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Multifocal Avascular Necrosis in an Alcoholic Male with Antiphospholipid Syndrome and Megaloblastic Anemia.

Valizade N*, Fattahzadeh A**.

* Assistant Professor, Section of Hematology and Medical Oncology, Department of Medicine, **Resident, Department of Medicine, Urmia University of Medical Sciences, Urmia, Iran.

Correspondence: Dr. Nasim Valizadeh, Department of Medicine, Urmia University of Medical Sciences, Urmia, Iran, Telephone: +98(441) 3370-234, Fax: +98(441) 3469-939, Email: nsedaha0@gmail.com .

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Abstract:

Any factor that damage blood supply to bone can cause osteonecrosis.Traumatic and non-traumatic factors can cause osteonecrosis.Important non-traumatic causes of avascular necrosis are alcoholism, steroid use, cigarette smoking, hyperlipidemia and systemic lupus erythematosus. We want to present a case of multifocal avascular necrosis (AVN) in an alcoholic man with antiphospholipid (APL) syndrome and associated megaloblastic anemia.

Keywords: Alcoholism, Megaloblastic anemia, Avascular necrosis, Antiphospholipid syndrome.

Introduction:

Traumatic and non-traumatic factors that decrease blood supply to the bone can lead to osteonecrosis.Alcohole use, corticosteroid administration, systemic lupus erythematosus, hyperlipidemia and cigarette smoking are etiologic factors for osteonecrosis.[1,2]

There is a case of alcohol-induced multifocal osteonecrosis in literature.[3] There was an association between antiphospholipid antibody syndrome and osteonecrosis.[4,5,6]Thiamine (Vitamin B1) is soluble in water and partly in alcohol. Its half-life is 9.5 to 18.5 days and it is cleared by the kidney.[7,8] It found in skeletal muscles, heart, brain, liver and

kidney.[9]Thiamine acts as cofactor for enzymes involved in carbohydrate and amino acid metabolism.[6]Nervous system involvement due to thiamine deficiency is called dry beriberi and cardiovascular involvement of thiamine deficiency is termed as wet beriberi.[7]We want to present multifocal osteonecrosis(bilateral femoral and humeral heads) in an alcoholic patient with megaloblastic anemia and antiphospholipid antibody syndrome.

Case Report:

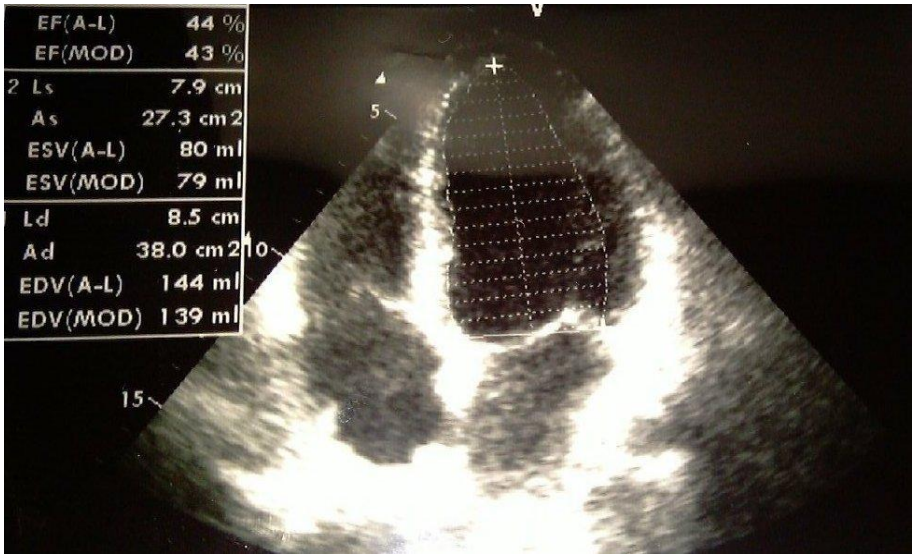
A 45 y/o muslim and divorced man was admitted with diarrhea and anemia. He complained memory loss, depression, fatigue, impotence, and paresthesis in upper and lower extremities. He had history of psychosis and one time seizure 2 years ago, history of unexplained dilated cardiomyopathy since 3 years ago which had underwent coronary angiography which revealed normal coronary arteries and prophylactic implantable cardioverter defibrillator(ICD) was inserted to him since 8 months ago. Past medical history was positive for recurrent deep vein thrombosis (DVT) in right and left lower extremities and a car accident which had leaded to right femural fracture about 4 years ago and underwent orthopedic surgery and during this operation the surgeon had noticed the avascular necrosis of right femoral head .Since 10 years ago he started to daily alcohol consumption and increased it to one bottle per day since 3 years ago.

Drug history was positive for lorazepam, warfarin, enalapril, serteraline,Inderal, aldacton, carvedilol, captopril, imipramin. Also, he had been receiving prednisolone intermittently due to hip and shoulder joints' pain for a short period (about 3 months). Physical examination showed pallor,icteric sclera, a pace maker on his chest wall, loss of memory and concentration.

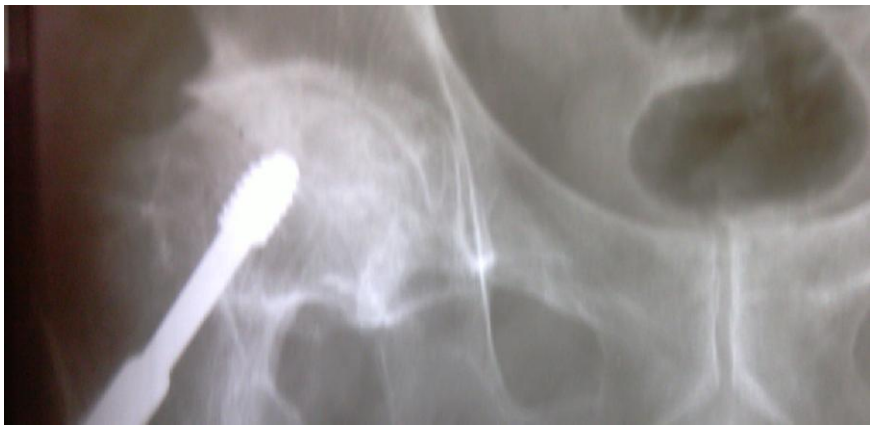
Laboratory findings are included: WBC=4,500/µL, Hg=11.6 g/dl, MCV=118 fl, Reticulocyte count=1.15,LDH=937 U/L,AST=275 U/L ,ALT=85 U/L ,Total bilirubin=2.39,direct bilirubin=0.87 ,LDL=51 mg/dl, HDL=48 mg/dl, TG=265 mg/dl, Ca=10.4 mg/dl, BS=131 mg/dl.HBS Ag and HCV Ab were negative. Stool exam and urine analysis were unremarkable. a=140 meq/l, K=3.5 meq/l. BUN, Cr, TSH and free T4 were negative.

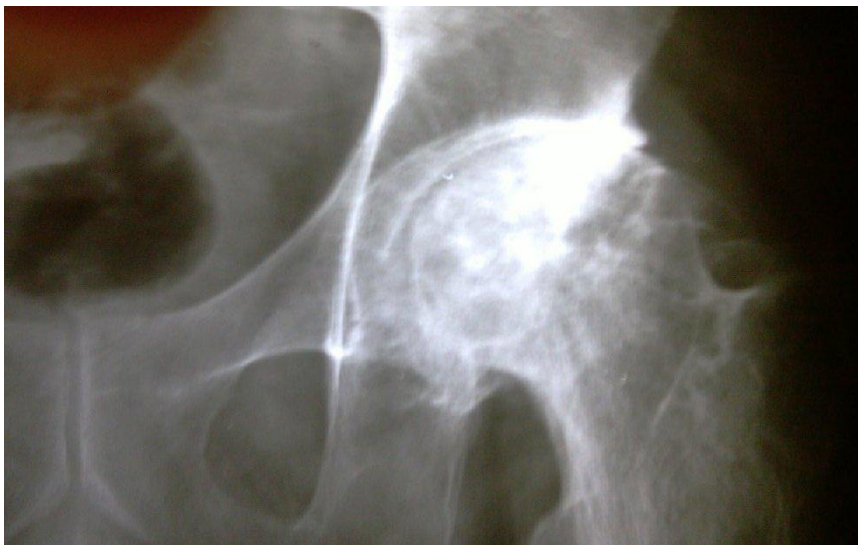
PT, PTT, INR, Protein S, protein S and anti-thrombin III all were in normal range. He had high titer of lupus anticoagulant 64.9 (normal range: 31-44) but, Antiphospholipid antibodies (IgM,IgG)and anti-ß2 glycoprotein-1(IgM,IgG),ANA and anti-DS DNA were normal.Coomb's (direct and indirect) was negative. Serum folic acid was 12.09 ng/ml (NL 3.1-17.5) and serum B12 was291.3pg/ml (NL 211-946). homocysteine level was 19 µmol/L(9.1-14.7).he had not antithrombinIII,protein C and S deficiency. Serum IgA level and anti-endomyosial Ab (IgA) were normal.

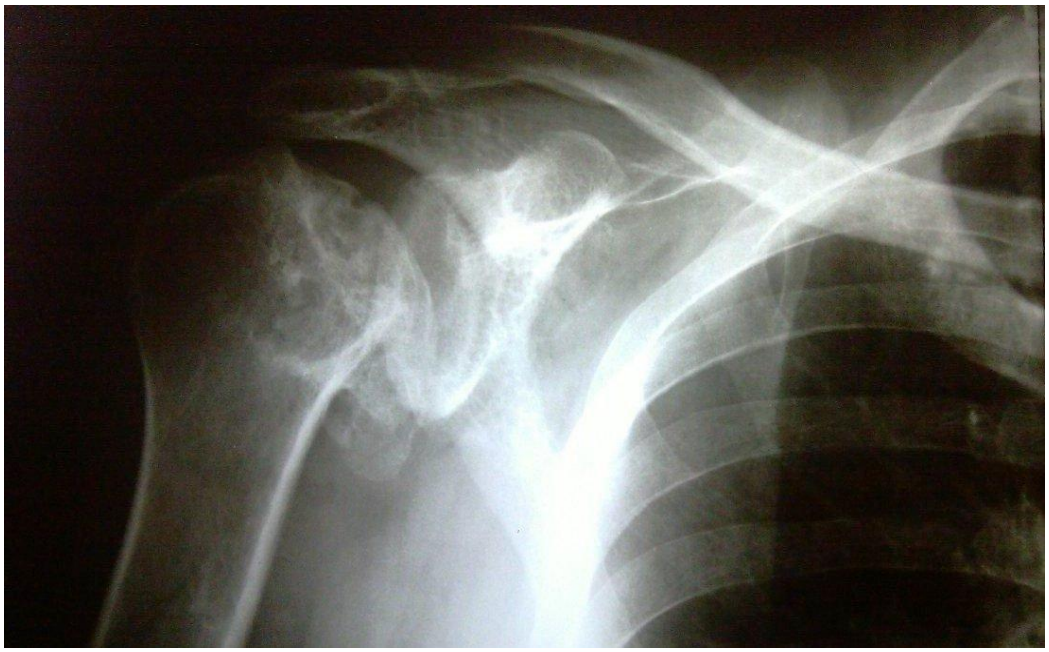
Figure 1, Echocardiography showed LVEF=25-30%, severe LV dysfunction and dilatation.

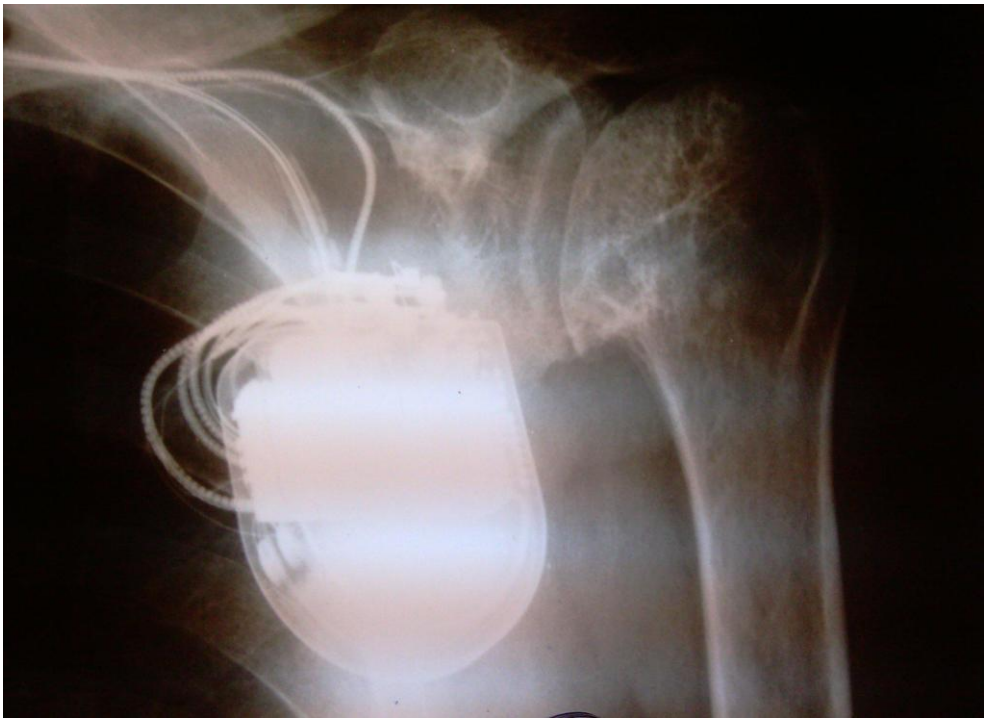


Figures 2,3,4,5, X-ray films of both hip and shoulder joints revealed bilateral avascular necrosis of femoral and humeral heads.









Abdomino-pelvic sonography was reported normally.

Chest –X ray showed cardiomegaly and shadow of pacemaker in chest wall.

Peripheral blood smear showed macrocytosiss, many target cells, teardrops, hypersegmented nutrophills. Brain MRI showed dilated sulcuses, increased size of subarachnoid space, brain and cerebellar atrophy.

According to history of anemia, alcoholism, recurrent DVT, neurological problems and evidence of macrocytic anemia , serum cobalamine level (which was in lower limit of normal range)and high titer of homocysteine level and lupus anticoagulant, avascular necrosis in both femur and humerus, brain atrophy in imaging and dilated cardiomyopathy, the diagnosis of megaloblastic anemia and thiamine deficiency(secondary to heavy alcohol consumption) associated with antiphospholipid antibody syndrome was made.

We started cobalamine(vitamin B12), folic acid, Vitamin B6,B-complex and thiamine (vitamin B1) and enoxparin for him. Also he received aldacton, digoxine, carvedilol, lozartan and heparin. During hospital course diarrhea was stopped but he had 2 episodes of tonic clonic seizure and neurologic consultation was recommended thiamine deficiency due to heavy alcohol abuse and started Phenobarbital and lorazepam to him. Episodes of seizure did not repeat in hospital course.3 days after giving cobalamine the diarrhea was stopped and one week after starting vitamin B12 ,AST,ALT ,Total and direct bilirubin and LDH were normalized. He was discharged with warfarin, thiamine, cobalamine, Phenobarbital, vitamin B6, folic acid and lozar,aldactone and digoxin. Abstinence from drinking was strongly recommended to the patient.

Results:

In this patient with megaloblastic anemia and alcoholism with history of dilated cardimyopathy, recurrent DVT and bilateral avascular necrosis in the humeral and femoral heads, we found antiphospholipid syndrome. Thiamine deficiency due to alcoholism is considered the causative agent for psychosis, seizure and also dilated cardiomyopathy in this patient. Our explanation for avascular necrosis of both femoral and humeral heads in this case was combination of risk factors including: alcoholism, antiphospholipid syndrome. Since, he had taken prednisolone for shoulder and hip joints' pain for a short time; it did not seem that prednisolone was leading cause of multifocal AVN in this alcoholic man.

This Muslim patient with alcoholism developed dilated cardiomyopathy, neurologic problems and brain and cerebellar atrophy, megaloblastic anemia and multifocal AVN in the heads of both femurs and humeri.Also, we found concurrent antiphospholipid syndrome in him.

Discussion:

Any factor that damage blood supply to bone can cause osteonecrosis. Traumatic and non-traumatic factors can cause osteonecrosis. Alcohol use is a known etiologic factor for osteonecrosis[1,2],although alcohol-induced AVN of femoral head is generally reported but alcohol-related multifocal AVN is very rare and there is a only case of alcohol-induced multifocal osteonecrosis in literature.[3]Antiphospholipil syndrome is diagnosed according to two criteria: the first is arterial and/or venous thrombosis ,pregnancy morbidity, or thrombocytopenia and the second is presence of at least one type of auto-antibodies which termed as anti-phospholipid antibodies

(apL).[10] There was an association between antiphospholipid antibody syndrome and osteonecrosis.(4,5,6)There is a few report regarding multifocal avascular necrosis associated with antiphospholipid syndrome.[11] In alcoholic patients ,who develop multifocal osteonecrosis ,we should search for coexistence factors such as antiphospholipid antibody syndrome especially in those with history of DVT. Also, we should think for thiamine deficiency in alcoholic patients who have unexplained CHF or dilated cardimyopathy. Patients with megaloblastic anemia have hyperhomocyteinemia and are susceptible for arterial or venous thrombosis, then starting cobalamine and/or folic acid would be effective in decreasing the risk of thrombotic events.

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