MMJ

Malta Medical Journal, 2026; 38(2)

http://mmsjournals.org/index.php/mmj/48

CASE REPORTS

A case of antiphospholipid syndrome associated with bilateral intermediate uveitis

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A 61 year old male presented with blurred vision after being treated for an unknown source of infection. He was found to have bilateral intermediate uveitis after urgent ophthalmological review. Blood results showed a genuine persistent thrombocytopenia. In view of the history of bilateral intermediate uveitis in association with a genuine thrombocytopenia, further blood investigations were taken. Further investigations revealed positive anticardiolipin antibodies, β2 glycoprotein antibodies and a strongly positive lupus anticoagulant test. Uveitis is an uncommon presentation of antiphospholipid syndrome. This case report outlines a case of bilateral intermediate uveitis in association with antiphospholipid syndrome.

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A 61 year old gentleman presented to the Accident and Emergency Department at Mater Dei Hospital, Malta with a self- reported history of fever in the previous two weeks, associated with back pain and an antalgic gait and that had persisted despite a course of Amoxicillin followed by a course of Doxycycline. This gentleman had sustained a mechanical fall in a quarry with trauma to the left lower limb one month prior to presentation, for which he had not sought medical advice. On presentation his blood pressure was within normal limits at 132/85, pulse rate was 74 beats per minute and he was afebrile.

Physical examination revealed an antalgic gait and a traumatic left lower limb laceration which appeared to be healing. Lower limb tone, reflexes and sensation were normal. On presentation he denied diplopia or any visual disturbance, with full cranial nerve examination also being normal.

Laboratory investigations on admission showed a genuine thrombocytopenia that was confirmed with a blood film. C-reactive protein was raised at 140 mg/L however erythrocyte sedimentation rate was within normal limits (13mm first hour). Liver function tests showed predominant transaminitis with a normal bilirubin level (12.8 micromoles/L). Alanine aminotransferase level was 95 U/L, alkaline phosphatase level 144 U/L and gamma glutamyl transferase 71 U/L. Blood and urine cultures returned negative.

A computerised tomography scan of the thorax, abdomen and pelvis excluded the presence of any abscesses. The lumbar spine was also imaged with magnetic resonance imaging, with the imaged axial skeleton showing red marrow persistence.

In view of sepsis with an unknown source of infection on admission, he was treated with broad spectrum intravenous antibiotics with combined tazobactam and piperacillin for two weeks. There was good clinical response with concurrent normalisation of inflammatory blood markers, but persistence of thrombocytopenia.

On the thirteenth day of hospitalisation, the patient developed visual disturbance which he described as seeing "black spots". Urgent ophthalmology review was sought, which confirmed bilateral intermediate uveitis with vitreous condensation in both eyes. This was treated with dexamethasone 0.1% eye drops every three hours for eleven days, which was then tailed down by one drop every 5 days. An improvement in vision was reported by the patient after two weeks of dexamethasone eye drops treatment and his vision was fully restored after 4 weeks.

In view of the history of bilateral intermediate uveitis in association with a genuine thrombocytopenia, further blood investigations were taken. Of particular note, anticardiolipin antibodies and β2 glycoprotein antibodies were positive as well as a strongly positive lupus anticoagulant test. Thrombocytopenia persisted despite improvement of the patient's clinical condition. Serum angiotensin converting enzyme was mildly elevated.

A diagnosis of antiphospholipid syndrome was made and low dose aspirin was started. Repeat serum testing after six weeks continued to confirm the persistence of antiphopholipid antibodies, B2-glycoprotein antibodies and lupus anticoagulant. Table 1 below shows other tests that were taken to exclude secondary causes of bilateral uveitis.

Table 1 *Table of results*

Serological tests	
Platelets	50 - 94 x10 ^{9}/L
Bilirubin	12.8 micromoles/L
Alanine aminotransferase	95 U/L (5-41)
Alkaline phosphatase level	144 U/L (40-129)
Gamma glutamyl transferase	71 U/L (8-61)
Complement 3 & complement 4	Normal
Serum protein electrophoresis	No monoclonal band detected
Anticardiolipin antibodies	Positive
B2 glycoprotein antibodies	Positive
Anti-nuclear Antibodies	Positive
ANCA	Negative
Lupus anticoagulant	Strongly Positive
Syphilis	Negative
Serum Angiotensin converting enzyme	88U/L (20-70)
HLA B27	Negative
HLA B51	Negative
Cytomegalovirus IgM & IgG	Negative
Toxoplasma IgM & IgG	IgM negative, IgG positive
Bartonella Serology	Negative
Borrelia Serology	Negative
Rickettsia conorii IgM antibodies	Negative
Radiological Imaging	
CT thorax, abdomen and pelvis	no evidence
MR lumbar spine	multilevel degeneration of the spine
MR head	Empty sella syndrome, but otherwise normal
MR orbits	Non-specific retro-orbital fat inflammatory changes.
Positron emission tomography	No signs of large vessel vasculitis

DISCUSSION

Antiphospholipid syndrome is a hypercoagulable disorder which is acquired later in life. The main presenting features leading to investigation and diagnosis are thrombotic conditions and pregnancy-related adverse outcomes. Thrombotic events may affect the venous, arterial and/or microvascular component. Antiphospholipid syndrome can be linked to other autoimmune diseases, such as systemic lupus erythematosus (SLE). In this case, this would be referred to as secondary antiphospholipid syndrome which accounts for half of the cases of antiphospholipid syndrome.[1]

Diagnosis depends on the presence of: lupus anticoagulant, anticardiolipin antibody, and anti-beta 2 glycoprotein I antibody. The antibody which is related most to thrombosis and adverse pregnancy outcomes is lupus anticoagulant which is detected in platelet-deplete plasma, particularly the presence of higher IgG titres compared to IgM and their persistence for at least 6 months.[1]

It is not uncommon to detect antiphospholipid antibodies in seemingly healthy individuals. This would however be detected at low titres. In fact, the lupus anticoagulant or anticardiolipin antibodies have been detected in 1-5% of young healthy subjects. Also, the anticardiolipin and anti-beta 2 glycoprotein I antibodies have been detected in 12% of the older portion of the population. Antiphospholipid antibodies can be induced through an infectious process, via both viruses and bacteria; such as: human immunodeficiency virus (HIV), hepatitis B and C, leprosy, and syphilis. However, antiphospholipid antibodies which are secondary to the above- named infectious processes are not linked to a pro-thrombotic state of the antiphospholipid syndrome. The detection of antiphospholipid antibodies can also be linked to underlying malignancy.[1]

Low platelet count is a feature common to one third of the patients with antiphospholipid syndrome. This happens via activation and aggregation of platelets secondary to the binding of beta 2 glycoprotein I receptors on platelets. Thrombocytopaenia is usually mild. In severe cases, corticosteroids, intravenous immunoglobulins and rituximab can be used.[1]

As mentioned earlier, antiphospholipid syndrome is a prothrombotic condition that can lead to thrombosis in the microvascular compartment including in the eye.[1] In a review and metanalysis by Turk et al, ocular complications in antiphospholipid syndrome occur in 35% of the cases, with retinal infarctions and haemorrhages being the more predominant features.[2]

Intermediate uveitis is linked to both infectious and non-infectious causes; with multiple sclerosis, sarcoidosis and intraocular lymphoma being the most mentioned for the latter category.[3] In 2021 a retrospective study that had been done showed that the presence of either of the antiphospholipid antibodies was found in 20.6% of patients with uveitis, that otherwise had no other features of systemic thrombosis suggestive of antiphospholipid syndrome. The majority of these patients, had exclusively anterior uveitis.[4]

Antiphospholipid syndrome is associated with HLA typing as demonstrated by both animal and human models, with: HLA-DR4, HLA-DR7, HLA-DRw53 and HLA-DQB1*0302 being the ones mostly shown to be related in the latter. However, there are inter-racial differences in the HLA associations. Major Histocompatibility complex genes have an effect on both disease manifestation and the production of antibodies.[5,6]

SUMMARY

Uveitis is an uncommon presentation of antiphospholipid syndrome.

Persistent thrombocytopaenia is a feature of antiphospholipid syndrome.

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