Case Report

Vitiligo in a Patient Receiving Adalimumab for Idiopathic Uveitis

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Abstract

In recent years, adalimumab has been increasingly used in the chronic treatment of non-infectious uveitis. This case report aimed to describe a drug-induced adverse event in a 34-year-old man who presented with blurred vision and floaters in the right eye and was being treated for intermediate uveitis. The patient had started topical treatment with a diagnosis of uveitis at another center. Best corrected visual acuity at presentation was 0.8 (decimal) in the right eye and 1.0 in the left eye. On examination, the anterior chamber in the right eye was clear, with anterior vitreous cells and mild haze, and snow banking and vitreous opacities in the inferior periphery. Fluorescein angiography (FA) showed hyperfluorescence in the right disc and leakage in the inferior periphery. As the inflammation did not resolve with local treatment, systemic cyclosporine was administered, after which the patient exhibited vomiting and weakness. Cyclosporine was discontinued and adalimumab treatment was started. On examination 5 months later, bilateral vitreous cells and mild vitreous opacity were noted, and FA showed mild leakage in the inferior periphery bilaterally. In addition, a depigmented patchy vitiligo lesion was observed on the chin. Due to the persistence of intraocular inflammation and on the recommendation of the dermatology clinic, adalimumab treatment was continued and topical tacrolimus was started for the lesion. On examination 3 months later, the inflammatory findings had resolved and there was no progression of the vitiligo lesion. The patient's treatment was continued. Taken together with the previous literature findings, no pathology was found in the patient's systemic examination, suggesting that this lesion was a side effect of the treatment. Ophthalmologists should be alert for this side effect in patients receiving adalimumab.

Keywords: Adalimumab, pars planitis, vitiligo

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Introduction

Tumor necrosis factor-α antagonists (anti-TNFα) are used in the treatment of dermatological, rheumatological, and gastroenterological diseases, as well as non-infectious uveitis.[1] Some case reports describe improvement of vitiligo in patients receiving anti-TNFα therapy for other conditions,[2,3] while others report patients who developed vitiligo after starting anti-TNFα therapy.[4,5,6] In cases of vitiligo subsequent to anti-TNFα use, the patients received the drug to treat systemic chronic inflammatory diseases. No previous study has described a patient developing vitiligo after using adalimumab for idiopathic uveitis.

In this case report, we aimed to report new-onset vitiligo in a patient receiving adalimumab therapy for pars planitis.

Case Report

A 34-year-old man with complaints of floaters and blurred vision for 3 weeks presented to another clinic where he was diagnosed with uveitis, prescribed topical steroid drops, and referred to our center. In the other clinic he was treated with topical dexamethasone (Maxidex, Novartis, Puurs, Belgium) 3 times daily for a week, followed by topical loteprednol drops (Lotemax, Bausch and Lomb, Rochester, NY, USA) 5 times daily. He presented to our center after 2 weeks of use. The patient's best corrected visual acuity (BCVA) at presentation was 0.8 (decimal) on the right and 1.0 on the left. Intraocular pressure (Goldmann applanation tonometry) was 13 mmHg on the right and 18 mmHg on the left. On anterior segment examination of the right eye, no cells or flares were observed in the anterior chamber, while cells and mild turbidity were observed in the anterior vitreous. The left eye was normal. On fundus examination, "snow banking" and vitreous opacities were observed in the inferior periphery of the right eye. Macular images obtained by optical coherence tomography were normal. Fluorescein angiography (FA) showed optic disc hyperfluorescence and peripheral vascular leakage in the right eye (Figure 1). Possible infectious causes

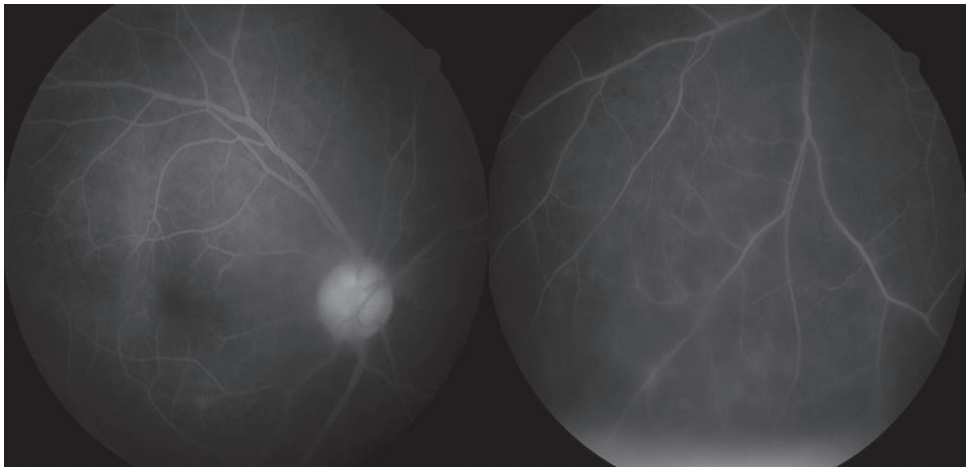

Figure 1. In the patient's initial examination, late fluorescein angiography of the right eye showed hyperfluorescence in the optic disc and vascular leakage in the lower periphery

of intermediate uveitis (tuberculosis, *Borrelia burgdorferi, Bartonella henselae,* syphilis, and toxocariasis) were ruled out. Consultations with the departments of neurology, rheumatology, and chest diseases were requested to investigate non-infectious causes (sarcoidosis, multiple sclerosis, inflammatory bowel disease, lymphoma, tuberculous interstitial nephritis and uveitis syndrome, and Sjögren's syndrome), but no systemic cause could be identified. With the diagnosis of pars planitis, three deep sub-Tenon injections of triamcinolone acetonide (Kenacort-A, Deva, Tekirdağ, Türkiye) were administered to the patient at 1-month intervals while topical steroid therapy was continued. As there was no regression in inflammatory findings with local treatment, systemic cyclosporine (Sandimmun Neoral, Novartis, Eberlach, Germany) treatment was initiated. However, due to complaints of fatigue and vomiting, it was discontinued and replaced with adalimumab (Humira, AbbVie, Ravensburg, Germany). Subcutaneous adalimumab injections were administered as a loading dose (80 mg) followed 1 week later by doses of 40 mg repeated at 2-week intervals.

Although the inflammation findings regressed, the development of a vitiligo lesion on the patient's lower jaw area was observed in month 5 of treatment (Figure 2). On examination, his BCVA was 1.0 (decimal) in both eyes and the anterior chamber was calm bilaterally. Sparse cells and minimal turbidity were observed in the vitreous of both eyes. Minimal peripheral vascular leakage was observed bilaterally on FA imaging (Figure 3). Ocular findings and examinations were reviewed for Vogt-Koyanagi-Harada (VKH) syndrome, but no additional pathology was detected. No side effects other than vitiligo were observed in the patient. Complete blood count and biochemistry test results were within normal limits. No pathology was detected in repeated consultations to investigate for both systemic diseases and extraocular findings of VKH syndrome. The dermatology clinic stated there was no contraindication to the continuation of adalimumab therapy. Tacrolimus (0.1%) pomade (Tacrolin, Farma-Tek, Sakarya, Türkiye) was started for the treatment of vitiligo as recommended by the dermatology clinic.

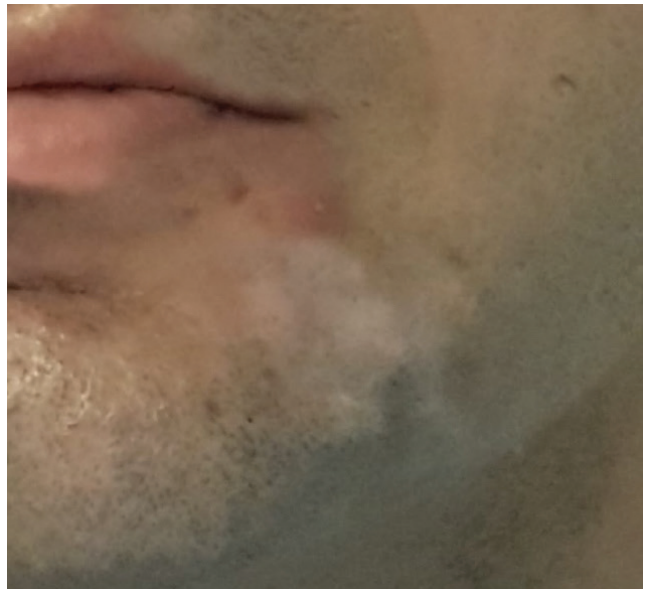

Figure 2. A vitiligo lesion is observed on the patient's left jaw

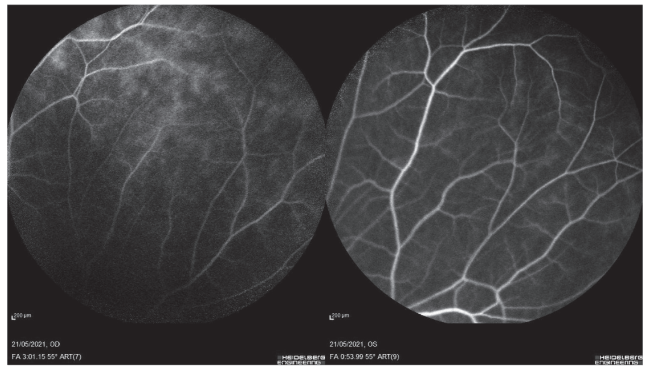

Figure 3. After 5 months of treatment, fluorescein angiography revealed persistent peripheral vascular leakage in the right and left eyes

No progression of the vitiligo lesion was observed at follow-up 3 months later. Treatment with adalimumab and topical tacrolimus was continued.

Discussion

Previous studies showed that TNF is an important mediator in various inflammatory diseases, leading to the development of various anti-TNF agents such as infliximab, etanercept, and adalimumab. Although anti-TNF therapy has been proven to be effective and safe in the treatment of chronic inflammatory conditions, the development of autoimmune diseases and conditions associated with anti-TNF therapy have also been reported.[7] These conditions include new-onset vitiligo or worsening of existing vitiligo.[4,5,6] However, anti-TNF drugs have also been shown to be beneficial in the treatment of vitiligo lesions, which are considered an autoimmune condition.[2,3]

TNF levels in vitiligo lesions have been shown to be increased and associated with disease activity.[8] Anti-TNF drugs were thought to be beneficial in the treatment of vitiligo and were reported to induce regression of the lesions in clinical studies.[2,3] In contrast, new vitiligo lesions may develop while receiving anti-TNF therapy for various autoinflammatory diseases.[4,5,6] Although several hypotheses have been put forward regarding the underlying cause of these contradictory findings, the most accepted of these hypotheses is that long-term TNF inhibition causes an imbalance in cytokine levels.[9] Studies on mouse models of vitiligo have shown that interferon (IFN) also plays a role in lesion formation,[10,11] and later reports also indicated that JAK inhibitors that inhibit IFN were effective in the treatment of vitiligo.[12,13] In an epidemiological study evaluating patients receiving anti-TNF and non-anti-TNF treatments for various autoinflammatory diseases, the risk of developing vitiligo was found to be twofold higher in patients receiving anti-TNF treatment than in patients undergoing conventional treatment.[14] In another case series, it was reported that anti-TNF agents both caused new-onset vitiligo and worsened vitiligo lesions that existed before treatment.[15] In our case, a detailed investigation for systemic disease was conducted both at first admission and after the development of the vitiligo lesion, and no underlying pathology that could cause uveitis was detected. When evaluated together with the previous literature, the fact that our case was under adalimumab treatment for idiopathic uveitis suggests that the development of vitiligo is a result of using adalimumab.

Continuing the anti-TNF agent with an additional topical treatment for the lesion is recommended for the treatment of new-onset vitiligo during anti-TNF therapy. In a multicenter retrospective study, it was reported that continuation of anti-TNF therapy was appropriate in patients with new lesions, but the prognosis was poor when anti-TNF therapy was continued in patients with worsening of existing lesions.[15] In the same publication, it was stated that while spontaneous regression was observed in some of the patients, others received additional topical treatments. Our case was also evaluated by the dermatology clinic, and because he had only a single lesion, continuation of anti-TNF and topical treatment were recommended.

Another point to keep in mind in our case is the exclusion of VKH syndrome in the differential diagnosis, as vitiligo and uveitis occurred together. Ocular signs of VKH syndrome include increased choroidal thickness, hyperemia and edema of the optic disc, multiple serous retinal detachments, and multiple early hyperfluorescent spots on FA.[16] After our patient developed vitiligo, we reassessed him for VKH syndrome. However, no suspicious findings were observed in our examinations, and there were no findings suggestive of VKH in the systemic investigations and evaluations made by the relevant clinics.

In summary, a review of studies in the literature documenting new-onset vitiligo after the use of various anti-TNFs shows that all patients were using these drugs because of systemic autoimmune diseases. In contrast, our patient was using adalimumab to treat idiopathic intermediate uveitis. Previous studies have not reached a definite conclusion on whether vitiligo occurs because of the underlying disease or the anti-TNF agents. However, the absence of an underlying systemic disease in our case supports the view that vitiligo lesions may be induced by adalimumab use.

In recent years, ophthalmologists increasingly prefer biological agents with high efficacy and reliability for the treatment of inflammatory eye diseases. Ophthalmologists should also be aware that vitiligo lesions may develop due to the use of adalimumab. In such cases, the patients should be re-evaluated in terms of systemic diseases, and treatment should be reviewed with the relevant departments using a multidisciplinary approach.

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Ethics

Informed Consent: Obtained.

Authorship Contributions

Surgical and Medical Practices: F.N.Y., Concept: M.F.K.D., Design: M.F.K.D., Data Collection or Processing: F.N.Y., M.F.K.D., Analysis or Interpretation: F.N.Y., M.F.K.D., Literature Search: F.N.Y., M.F.K.D., Writing: F.N.Y., M.F.K.D.

Conflict of Interest: No conflict of interest was declared by the authors.

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