, and normal pupils can differentiate it from inflammatory optic neuropathy.

RP patients with AR-Abs are more likely to have macular edema than those without. However, it is unclear if they precede retinopathy or are simply a consequence of retinal damage.[1]

Various immunomodulatory therapies have been tried in AIR including systemic or local corticosteroids, intravenous immunoglobulin, plasmapheresis, and immunosuppressive treatment.[10]

A combination of treatment modalities has shown improvement in visual acuity, visual fields, and/or CME.[2]

Serial functional testing serves as an indicator of treatment response. At 18-month follow-up on treatment, serial testing showed improved retinal sensitivity on visual fields without further clinical and functional deterioration. Thus, AIR, if diagnosed early and differentiated from RP variants, may have a better outcome with treatment. There are multiple challenges in the diagnosis and treatment of this entity, especially in a country like India, where, owing to consanguinity, similar cases may be diagnosed as RP and left untreated. To the best of our knowledge, this is the first report of a case of AR-Ab-proven AIR from India.

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Conflicts of interest

There are no conflicts of interest.

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