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A CASE OF VKH SYNDROME WITH RHEUMATOID ARTHRITIS

Rheumatology

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ABSTRACT

VKH disease is considered to be a T- cell mediated autoimmune response directed against melanocyte although the exact antigen involved are incompletely understood. Immunohistochemical study of eyes affected by VKHD, revealed an increased T helper/ T suppressor cells ratio and CD25+ and CD26+ T lymphocytes within choroidal inflammatory foci. Despite a common genetic susceptibility, the association between VKH syndrome and RA has been rare. Here we present a case of 43-year-old lady presented with chief complaints of headache, redness of eyes and aural fullness for 9 months. Initially it was thought to be uveitis and she was put on steroids and her complaints resolved completely but recurred after steroid withdrawal. She had such 4-5 episodes during the course of 9 months. She also complained of arthralgia for last 8-9 years for which she took multiple treatments before she presented to us for uveitis. Rheumatoid arthritis was suspected and Anti CCP was sent which came out to be strongly positive suggestive of rheumatoid arthritis. Ophthalmological examination was suggestive of total vitreous detachment and active anterior uveitis. Fundus examination showed a festooned pupil and hyperemic disc with macular edema which being confirmed by OCT. Audiometry was suggestive of bilateral mild sensorineural hearing loss at higher frequency. Hence a diagnosis of Vogt-Koyanagi-Harada in a patient of seropositive RA was put forth.

KEYWORDS

INTRODUCTION -

The 43-year-old lady presented to OPD with chief complaints of headache, redness of eyes and aural fullness for 9 months. Patient had headache which was holocranial, persistent associated with photophobia, phonophobia, neck stiffness and painful neck movements. She complained of diminution of vision, redness of both eyes with peri orbital dull aching pain which was not associated with epiphora, itching, fever. Following this she complained of aural fullness and dysacusis. No active complaint of fever, cough, cold, rhinitis, burning micturition, oral ulceration, skin pigmentation-rashes back then. After 2 months the patient complained of hair loss without scarring and increased blurring of vision following which consulted an ophthalmologist and she was put on steroids leading to dramatic clinical improvement. Later she experienced multiple episodes of blurring of vision and redness of eye. Patient has been better in terms of ocular and audiological complaints after initiation of steroids but not completely resolved.

Patient has arthritis for last 8-9 years for which she took multiple treatments. No documentation available, then she presented to us for uveitis and then Anti- CCP report strongly positive suggestive of rheumatoid arthritis. She is off treatment for this since the last 7-8 months and no active joint pain at present.

Investigation:

HB/TC/PLT	**8.6/7500/318000**	**ESR**	**22**
CREAT	0.59	CRP	1.04
TP/ALBUMIN	6.86/3.87	TIBC (250-450)	327.5
URINE RM	PROTEIN -TRACE	IRON (49-181)	28.56
ACE ENZYME	18.5 (8-52)	SGPT/SGOT	34/30
ANTI TPO	<3.0	FERRITIN (70-435)	3.06
S.TSH-(0.25-5.0)	9.16	FT4 (9.55-25)	18
R FACTOR	NEGATIVE	ANTI CCP (0-5)	134
VIT B12	211	ANA BY IF	NEGATIVE
TB GOLD(IGRA)	NEGATIVE	VDRL (SLIDE/ELISA)	NEGATIVE
2D ECHO	NORMAL	MANTOUX TEST	NEGATIVE
HIV	NEGATIVE	HCV	NEGATIVE
HBSAG	NEGATIVE	ASO TITRE	NEGATIVE

X RAY pelvis with both hip joint: Normal, No sacroiliitis.

X RAY chest: Normal

HRCT Thorax:
Bilateral mildly hyperinflated lung fields.
Few thin plates like atelectasis involving the right middle lobe and lingula.

Sub-centimetre mediastinal lymphadenopathy.

Bilateral minimal pleural thickening.

Ophthalmological examination: (6 months ago)
Findings suggestive of total vitreous detachment and active anterior uveitis.

Ophthalmic -B scan: (6 Months back)

BILATERAL EYE:
Chorio-retinal layer is thickened.

Fine bands with after eye movements are noted s/o total vitreous detachment.

Ophthalmological examination (At present):
Her BCVA in both the eyes is 6/18 and intraocular pressure by applanation tonometry in RE 14 mm hg LE 16 mm hg. Slit lamp

examination shows grade 2 nasal pterygium with KP's, posterior synechiae, iris pigment dispersion over corneal endothelium and anterior lens capsule in both eyes' s/o previous attack of uveitis.

Gonioscopy shows open angle with few pigments' dispersion in both eyes.

Fundus examination shows a festooned pupil with healthy disc and macula with normal periphery in RE. LE shows a festooned pupil with normal disc with macular oedema with hyperaemic disc which is being confirmed with OCT.

Audiometry (at present):
Mild sensorineural hearing loss bilateral specially at high frequency.

Plan of management further:
Plan to start Injection adalimumab (40 mg/0.8ml) subcutaneously every 2 weeks.

Diagnosis
VKH Syndrome in a patient of rheumatoid arthritis (8-9 years) and hypothyroidism (newly diagnosed).

DISCUSSION:
VKH disease is considered to be a T-cell–mediated autoimmune response directed against melanocytes, although the exact antigens involved are incompletely understood.

Immunohistochemical study of eyes affected by VKHD, revealed an increased T helper/T suppressor cells ratio and CD25+ and CD26+ T lymphocytes within choroidal inflammatory focii. These authors also observed class II major histocompatibility complex (MHC) expression in choroidal melanocytes and endothelium of choriocapillaris.

Helper T cell subsets producing Th1 cytokines (interferon-gamma and interleukin-2) after melanocyte derived peptides may produce pathological changes in VKHD, such as the granulomatous choroid inflammation in acute phase. [1][2][3]

Tyrosinase peptide is a known target of T-cells, specifically in melanocytes expressing HLA DRB1-04*05. This inflammatory cascade leads to the formation of non-necrotizing granulomas in affected organs. In the eye, these are seen as sub-retinal pigment epithelial (RPE) aggregates named Dalen-Fuchs nodules, which may also be seen in other granulomatous processes, especially sympathetic ophthalmia.

The clinical course of VKH syndrome can be divided into prodromal, acute uveitis, convalescent, and chronic recurrent stages. Neurological and auditory involvement occur in the prodromal stage. Ocular involvement occurs in acute uveitic, convalescent, or chronic recurrent stages, whereas skin involvement occurs in the convalescent stage. History of ocular trauma or surgery must be absent. Based on the diagnostic criteria, a patient can be classified as having complete, incomplete, or probable VKH.

VKH disease can be associated with other autoimmune disorders, such as autoimmune polyglandular syndrome, hypothyroidism, Hashimoto thyroiditis, diabetes mellitus, Guillain-Barré syndrome, immunoglobulin A (IgA) nephropathy and malignant lymphoma. Decreased Vit-D3 level is associated with increased intraocular inflammation in VKH syndrome. [1][2][3]

Cataract, glaucoma, choroidal neovascularization and subretinal fibrosis are the common complications of VKH syndrome.

Corticosteroid is the mainstay of treatment for 3-6 months in gradual tapering course, IV methylprednisolone 1-2 mg/kg /day for 3 days followed by oral prednisolone in tapering dose for minimum 3-6 months until the inflammation subsides. Refractory cases are treated by immunosuppressive agents like cyclosporine, mycophenolate mofetil or azathioprine. Anti TNF alpha monoclonal antibody-adalimumab is also used for refractory cases.

Here the patient has rheumatoid arthritis as well, VKH syndrome association with rheumatoid arthritis is very rare. Uveitis without scleritis/episcleritis is very rarely associated with rheumatoid arthritis.

Differential Diagnosis:

1: HLA B27 uveitis: Ankylosing spondylitis can present with uveitis but in this case the patient is not having any axial joint pain, X-ray pelvis is normal, HLA B27 is negative so it is less likely.

2. Sarcoidosis: It can sometimes present with posterior uveitis or anterior uveitis with B symptoms (fever, weight loss, night sweats), but the patient is not having any B symptoms and Angiotensinogen Converting enzyme is not raised, so sarcoidosis can be rule out. [12]

3. Sympathetic ophthalmia: Sympathetic ophthalmia is an autoimmune condition that is a direct response of penetrating trauma or surgery to the eye, exposing ocular molecules as antigenic material leading to the immune system developing an inflammatory response to the uvea. This condition also leads to bilateral non-necrotizing granulomatous uveitis, but there is no history of trauma.[11]

4.Syphilis: Treponema pallidum infection can present with uveitis but the patient is not having any significant skin lesions or oro-genital ulceration so it is highly unlikely.

5. Rheumatological conditions: Anterior uveitis can be a manifestation of many rheumatologic diseases such as juvenile rheumatoid arthritis/juvenile idiopathic arthritis (JRA/JIA), reactive arthritis (Reiter's syndrome), inflammatory bowel disease (IBD), psoriatic arthropathy, Wegener's granulomatosis, and relapsing polychondritis, SLE [13]. But the patient does not complain of any symptom that might point towards these disorders.

6. Cogan syndrome: Cogan syndrome is the closest differential for VKH. But the patient is not having interstitial keratitis.

7. Choroidal melanoma: Patients with choroidal melanoma may develop serous retinal detachments, and non-pigmented melanomas may appear as subretinal pigmentary loss similar to VKH.

8. Alport syndrome: Alport syndrome shows choroidal thickening but is characterised by significant inner retinal changes. Sensorineural hearing loss is also seen in Alport syndrome. [10]

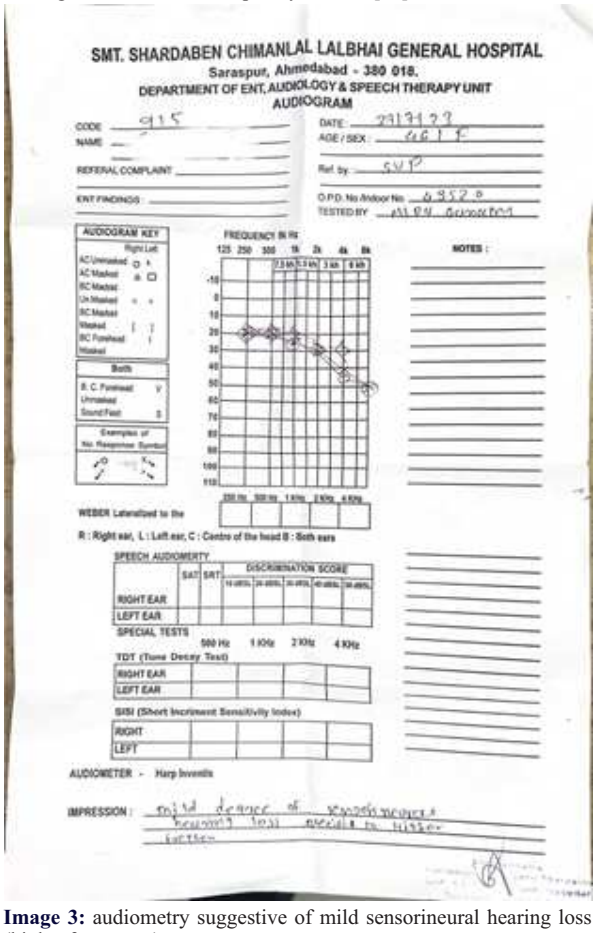

Image 3: audiometry suggestive of mild sensorineural hearing loss (higher frequency).

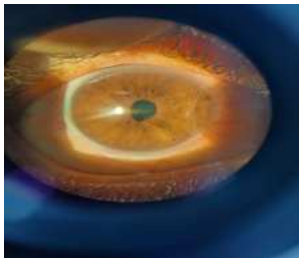

Image1: Right Eye with posterior synechiae and KP's over endothelium

Image 2: Left Eye with posterior synechiae

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