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What Caused Her Fall? A Clinical Case of Leg Swelling

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WHATCAUSEDHERFALLACLINICALCASEOFLEGSWELLING

Strictly as per the compliance and regulations of:

What Caused Her Fall? A Clinical Case of Leg Swelling

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Abstract- **Minimal change disease (MCD) is typically not a disease seen in adults as it comprises only 10-15% of cases (1). Disease can be further characterized as primary/idiopathic or secondary. Typical secondary causes include drugs such as NSAIDs and Lithium and malignancies including Non-Hodgkin Lymphoma. Thus, secondary causes are often the culprit. We present a 47-year-old African-American female patient with a history of Multiple Sclerosis (MS) and HIV who presented with sudden onset worsening lower extremity edema and 6.6 grams (g) urine protein to creatinine ratio with primary MCD.**

I. Introduction

Minimal change disease (MCD) is a nephrotic syndrome primarily seen in children and early teens (1). In adults, the major nephrotic disease remain Focal Segmental Glomerulosclerosis (higher prevalence in people of African origin) and Membranous nephropathy (higher prevalence in people of European descent). It is rare to see MCD in adults as it comprises only 10-15% of cases (2). Patients usually present with sudden onset edema, proteinuric kidney injury, and hyperlipidemia. Disease can be further characterized as primary/idiopathic or secondary. Typical secondary causes include drugs such as non steroidal anti-inflammatory drugs (NSAID) and Lithium, infections such as Syphilis, Mycoplasma, allergens, autoimmune disorders like Systemic Lupus Erythematous (SLE), Celiac disease, diabetes, as well as malignancies including Non Hodgkin Lymphoma and bronchogenic carcinoma (1). The pathogenesis hypothesis states that disruption of actin cytoskeleton within the podocyte and basement membrane in conjunction with a disrupted immune system cause an increase in mediating factors leading to filtration of albumin into the urinary system (2).

II. Case Report

We present a case of a 47 -year old African-American woman with biopsy proven MCD.

The patient presented to the Emergency Department (ED) after sustaining a fall at home. She hit her head albeit did not lose consciousness. She reports myalgia, nausea, and acute worsening of paresthesia in her hands and lightheadedness over the past one month. In addition, she notes worsening leg swelling spanning three weeks and involuntary 30 pound weight gain over the past month. She denies any herbal medication use, illicit drug use, or recent illness. The last time she took NSAIDs was for menses four months prior to presentation and totaled no more than six doses.

Her past medical history is significant for Multiple Sclerosis (MS) diagnosed in 2005 and her last flare in 2008. Flares are characterized by fatigue, frequent fall, and dizziness. Her disease is managed with Glatramer injections three times weekly. She also has a history of HIV with undetectable viral load and takes Biktarvy daily. CD4 count at time of admission 976. Finally, patient has leiomyomas and follows with outpatient gynecology.

Her vitals: heart rate 101 beats per minute Blood pressure 150/90mm Hg, 16 Respirations per minute and oxygen saturation of 99% on room air.

Upon admission, lab investigations demonstrated:

C3, serum	95.62 (mg/dl) (79-152)
C4, serum	13.75 (mg/dl) (16-38)
Albumin ,serum	Less than 1.5 (g/dl)
Calcium, serum	7.3 (mg/dl)
Brain natriuretic peptide (BNP)	7.5 (pg/mL) (less than 100)
CPK	9 IU/L (35-230)
D dimer	2.58 (ug/ml) (0-0.48)
White blood cell count	4.36x10 ^ 9 per microliter (3.2-10.6)
Hemoglobin	12.5 (g/dl) (12.1-15.9)
Platelet	120x10 ^ 9 per microliter (177-406)

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Sodium	138 (meq/L)
Potassium	5.3(meq/L)
Chloride	109 (meq/L)
Bicarbonate	26 (meq/L)
BUN	29(mg/dl)
Creatinine	1.3 (mg/dl) (baseline 0.7-0.8)
Glucose	97(mg/dL)

Lipid panel

Cholesterol	341 (mg/dL)	(125-200)
HDL	35.6 (mg/dL)	(>47)
LDL	169.7 (mg/dL)	(less than 130)
Triglyceride	424 (mg/dL)	(less than 150)

Urine studies

Urinalysis:	Amber appearing urine, with greater than 500mg/dL protein with few bacteria, 16-25 WBC (normal 0-4 per high powered field). No nitrites, no leukocyte esterase, and no Redblood cell cast. Specific gravity: 1.032 (normal 1.01-1.03)
Urine protein	>1500 mg/dL
Urine Creatinine	225.66 mg/Dl
Urine BUN	1780 mg/dL
Urine Sodium	20 mg/dL

Imaging

Renal ultrasound	Patent renal veins and normal sized kidneys
Lower extremity Vein Doppler	NEGATIVE for deep vein thrombosis
CT Head and Cervical spine	No acute intracranial process and evidence of multi-level disk disease.

Exam notable for obese woman with generalized edema, normal heart sound intensity, no adventitious breath sounds, and no focal neurological deficits. Patient oriented to person, place, and situation.

Neurology initially consulted due to concern for MS flare and patient completed four day course of daily Solumedrol. Head imaging showed no evidence of acute flare.

Nephrology consulted due to concern for nephrotic syndrome. Urine studies, autoimmune workup including SPEP, UPEP, ANCA, RPR, serum free light chains recommended. Results all negative. ANA positive and reflex to titre pending. Double stranded DNA (dsDNA) quantified as indeterminate. Urine protein: creatinine ratio is 6.64g/day. Interventional Radiology (IR) consulted for kidney biopsy. Patient started on IV Furosemide , IV albumin, and anti hypertensives. Protein and sodium restriction intake enforced. Plan for biopsy of kidney.

Biopsy results on electron microscopy demonstrated effacement of podocytes and absence of tubule-reticular structures. On light microscopy normal appearing glomeruli seen with some evidence of interstitial edema. Immunofluorescence demonstrated no glomerular positivity with IgG, IgA, IgA, C3, C1q, kappa, lambda, or fibrinogen. Faint one plus glomerular positivity seen with IgM, however non specific. No specific tubulointerstitial or vascular positivity with any of the above mentioned immunoreactants.

Patient started on prednisone 80mg every morning. Testing for G6PD negative, and patient started on Dapsone 100mg day for Pneumocystis jiroveci pneumonia (PJP) prophylaxis.

At time of discharge, labs demonstrated

Sodium	138 (meq/L)
Potassium	3.6 (meq/L)
Chloride	99 (meq/L)
Bicarbonate	32 (meq/L)
BUN	17(mg/L)
Creatinine	0.8 (mg/L) (baseline 0.7-0.8)
Glucose	112 (mg/L)

White blood cell count	16.46x10^9 per microliter	(3.2-10.6)
Hemoglobin	10.5 (g/dl)	(12.1-15.9)
Platelet	179x10^9 per microliter	(177-406)
Glucose 6 phosphate dehydrogenase	9 u/g of Hemoglobin	(7-20)

III. Discussion

The incidence of primary MCD in adults is not well defined (1). The hallmark of biopsy results is absence of immunofluorescence staining for varying antigens/immunoreactant (IgG, IgM, IgA, C1, etc.) and effacement of podocytes (1) on electron microscopy. If other features are seen, it cannot be MCD (1). Nonetheless, low intensity staining of C3 and IgM can be normal (8). This was seen in our patient. Typically, this disease has a higher prevalence in children who are often steroid responsive. By two weeks, 50% of kids have responded, whereas the percentages are more sobering in adults. Here, 75% have responded by 13 weeks (8). Furthermore, adults have greater risk for progression to renal failure in adults. In study by Nolasco et. al, ten of nineteen patients progressed to renal failure, with eight of those eventually requiring dialysis (9).

There have been few reports of adults with MCD and even fewer in patients with comorbidities such as HIV and MS, as in our patient. However, given the biopsy results this remains a case of primary MCD. In spite of the patient's history of well controlled HIV, HIV Associated nephropathy (HIVAN) remained on the differential. It is important to recognize that anti retroviraltherapy (ART) does not protect against MCD. In fact, seven of eight patients were diagnosed with MCD while on ART. HIVAN detected in only one case (4). On the other hand, a viral load of greater than 400 was also not a good predictor of HIVAN, as only 37% of such patients diagnosed with HIVAN (6).

While the patient did have abrupt onset edema, hyoalbuminemia, and proteinuria, her serum creatinine was not greater than 2. Above 2 is more typical for HIVAN (5). Variability in labs and presentation echo the importance of biopsy. Biopsy will demonstrate tubular atrophy and dilation as well as flattened epithelial cells in setting of collapsing FSGS (due to podocyte proliferation). Furthermore, a large number of tubular and glomerular cells coated with HIV RNA (4). Important to note that low CD4 count and presence of proteinuria are not predictive of HIVAN. Furthermore, a viral load of greater than 400 was also not a good predictor of HIVAN, as only 37% of such patients diagnosed with HIVAN (6).

Our patient did not have HIVAN in spite of medical history. Similarly, one could postulate MCD secondary to MS drugs. While the patient was treated for presumed flare on admission, there are very little reports in the literature of Glatiramer induced nephrotic syndrome. On the other hand, Interferon gamma B (IFN B) has been linked to MCD after long time use. Kumasake et al. describe case of a woman with MS on IFN B who develops MCD after 21 months on MS treatment (7). Our patient was never treated with IFN B and no evidence seen on renal biopsy.

IV. Conclusion

MCD is a type of nephrotic syndrome, characterized by a urine protein/creatinine of 3500mg and greater. Patients usually present with sudden onset edema, proteinuric kidney injury, and hyperlipidemia. It is believed that disruption of actin cytoskeleton within the podocyte and basement membrane in conjunction with a disrupted immune system cause an increase in mediating factors leading to filtration of albumin into the urinary system and marked proteinuria. Patients need close follow up to ensure steroid responsiveness, as measured by reduction in proteinuria. Due to long duration of steroid therapy, patient's need PJP prophylaxis. This includes Atovaquone or Dapsone. It is prudent to be aware that adults have greater risk for progression to renal failure (than children). In a study by Nolasco et. al, ten of nineteen patients progressed to renal failure, with eight of those eventually requiring dialysis. If adults have truly failed steroid therapy, there will be no improvement after four months. The next step is to discuss the efficacy of second line non-steroidal therapies such as calcineurin inhibitors. This case highlights a case of primary MCD in a woman with HIV and MS, while illustrating that even when patients have other comorbidities or concern for secondary causes of MCD, it is imperative to obtain a renal biopsy to clarify the picture.

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