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An extrapyramidal manifestation of antiphospholipid syndrome (APS) and approach to its treatment; a case report

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Abstract
Antiphospholipid syndrome (APS) is an autoimmune disease categorized by recurrent thrombotic events and/or obstetrics complications with persistently positive antiphospholipid antibodies. APS could be presented with non-thrombotic features, the most important of which are neurological dysfunctions such as migraine, epilepsy, multi-infarct dementia and chorea. But among them, one of the less common cases is extrapyramidal manifestation, namely athetosis. we report a case of primary APS presenting with an unusual neurological manifestation (left hand athetosis) in which due to the positivity of antiphospholipid antibodies(aPL) without thrombotic features or pregnancy complications and SLE, she was diagnosed as non-thrombotic primary APS. In this case report, we purpose to discuss our case in the light of current knowledge on APS and share our treatment approach. **Cell, Gene and Therapy, Vol.2, Number 4, Winter 1st, 2021; 122- 125**
Key words: Antiphospholipid syndrome, APS, extrapyramidal manifestation

Introduction

Antiphospholipid syndrome (APS) is one of the autoimmune disorder characterized by recurrent arterial and venous thrombosis and/or pregnancy complications and/or non-thrombotic manifestations with circulating antiphospholipid antibodies(aPL). (1)(8). It could be isolated (primary APS) or associated with autoimmune disease, typically systemic lupus erythematosus (SLE). (2) (11) ultimate diagnosis of APS is determined by presence of at least one clinical feature and one laboratory abnormality in which Presence of aPL in serum, including anticardiolipin antibody (aCL), lupus anticoagulant (LA), and anti-β2 Glycoprotein-I antibody (anti-β2GPI), as a specific indicator of APS, must be existed on two or more times at least 12 weeks apart. (3)(4) one of the most common and significant clinical manifestations of antiphospholipid syndrome (APS), which is responsible for high morbidity and mortality, is neurological disorders, such as: stroke, transient ischemic attack, dementia, convulsions, epilepsy, ocular symptoms, cognitive deficits, headaches, migraine, chorea, multiple sclerosis-like, transverse myelitis and Guillain–Barre´ syndrome. (5) Anticoagulants with or without additional immunosuppression are used to treat antiphospholipid antibody–associated neurologic disease. (6) In this article, we will explain one aPL-positive patient with the initial extrapyramidal manifestations and describe its treatment.

Case presentation

A 30-year-woman was referred to our clinic with speech problems, upper and lower limbs paresthesia, insomnia, memory problems, stress and anxiety, which had been recently emerged. She had chronic severe headache as well. Brain MRI investigations was performed. On the brain MRI she had a few tiny non- specific foci. The result was not in favor of demyelination syndromes like Multiple Sclerosis

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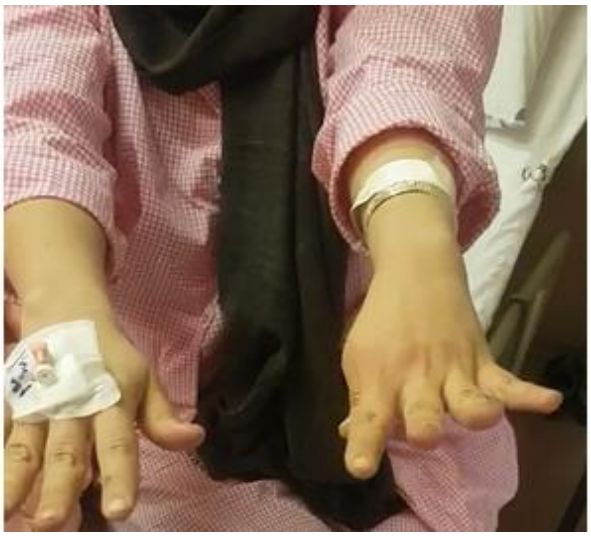
(MS) but On the cervical MRI, she had normal findings. Her medical history included a single episode of seizure when she was 1-year-old and the left hand myoclonus when she was pregnant. On the examination, she has the left hand atethosis (picture 1) and the right side CTS otherwise normal findings. For more diagnostic evaluations, we admitted her at the hospital and did Para clinic studies to check other autoimmune reasons which could represent with neurological disturbances especially extrapyramidal manifestation. The collagen vascular disease tests namely ANA, RF, Anti NMO Ab, and Anti MOG Ab, Anti ds-DNA, Anti SS-A, Anti SS-B, were negative, but the Anti-Cardiolipin Ab IgG (>120) and IgM (108), Lupus anticoagulant Ab (47) and anti-β2 Glycoprotein-I antibody (anti-β2GPI) were positive. For definite diagnosis of APS, the aPL was rechecked about12 weeks later, and those tests were positive again. Based on the diagnostic criteria of APS, due to the presence of clinical symptoms (non-thrombotic feature) and positivity of laboratory tests, the diagnosis of anti- phospholipid syndrome was confirmed. [3,4]. This case had no history of pregnancy complications or stroke. Eventually, we gave the patient low dose aspirin and statin along with medications (biperiden and haloperidol) to control extrapyramidal symptoms.



Picture1. left hand athetosis

Discussion

Our patient was a woman who has had just neurologic manifestations of which the most interesting was the presence of athetosis classified in extrapyramidal features. According to researches, chorea is one of the rare sign of APS, so that its prevalence is estimated at about 1.3 percent. (5) Based on the study of Cervera et al. research group on 50 patients with chorea and APS, of whom 12% had lupus-like syndrome, 15% had systemic lupus erythematosus, and 30% had primary APS (62). Moreover, 66% of the APS patients had only one episode of athetosis. our case, diagnosed as primary APS, also had experienced one episode of this sign that was treated with haloperidol 0.5mg per ml and biperiden 2mg per ml. studied have revealed that in 55% of cases, chorea was bilateral, and imaging studies shown cerebral infarction in 35%. (5) However, in our patient, athetosis was unilateral and there was no evidence of cerebral infarction on imaging. Movement disorders and multiple sclerosis-like features in APS patients are due to damage to the basal ganglia and destruction of white matter caused by aPl. despite basal ganglia involvement is usual in primary APS, dystonia is a quite uncommon clinical sign of APS (5). if lesions are found on brain MRI of APS patients, they are mostly statics and located in the subcortical areas. (4) but in our case, on the brain MRI, she had a few tiny non- specific foci.

In general, the treatment of this syndrome depends on its various clinical manifestations and focuses on low-dose aspirin, vitamin K antagonists, heparin and immunosuppression. Recently, direct oral anticoagulants are not suggested in APS. Antithrombotic strategies are usually not advantageous for the non-thrombotic signs of APS, because these kind of medications can develop these manifestations (8). Therefore, considering that our patient had only neurological symptoms with no other features, we only used low dose aspirin, which is confirmed by another study. According to this study, in aPL Positive patients without any vascular thrombosis or obstetric complications, with a high-

Table 1. Definition of aPL profile

low-risk aPL profile	LA: negative + low level* of aCL or ab2GPI IgG or IgM
medium-risk aPL profile	LA: negative + moderate- to high-level* aCL or ab2GPI IgG or IgM
high-risk aPL profile	LA: positive and/or moderate- to high-level* aCL or ab2GPI IgG or IgM (8)

*low level is 20-39 GPL/MPL units.
(GPL, IgG phospholipid units; MPL, IgM phospholipid units.)

risk aPL profile (table1), prophylactic treatment with low-dose aspirin (LDA) (75–100 mg daily) is suggested. High-risk antiphospholipid antibody (aPL) profile is accompanied with greater risk for thrombotic and obstetric APS. (7)(9) Since all three antibodies (LA, aCL, ab2GPI) with high titers were positive in our case, she was a high-risk aPL profile patient, but she did not have any vascular thrombosis or pregnancy mortality.

According to anecdotal experience, traditional immunosuppressive medications are useful for some of the aPL-related non-thrombotic or micro thrombotic signs. (8)

Hydroxychloroquine(HCQ) with anti-inflammatory and antithrombotic effects can be used as an add-on therapy in APS patients. Moreover, statins apply anti-inflammatory and antithrombotic effects in aPL-positive patients as well. statins may have a part as an add-on treatment in APS patients when anticoagulation alone is not enough. (8) we also used the beneficial anti-inflammatory effect of statins in our case.

In addition, some other adjunctive therapies are recommended such as coenzyme Q10, adenosine receptor agonists and vitamin D. (10) In our case, level of vitamin D was insufficient(<30ng/ml), so she was given vitamin D.

Conclusion

Antiphospholipid syndrome could be presented with non-thrombotic manifestations, the most important of which are neurological manifestayions. But among them, one of the less common cases is athetosis, which was the initial symptom of our patient. Therefore, we must be careful that if the patient presents with the initial extrapyramidal manifestations, after ruling out other causes, collagen vascular disease should be considered and the antibodies namely aPL should be checked, because it can be a sign of APS. For treatment, we use both symptomatic therapy to relieve extrapyramidal features and low dose aspirin for initial thromboprophylaxis. In addition, adjuvant therapies including vitamin D, coenzyme Q10, hydroxychloroxene, may be useful.

References

1. Hallab A, Naveed S, Altibi A, Abdelkhalek M, Ngo HT, Le TP, Hirayama K, Huy NT. Association of psychosis with antiphospholipid antibody syndrome: A systematic review of clinical studies. Gen Hosp Psychiatry. 2018 Jan-Feb;50:137-147. doi: 10.1016/j.genhosppsych.2017.11.005. Epub 2017 Nov 16. PMID: 29241089.
2. Warriach SA, Mustafa M, O'Keeffe D, Watts M. Unusual case of antiphospholipid syndrome presenting as adrenal insufficiency. BMJ Case Rep. 2020 Mar 17;13(3):e233631. doi: 10.1136/bcr-2019-233631. PMID: 32188612; PMCID: PMC7078771.
3. Zhu DS, Fu J, Zhang Y, Li SX, Zhang GX, Guan YT, Dong Q. Neurological antiphospholipid syndrome: Clinical, neuroimaging, and pathological characteristics. J Neurol Sci. 2014 Nov 15;346 (1-2):138-44. doi: 10.1016/j.jns. 2014.08.010. Epub 2014 Aug 14. PMID: 25173939.
4. Shahbeigi, S., et al. The Neurological Manifestations as an Onset Symptom of Anti-Phospholipid Syndrome: Report of Two Cases International Journal of Neurology and Brain Disorders the Neurological Manifestations as an Onset Symptom of Anti-Phospholipid Syndrome:

Report of Two Cases, Doi: - 10.15436/2377-1348.19.2033, Published date: January 28, 2019
5. Rodrigues CE, Carvalho JF, Shoenfeld Y. Neurological manifestations of antiphospholipid syndrome. Eur J Clin Invest. 2010 Apr;40(4):350-9. doi: 10.1111/j.1365-2362.2010.02263.x. Epub 2010 Feb 19. PMID: 20192975.
6. Graf J. Central Nervous System Manifestations of Antiphospholipid Syndrome. Rheum Dis Clin North Am. 2017 Nov;43(4):547-560. doi: 10.1016/j.rdc.2017.06.004. PMID: 29061241.
7. Tektonidou MG, Andreoli L, Limper M, Amoura Z, Cervera R, Costedoat-Chalumeau N, Cuadrado MJ, Dörner T, Ferrer-Oliveras R, Hambly K, Khamashta MA, King J, Marchiori F, Meroni PL, Mosca M, Pengo V, Raio L, Ruiz-Irastorza G, Shoenfeld Y, Stojanovich L, Svenungsson E, Wahl D, Tincani A, Ward MM. EULAR recommendations for the management of antiphospholipid syndrome in adults. Ann Rheum Dis. 2019 Oct;78(10):1296-1304. doi: 10.1136/annrheumdis-2019-215213. Epub 2019 May 15. PMID: 31092409.
8. Sevim E, Willis R, Erkan D. Is there a role for immunosuppression in antiphospholipid syndrome? Hematology Am Soc Hematol Educ Program. 2019 Dec 6;2019(1):426-432. doi: 10.1182/hematology.2019000073. PMID: 31808842; PMCID: PMC6913487.
9. Uthman I, Noureldine MHA, Ruiz-Irastorza G, et alManagement of antiphospholipid syndromeAnnals of the Rheumatic Diseases 2019;78:155-161.
10. Cohen H, Cuadrado MJ, Erkan D, Duarte-Garcia A, Isenberg DA, Knight JS, Ortel TL, Rahman A, Salmon JE, Tektonidou MG, Williams DJ, Willis R, Woller SC, Andrade D. 16th International Congress on Antiphospholipid Antibodies Task Force Report on Antiphospholipid Syndrome Treatment Trends. Lupus. 2020 Oct;29(12):1571-1593. doi: 10.1177/0961203320950461. PMID: 33100166; PMCID: PMC7658424.
11. Taipa R, Santos E. Primary antiphospholipid antibody syndrome presenting with encephalopathy, psychosis and seizures. Lupus. 2011 Nov;20(13):1433-5. doi: 10.1177/0961203311405373. Epub 2011 Jul 18. PMID: 21768180.