An unusual case of rapidly progressive chronic kidney failure in patient with insulin treated Type 2 diabetes and chronic microvascular complications

M Marga [1*], LP Pinto [1], RM Coulson [1], C Carrington [2], G Roberts [2]

[1]*Department of Diabetes and Endocrinology, Nevill Hall Hospital, ABUHB;*

[2]*Department of Nephrology Royal Gwent Hospital, ABUHB; Department of Pathology, UHW.*

GIG CYMRU NHS WALES
Bwrdd Iechyd Prifysgol Aneurin Bevan University Health Board

Abstract:

68 yrs old lady with insulin requiring diabetes of 15 years and chronic microvascular diabetes complications including microalbuminuria and stable CKD2 presented to the diabetes follow up clinic with 2 weeks history of the variable minor symptoms including lethargy, nosebleeds, and eye symptoms (watering and stinging). PMHx include a previous episode of Granulomatous poliangiitis 24 years ago, treated with immunosuppressive agents for two years. The routine bloods showed rapidly increasing creatinine, nephritic proteinuria of 3.1gm/24 hrs, red blood cells in urine sediment and negative Bence-Jonce protein.

The vasculitis screening showed positive ANCA 1:320 and positive MPO 57. She was reviewed by Nephrologists, the kidney biopsy confirmed relapsing ANCA associated vasculitis. The Granulomatous poliangiitis affects primarily lungs and kidneys, the incidence rate is 10-20: 100 000. Patient responded well to the treatment course with Cyclophosphamide and steroids and continues under joint care with Nephrology and Diabetes Consultants and Teams. This case highlights the relevance of detailed past medical history and multidisciplinary approach in treatment of complex diabetic patients.

Case History

A 68 year old woman presented to diabetes clinic with insulin requiring diabetes of 15 years and chronic microvascular diabetes complications (background retinopathy and microalbuminuria, eGFR 53ml/min.). She reported nosebleeds, lethargy, watering and stinging to her eyes over past 2 weeks. Previous medical history was one of Granulomatosis with poliangiitis (formerly known as Wegener's granulomatosis) 24 years ago, treated with immunosuppressive agents for 2 consecutive years and discontinued subsequently. There was no remarkable family history. Diabetes was treated with basal bolus insulin, patient was taking Lisinopril and Simvastatin.

Examination revealed BMI 28, consistent with recent weight loss of 4 kg over past 4 months, resting tachycardia of 92, sinus rhythm, new mild systolic ejection murmur on AV and negative JVP. Blood pressure 125/57 mmHg. Peripheral pulse was vague, though symmetrical, no lower limb oedema. Peripheral sensation with C 128Hz and monofilament 10g mm^2 was intact. The blood shot eyes exhibited injected blanching conjunctival vessels and vaguely reactive small symmetrical small Ø 2mm pupils. The erythema with contact bleeding and small clots was found on septum and turbinate area on bilateral external rhinoscopy. The annual screening report was consistent with static background retinopathy. The screening tests for Granulomatous poliangiitis were requested. The results of our extensive investigation confirmed proteinuria 1.82 g/L with Protein-creatinine ratio (PCR) 247; microhaematuria in urine sediment, positive ANCA 1:320 and P-ANCA pattern along with more than ten-fold increased Anti-MPO antibodies of 57.0 U/ml. The renal biopsy confirmed ANCA-associated vasculitis, the cause of rapid progression of CKD[1].

Patient responded well to cyclophosphamide and steroids. EGFR level improved from 20 to 35-42 ml/min, proteinuria is resolved and the recent ACR was 4.1 (back to baseline) January 2017. She continues under joint care of Nephrology and Diabetes Teams. Diabetes control has temporarily deteriorated (HbA1c 85-96 mmol/mol) over past 18 months however the steroid treatment is now stopped and insulin regimen and doses are optimised. Her vasculitis is under control and patient exhibits no other complications of kidney disease apart from CKD3, static. This case highlights the relevance of detailed past medical history and emphasizes impact of efficient multidisciplinary approach in management of complex diabetic patient.

Investigation results

HbA1c	82 mmol/mol
Creatinine	158 µmol/L (baseline 99)
EGFR	28 ml/min/1.73m2
Morning urine Albumin	>500 mg/L
Bence Jones protein screening	No paraprotein identified
Urine Proteine Creatinine ratio	247 mg/mmol
Urine protein	1.82 g/L
24 Hr urine proteine	3.1 gramm /24 hrs
S.Cholesterol	4.7 mmol/L
HDL Cholesterol	0.9
Immunoglobulin A	5.22 g/L
ANCA screen	Positive (titre > 1:320)
ANCA pattern	P-ANCA pattern
Anti-nuclear	Ab screen negative
Anti-MPO Antibodies	57.0 (0.00-5.0)
Anti-PR3 Antibodies	2.4 U/ml
Complement C3	1.79 g/L
Complement C4	0.32 g/L

Summary of CELLULAR PATHOLOGY REPORT
Lab No 4696/15 Consistent with a recurrent pauci immune vasculitis (31% active crescents) on a background of focal segmental sclerosis as evidence of previous episode of acute vasculitis.
Reporting & Consulting pathologist: Dr D Griffiths. Date reported: 18.03.15

Real time test results

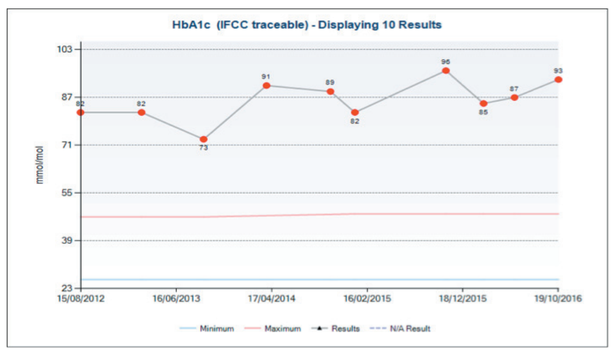


Table 1. HbA1c

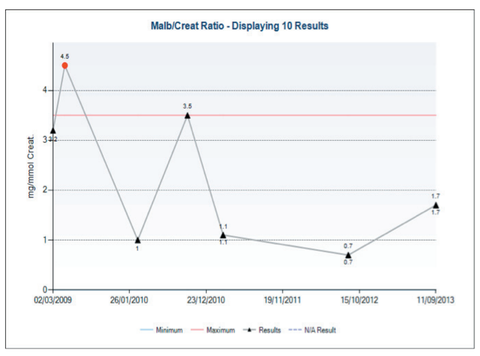


Table 2. Urine ACR

Real time test results

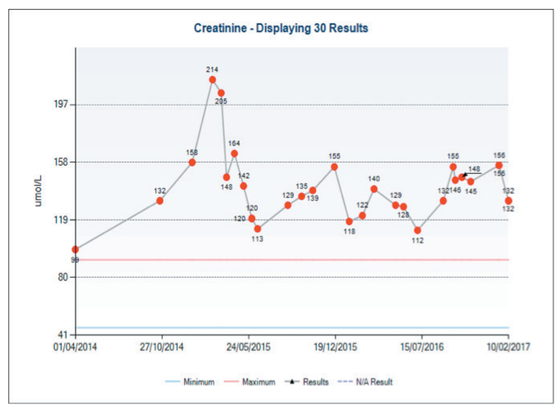


Table 3. Creatinine

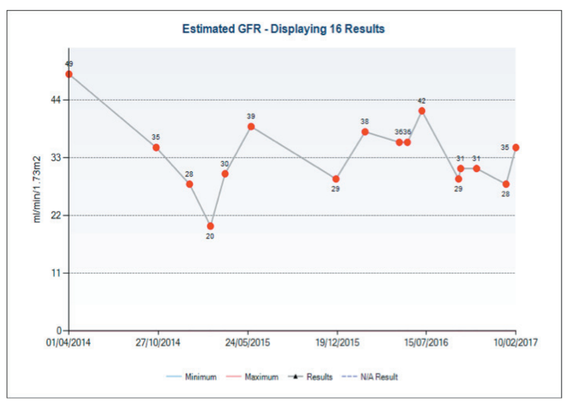
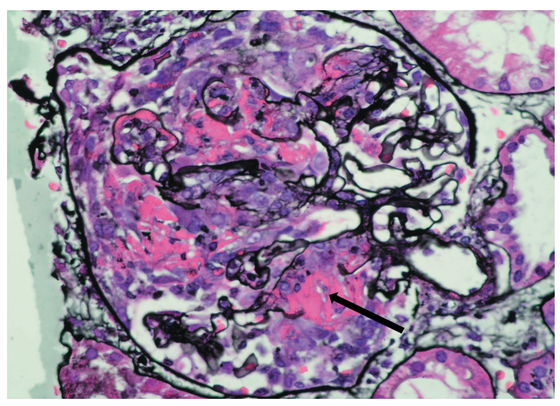
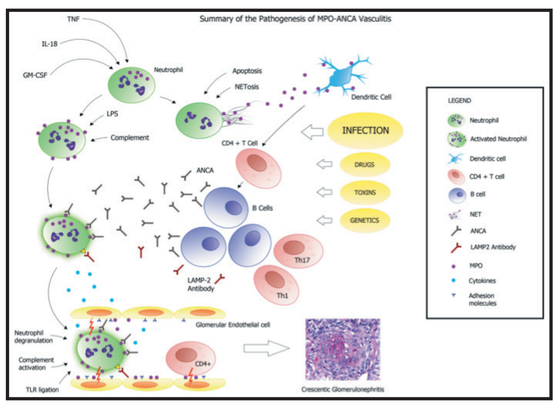


Table 4. Estimated GFR



Renal biopsy from a patient with AAV and severe renal failure showing a Glomerulus containing an extensive cellular crescent with a break in the basement membrane and surrounding fibrin deposition (arrowed) Methenamine silver stain, X400. Abbreviation: AAV, ANCA-associated vasculititis.



From Chapter 2. The Pathogenesis of Antineutrophil Cytoplasmic Antibody Renal Vasculitis by SL Ford, SR Holdsworth, SA Summers. Updates in the Diagnosis and Treatment of Vasculitis, edited by Laszarus I et al., 2013, ISBN 978-953-51-1008-8

Illustration from Therapeutics and Clinical Risk Management 2010:6 253–264© 2010 Hamour et al, publisher and licensee Dove Medical Press Ltd. This is an Open Access article which permits unrestricted noncommercial use, provided the original work is properly cited.

Discussion

Granulomatosis with polyangiitis (GPA) was initially described by Klinger in 1931 as a variant of polyarteritis nodosa and subsequently, as a separate syndrome, by Wegener in 1936 and 1939 respectively. The term Wegener's granulomatosis was introduced into English–language literature by Drs Godman and Chrug in 1954. Granulomatosis with poliangiitis has previously been proposed as an alternative for Wegener's granulomatosis. The move towards a vasculitis nomenclature based on pathology rather the historical reference was triggered by evidence that Dr Friedrich Wegener was a member of the Nazi party before and during World War II. As a result The Board of Directors of American College of Rheumatology (ACR), American Society of Nephrology and European League Against Rheumatism (EULAR) in 2011 have recommended a gradual shift from honorific eponyms to aetiology-based nomenclature [2].

Granulomatosis with polyangiitis (GPA, Wegener's) is type of antineutrophil cytoplasmic antibody (ANCA) associated vasculitis with annual incidence rates 2.1-14.4 per million in Europe. The 5 years survival rate for GPA is estimated to be 74 - 91%. It is most common in middle age and elderly, affecting men and women equally [3]. The cause is not yet known. The antineutrophil cytoplasm antibody (ANCA) - associated vasculitis is idiopathic and multisystemic by nature and characterised by the production of ANCA, reactive to either proteinase-3 (PR3-ANCA) or myeloperoxidase (MPO-ANCA) which are constituents of neutrophil granules and monocyte lysosomes. It causes a destructive inflammation of mainly small calibre arterial vessels and along with microscopic polyangiitis (MPA), renal-limited vasculitis (RLV) and Churg-Strauss syndrome represents the *group of ANCA- associated vasculitides* (AAV) [4&6]. The latter ones cause an end-stage renal failure developing in > 20% of patients at 5 years. *By the introduction of steroids and cyclophosphamide (CYP) in the early 1970s the survival rate has increased from median survival of five months to five year survival rate around 75% for patients with generalised GPA*. The induction of remission is now achieved in over 90% patients by six months, however the relapse rate remains high, up to 50% over 5 years[5].

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Contacts: 1. *Mara Marga,MD, Endocrinologist, Staff/Specialty Grade. Dept of Diabetes and Endocrinology, Nevill Hall Hospital, Aneurin Bevan University Health Board, Mara.Marga@wales.nhs.uk 2. Dr G Roberts, Consultant Nephrologist, Royal Gwent and Nevill Hall Hospitals, Aneurin Bevan University Health Board