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Case Report

Hepatitis C and Secondary Antiphospholipid Syndrome (APS) in a Diabetic Patient with Renal Failure on Haemodialysis.

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Summary

Case of Hepatitis C in a 15-year-old girl who has been suffering from Antiphospholipid syndrome, Type 1 Diabetes Mellites for 14 years, atherosclerosis, chronic kidney failure and cachectic appearance.

Background

Hepatitis C is a very common problem encountered in a third world country like Pakistan and is a major cause of mortality and morbidity in patients suffering from chronic kidney disease dependant on haemodialysis and awaiting the kidney transplantation. Co-morbid conditions like Antiphospholipid syndrome have also been reported to have been diagnosed in patients having diabetes and hepatitis C, which has been noted to be increasingly difficult to manage especially in a third world country like Pakistan.

Case Presentation

This is a case of Type 1 Diabetes diagnosed at age of one year, she has been started on twice daily injections regimen, she has been having erratic glycaemic control, & since in Pakistan, services for annual screening & monitoring for the micro & macrovascular complications of diabetes has not been fully developed, Unfortunately this patient developed Diabetic Nephropathy at age of thirteen years and started showing signs and symptoms of Chronic Renal Failure at the age of thirteen.

Patient has been stable for a one year without need for any haemodialysis, however patient developed Acute renal failure on Chronic Renal Failure secondary to Cellulitis/Carbuncle on her back, following which she developed post streptococcal glomerulonephritis, due to which she went into septicaemia from skin infection and the renal failure which never reversed, this happened when she was fourteen years old.

During the Haemodialysis treatment she also developed anaemia of chronic disease (lowest Hb of 6.9g/dl), for which she needed four blood transfusions and haemoglobin stabilised afterwards.

Patient also used to have Transient Intermittent dyspnoea secondary to Fluid overload after her dialysis dependency which used to respond very well to more frequent Haemodialysis.

A port-a-Cath was inserted in view of frequent need for haemodialysis, and she used to have Intermittent central line infections due to un-hygienic access of the central line, which resolved later following strict aseptic techniques during Haemodialysis and intermittent vancomycin locks of the central line.

She also suffered from hypertension secondary to renal failure which was well controlled with antihypertensives.

Unfortunately, within four months of the start of the haemodialysis she contracted Hepatitis C (type 1 a genotype), which was successfully eradicated with help of Ledipasvir 90mg/ Sofosbuvir 400mg course for 3 months.

She was noted to have cachectic appearance, with weight loss & feeling of lethargy/extreme weakness due to ongoing multiple Co-morbid conditions & due to the adverse effects of drugs used for HepC & Hypertension.

She has been complaining of unbearable aches and pains in her fingers of both hands about six months after onset of renal failure and the need for haemodialysis.

Patient started to have gangrenous fingers of both hands around seven months after onset of renal failure and need for haemodialysis.

For the gangrenous fingers of the hands bilaterally, she was extensively investigated for the cause and eventually it was established that gangrenous fingers were secondary to thromboembolic phenomenon due to secondary antiphospholipid syndrome as shown in confirmatory investigations done repeatedly in the context of clinical picture and due to the fact that other aetiologies out-ruled by testing as mentioned in differentials section.

Raynaud's phenomenon was one of the differentials as some degree of digital pain associated with low temperatures, but temperature regulation still couldn't control symptoms and was unlikely the diagnosis.

Cryoglobulinemia from Hep C was also one of the differentials but was unlikely as Hep C successfully eradicated, and symptoms started at the tail end of successful eradication treatment for Hepatitis C.

Other differential on the list was Scleroderma, but other features of Scleroderma like swelling of the feet and hands and skin hardenings was not in this patient.

Another unlikely differential was Intermittent Atrial Fibrillation as Echo and 72-hour ECG tape was normal.

Primary APS was also in question but since the symptoms started showing after the infection with Hepatitis

C, its most likely favouring the secondary APS.

Since there was no significant response to steroids course it was unlikely to be Small Vessel vasculitis

Falsely positive APS antibodies/investigations associated Hep C, Drug-induced APS , unlikely a diagnosis as the manifestations of APS in form of Thrombosis were also in presentation.

Microangiopathy due to poorly controlled diabetes could be one of the differentials but the blood smear and platelets counts were normal.

DIC, Fulminant purpura, Vit.K deficiency also unlikely as she has been having symptoms for nearly 2-3 months, while DIC and Fulminant Purpura would have resulted in rapid deterioration within hours to days.

Uremic arterial calcification secondary to complications of bone, mineral disorder of chronic kidney disease was also one of the differentials but wouldn't explain digital ischemia and gangrene.

In past medical history she was noted to have features suggestive of primary APS, and was under investigation for APS (antiphospholipid syndrome)

She used to have episodes of supraventricular tachycardias (SVT), which was treated with radio ablation and EPS done at age of ten years.

Family history positive for diabetes, kidney stones.

Investigations

Workup for Anti Phospholipid antibodies. Increased LA screen: 50.9 seconds, 55.8 seconds LA present in plasma, on two occasions twelve weeks apart (tests done after diagnosis of Hepatitis C).

Increased LA confirmatory 47.3 seconds, and 53.2 seconds twelve weeks apart.

Normal LA ratio 1.1 and 1.5 twelve weeks apart (tests done after diagnosis of Hepatitis C).

Anti-cardiolipin IGG (1.90GPL/ml), IgM 3.78 MPL/ml (Normal), but on two other occasions 12,24 weeks apart (tests done after diagnosis of Hepatitis C) Anticardiolipin Antibodies igG noted to be 15 GPL/ml and 18 GPL/ml respectively and anti-cardiolpin antibody igM were 8 MPL/ml and 10 MPL/ml respectively after

diagnosis of Hepatitis C (confirmatory results in presence of clinical presentation of vascular thrombosis not explained by other tests/aetiologies).

Autoimmune workup including

ANA Negative,

Anti-Smooth Muscle Antibodies and Anti Mitochondrial Antibody came back as Negative.

Serum Anti DsDNA 1.84IU/ml as Negative,

Serum Cryoglobulin Negative at 4,22,35 C after 72 hours incubation period

RF Quantitative <15 IU/ml (Neg)

Increased C4 0.62 G/L (0.15-0.57)

C3 1.55 G/L (normal)

CH50 not done as not available in area of practice.

Raised APTT 44.3, PT =10.9, INR=1.2, D-Dimer 1ug/ml

ESR 140mm/h

HCV RNA done 8 months and nine months post renal failure not Detected <20 HCV IU/ML

Normal arteriography study but clinically weak peripheral pulses.

Increased PTH levels [156.7 pg/ml (normal range 12-88]

Ultrasound and CT Neck Normal (no PTH Adenoma detected)

Blood group A Rh D positive.

Differential Diagnosis

- Raynaud's phenomenon (some degree of digital pain associated with low temperatures)
- Cryoglobulinemia from Hep C (unlikely as Hep C successfully eradicated)
- Scleroderma
- Intermittent Atrial Fibrillation (Unlikely as normal Echo, 72 hours ECG)
- Primary APS
- Small Vessel vasculitis

- Falsely positive APL investigations (associated Hep C)
- Microangiopathy due to poorly controlled diabetes
- DIC
- Fulminant purpura
- Secondary APS (Drug-induced)
- Vit.K deficiency
- Uremic arterial calcification secondary to complications of bone, mineral disorder of chronic kidney disease

Treatment

Ledipasvir 90mg/ Sofosbuvir 400mg 1 tablet daily (3 months course)

FOLIC ACID 5MG

Insulin HUMILIN 25 (24 bd s/c am, 20 pm) +Humulin R prn

Itopride HCL 50mg po od

Famotidine prn

Nifedipine 30mg

Valsartan 80 mg O.D

Aspirin 75 mg OD

Furosemide 40 MG OD

Tricardine

Benprost

High doses of steroids for 8 weeks started at ninth month of onset of renal failure with tapering doses afterwards.

Patient was advised to commence long term anticoagulation with close monitoring, but unfortunately advice wasn't followed by patient.

Outcome and Follow-Up

Patient has developed vascular (arterial) calcification secondary to renal osteodystrophy as X-rays of hands did show calcified vessels, U/S neck didn't show any parathyroid adenoma.

PTH levels were Elevated (156.7 pg/ML).

CKD Related Bone, mineral disorders manifested as vascular calcification.

The rapid progression of her disease seems unusual for simple diabetic Nephropathy.

It seemed more likely due to anti phospholipid antibody syndrome.

Cause of death from septic shock secondary to gangrenous digits.

Discussion

Antiphospholipid lipid syndrome is characterised by arterial/ venous thrombosis and adverse pregnancy outcomes in patients positive for antiphospholipid antibodies[1]. Antiphospholipid lipid syndrome is one of the most common cause of acquired thrombophilia, the only difference to the genetic causes of thrombophilia is that Antiphospholipid syndrome causes thrombosis in both arterial and venous systems[1]. Antiphospholipid lipid syndrome occurs either as a primary condition or in the setting of an underlying disease like systemic lupus erythematosus (SLE)[2]. It might present in its more aggressive form called catastrophic APS as well, which results in widespread thromboembolic phenomenon and multi-organ involvement[3].

Antiphospholipid lipid syndrome has also been observed in association with some infections particularly viral infections[4,5,6], but most of the times its not associated with thromboembolic events although rare cases have been reported as well showing thrombosis[4,5,6].patients with chronic hepatitis C have been observed to have both clinical and laboratory evidence of presence of thrombosis observed in Antiphospholipid syndrome[7].

Learning Points/Take Home Messages

Antiphospholipid should be suspected in adolescent patients presenting with Unexplained vascular

thrombosis.

Long term anticoagulation should be advised for any suspected case of Antiphospholipid syndrome case after doing the initial clotting studies.

Poorly controlled Diabetes could have catastrophic complications and can result in poor quality of life.

Progression to renal failure and dialysis dependency makes such patients prone to develop more complications of diabetes and renal failure.

Autoimmune conditions could get triggered from diabetes and HCV Infection.

Positive APL antibodies and other tests supporting clinical presentation could be true or false positive.

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