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"More than meets the eye" non secretory myeloma presenting as cidp in a patient with longstanding diabetic polyneuropathy. a diagnostic and therapeutic challenge.

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"MORE THAN MEETS THE EYE" NON SECRETORY MYELOMA PRESENTING AS CIDP IN A PATIENT WITH LONGSTANDING DIABETIC POLYNEUROPATHY. A DIAGNOSTIC AND THERAPEUTIC CHALLENGE.

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ABSTRACT

Diagnosing chronic inflammatory polyradiculopathy in patients with pre-existing diabetic sensorimotor polyneuropathy is a diagnostic challenge. We present a case of a 69 years old who presented with weakness of legs for two months,he was diagnosed as having CIDP on the background of diabetic sensorimotor polyneuropathy, further and extensive workup revealed the final diagnosis of nonsecretory myeloma. Diagnosing non secretory myeloma is itself a diagnostic challenge and usually first line investigations for the workup of myeloma are negative as was the case in our patient. Our patient with CIDP had raised free light chains of kappa which made the final diagnosis of kappa associated plasma cell dyscrasia.

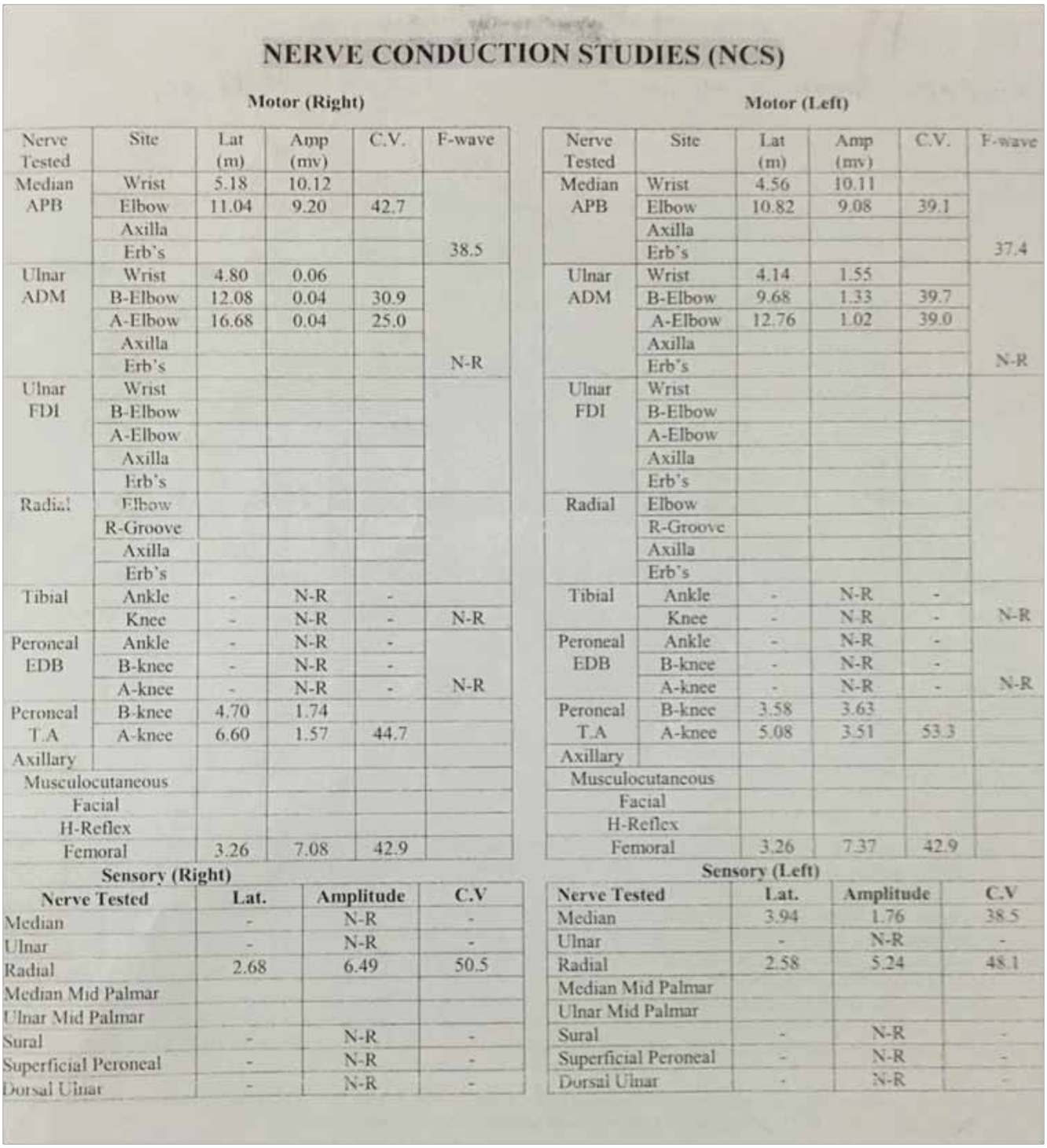
Key words: Chronic inflammatory polyradiculopathy (CIDP), Non secretory myeloma, Diabetic sensorimotor neuropathy

INTRODUCTION

Chronic inflammatory polyradiculopathy (CIDP) is clinically defined as 'chronically progressive, stepwise or recurrent proximal and distal and sensory dysfunction of all extremities, developing over at least 02 months, with absent or reduced tendon reflexes in all limbs and sometimes with cranial nerve involvement[1].The diagnosis of CIDP in diabetes patients may be significantly more difficult than in non-diabetics, due to mild demyelinating changes associated with diabetic sensorimotor polyneuropathy (DSP), in the setting of poor glycemic control[2].We present such a challenging case of 69 year old male from Islamabad where reaching to a final diagnosis was an arduous journey and in itself was a diagnostic challenge.

CASE REPORT:

A 69 years old male with 35 years long history of type 2 diabetes Mellitus with complications of diabetic neuropathy, nephropathy CKD III, retinopathy, diabetic foot ulcer presented with two months history of gradual but rapid worsening of weakness in both legs, he was independent with activities of daily living prior to two months and was driving. The weakness was asymmetrical and involved left leg more than right and involved both proximal and distal muscles equally and at the same time. He denied any symptoms in upper limbs. There was no significant backache or urinary symptoms. There was longstanding numbness in both his feet for more than six years which was unchanged. Examination revealed wasting of left leg, marked ischemic lower limbs skin changes, diabetic foot ulcer on right first metatarsal. There was prominent wasting of small muscles in hands as well. Power was 4/5 on left leg both proximally and distally. Power was 4+ on right leg both proximally and distally. He had normal power in upper limbs.Sensory system examination revealed impaired pin prick sensation in gloves and stocking distribution, impaired vibration and position sense in legs upto ankles.Investigations revealed HB of 10.5g/dL microcytic hypochromic.His renal functions revealed creatinine of 2.7mg/dL and urea of 40mg/dL. Serum electrolytes showed low sodium of 128mmol/L, normal potassium and low bicarbonate of 16. His HbA1c was 8.7.His nerve conduction studies and Electromyography revealed changes suggestive of sensorimotor predominantly polyneuropathy with demyelination changes as shown in figure 1&2.Was it just the rapid progression of Diabetic Sensorimotor



NERVE CONDUCTION STUDIES (NCS)

Motor (Right)

Nerve Tested	Site	Lat (m)	Amp (mv)	C.V.	F-wave
Median APB	Wrist	5.18	10.12		
	Elbow	11.04	9.20	42.7	
	Axilla				
	Erb's				38.5
Ulnar ADM	Wrist	4.80	0.06		
	B-Elbow	12.08	0.04	30.9	
	A-Elbow	16.68	0.04	25.0	
	Axilla				
	Erb's				N-R
Ulnar FDI	Wrist				
	B-Elbow				
	A-Elbow				
	Axilla				
	Erb's				
Radial	Elbow				
	R-Groove				
	Axilla				
	Erb's				
Tibial	Ankle	-	N-R	-	
	Knee	-	N-R	-	N-R
Peroneal EDB	Ankle	-	N-R	-	
	B-knee	-	N-R	-	
	A-knee	-	N-R	-	N-R
Peroneal T.A	B-knee	4.70	1.74		
	A-knee	6.60	1.57	44.7	
Axillary					
Musculocutaneous					
Facial					
H-Reflex					
Femoral		3.26	7.08	42.9	

Motor (Left)

Nerve Tested	Site	Lat (m)	Amp (mv)	C.V.	F-wave
Median APB	Wrist	4.56	10.11		
	Elbow	10.82	9.08	39.1	
	Axilla				
	Erb's				37.4
Ulnar ADM	Wrist	4.14	1.55		
	B-Elbow	9.68	1.33	39.7	
	A-Elbow	12.76	1.02	39.0	
	Axilla				
	Erb's				N-R
Ulnar FDI	Wrist				
	B-Elbow				
	A-Elbow				
	Axilla				
	Erb's				
Radial	Elbow				
	R-Groove				
	Axilla				
	Erb's				
Tibial	Ankle	-	N-R	-	
	Knee	-	N-R	-	N-R
Peroneal EDB	Ankle	-	N-R	-	
	B-knee	-	N-R	-	
	A-knee	-	N-R	-	N-R
Peroneal T.A	B-knee	3.58	3.63		
	A-knee	5.08	3.51	53.3	
Axillary					
Musculocutaneous					
Facial					
H-Reflex					
Femoral		3.26	7.37	42.9	

Sensory (Right)

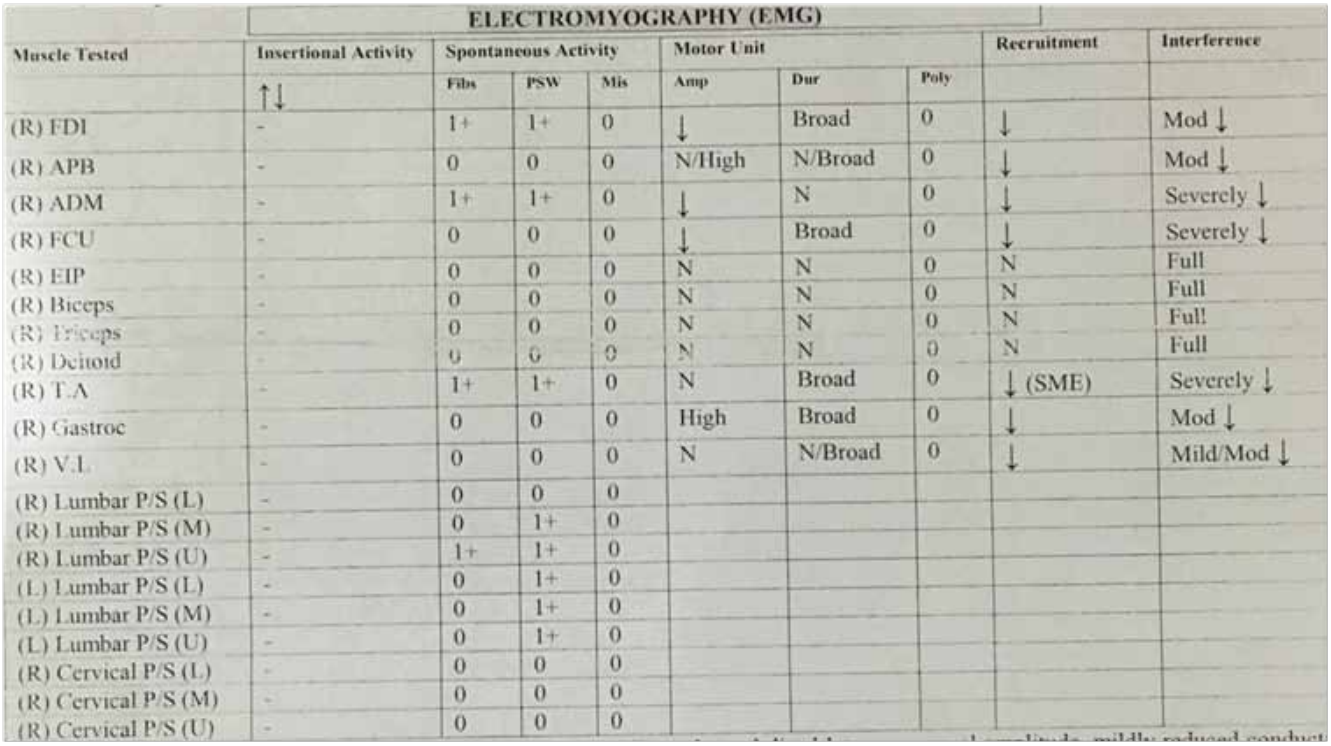
Nerve Tested	Lat.	Amplitude	C.V
Median	-	N-R	-
Ulnar	-	N-R	-
Radial	2.68	6.49	50.5
Median Mid Palmar			
Ulnar Mid Palmar			
Sural	-	N-R	-
Superficial Peroneal	-	N-R	-
Dorsal Ulnar	-	N-R	-

Sensory (Left)

Nerve Tested	Lat.	Amplitude	C.V
Median	3.94	1.76	38.5
Ulnar	-	N-R	-
Radial	2.58	5.24	48.1
Median Mid Palmar			
Ulnar Mid Palmar			
Sural	-	N-R	-
Superficial Peroneal	-	N-R	-
Dorsal Ulnar	-	N-R	-

Figure1. Nerve conduction studies of the patient showing prolonged distal latencies, reduced amplitudes and reduced conduction velocities of majority of upper limb nerves. Majority of lower limb nerves show no response. Sensory nerves are affected as well.

Polyneuropathy or this presentation suggestive of CIDP was the main diagnostic dilemma here. Diagnosing CIDP is a challenge in diabetics with pre-existing sensorimotor polyneuropathy.Our patient had neurological deterioration in 02 months and had raised CSF proteins of 136.6mg/dl which further supported the diagnosis of CIDP and there was evidence of demyelination on nerve conduction studies, however



ELECTROMYOGRAPHY (EMG)									
Muscle Tested	Insertional Activity	Spontaneous Activity			Motor Unit			Recruitment	Interference
	↑↓	Fibs	PSW	Mis	Amp	Dur	Poly		
(R) FDI	-	1+	1+	0	↓	Broad	0	↓	Mod ↓
(R) APB	-	0	0	0	N/High	N/Broad	0	↓	Mod ↓
(R) ADM	-	1+	1+	0	↓	N	0	↓	Severely ↓
(R) FCU	-	0	0	0	↓	Broad	0	↓	Severely ↓
(R) EIP	-	0	0	0	N	N	0	N	Full
(R) Biceps	-	0	0	0	N	N	0	N	Full
(R) Triceps	-	0	0	0	N	N	0	N	Full
(R) Deltoid	-	0	0	0	N	N	0	N	Full
(R) T.A	-	1+	1+	0	N	Broad	0	↓ (SME)	Severely ↓
(R) Gastroc	-	0	0	0	High	Broad	0	↓	Mod ↓
(R) V.L	-	0	0	0	N	N/Broad	0	↓	Mild/Mod ↓
(R) Lumbar P/S (L)	-	0	0	0					
(R) Lumbar P/S (M)	-	0	1+	0					
(R) Lumbar P/S (U)	-	1+	1+	0					
(L) Lumbar P/S (L)	-	0	1+	0					
(L) Lumbar P/S (M)	-	0	1+	0					
(L) Lumbar P/S (U)	-	0	1+	0					
(R) Cervical P/S (L)	-	0	0	0					
(R) Cervical P/S (M)	-	0	0	0					
(R) Cervical P/S (U)	-	0	0	0					

Figure 2. Electromyography of the patient showing neuropathic changes in form of broad motor unit potentials, some showing high amplitude and reduced interference pattern.

exact electrophysiological criteria could not be applied due to the presence of diabetic sensorimotor polyneuropathy.Rest of the diagnostic workup showed negative antiganglioside antibodies including Anti GM1 antibodies. His ANA, ENA(extractable nuclear antigen antibodies) were negative. His serum electrophoresis was normal, showing no evidence of para proteins. ESR was 49 and CRP was negative. MRI lumbosacral spine showed mild to moderate lumbar spondylosis as shown in figure 3.IVIG were contraindicated in our patient due to diabetes associated renal impairment. As oral corticosteroids are considered as first line treatment of newly diagnosed CIDP, patient was started on steroids. Plasma exchange was high risk in our patient due to presence of cardiovascular compromise and was offered but refused by patient. Patient was given corticosteroids along with Azathioprine for 06 weeks. At 06 weeks he showed no improvement in his disability. However, he further developed malena, steroid induced gastropathy was confirmed on endoscopy which confirmed marked antral gastritis and gastric erosions. His haemoglobin dropped from 10.5 to 7.5 mg/dL. He also developed neutropenia probably due to azathioprine and developed marked oral ulcers and thrush rendering him nil by mouth. Steroids and azathioprine were therefore discontinued. As patient did not respond to first line treatment and we had difficulties with first line treatments. We underwent second-line investigations. Further diagnostic workup revealed raised serum free light chain. Free kappa were found to be >4380mg/L (range 3.3-19.4mg/L).Serum protein electrophoresis of the patient was normal but the serum light chains were very high making the final diagnosis of non secretory myeloma. So final diagnosis was non secretory Kappa plasma cell dyscrasia

DISCUSSION

Diabetes patients who have changes suggestive of demyelination on nerve conduction studies (NCS) are usually considered to have a superimposed immune-mediated polyneuropathy, such as chronic inflammatory demyelinating polyneuropathy (CIDP)[3]. The differentiation of CIDP from DSP in patients with diabetes is important due to the implications for therapy and prognosis[4]. The finding of raised CSF proteins helped us in making the diagnosis of CIDP. In such difficult cases finding of raised CSF proteins without CSF leucocytosis further supports the diagnosis of CIDP[1] and this is next important investigation to

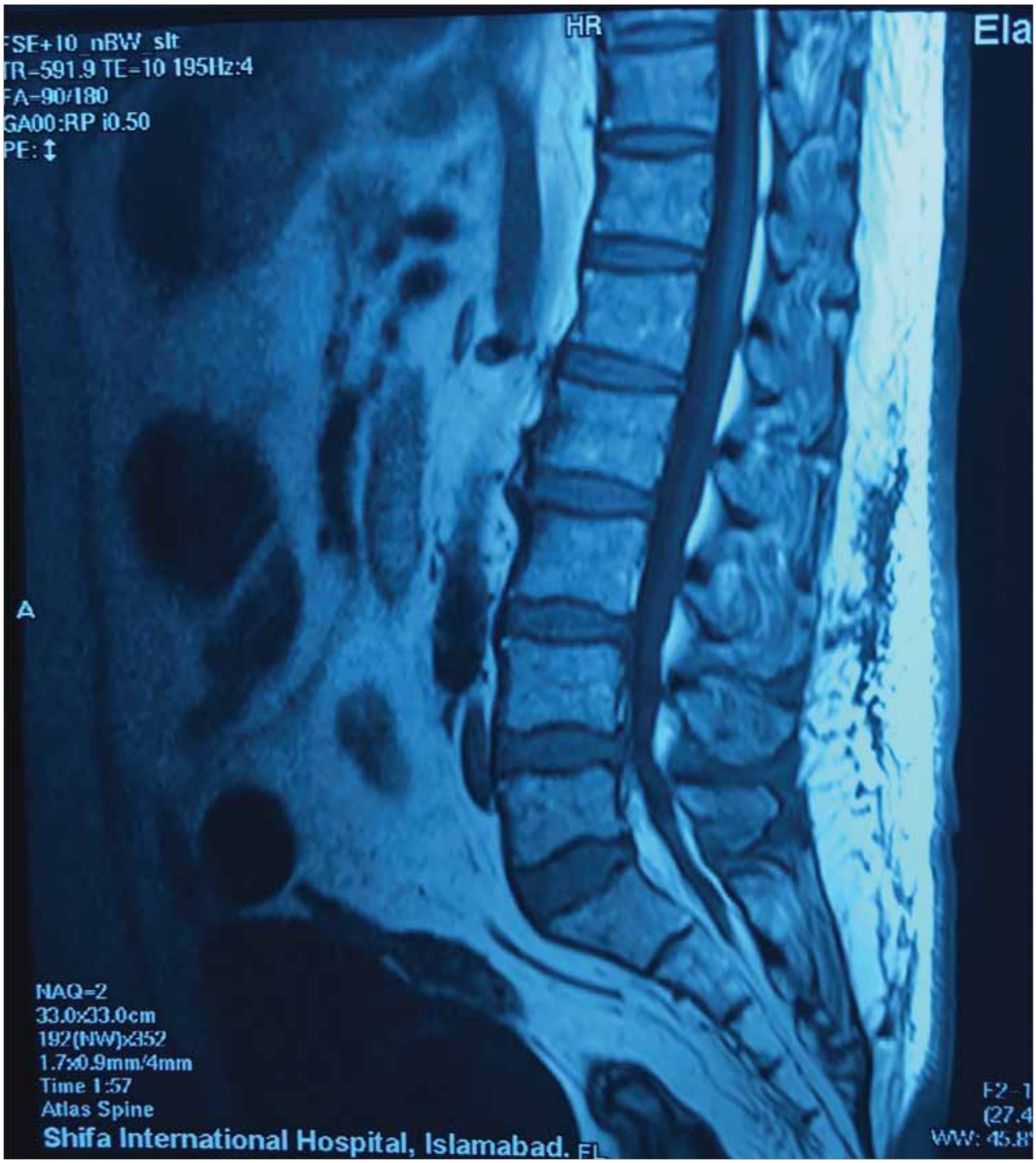


Figure 3.MRI lumbosacral spine of the patient showing mild to moderate lumbar spondylosis.

undertake in this regard.The quality of evidence for the efficacy for intravenous immunoglobulin and plasma exchange is moderate to high, with plasma exchange providing significant short term improvement in disability, clinical impairment and motor nerve conduction velocities, although there may be rapid deterioration post exchange[5]. Seventy percent of patients of CIDP respond to one or another of the three standard therapies and probably 90% respond overall I[1]. The lack of response to treatment and minimal electrophysiological progressin over time should lead one to suspect the diagnosis and undergo secondlineinvestigations[1]. Same was the case in our patient, he did not respond to steroids so we opted for

second line investigations and further extensive workup which revealed diagnosis of non secretory myeloma. Serum protein electrophresis has only a 60% sensitivity for detecting paraproteins in the context of neuropathy, so immunofixaton,95% sensitivity along with bence jones proteins and serum free light chains should be performed[1]. Non secretory myeloma are one of the rare cause of myeloma found in only 1 to 5% of the cases of multiple myeloma[6].They often present as diagnostic challenge[6].

CONCLUSION

We conclude that diagnosing CIDP in patients with background diabetic sensorimotor neuropathy is a diagnostic challenge.We also recommend diagnostic workup for myeloma in CIDP should not just include serum and urine electrophoresis but should include immunofixation as well as serum free light chains ratio especially if the response to first line therapy is poor.More than meets the eye,never stop at any step, keep on looking for the rare causes which can make a single unifying diagnosis of all symptoms, as in this case of non secretory myeloma

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FarheenNiazi; Study concept and design, protocol writing, data collection, data analysis, manuscript writing, manuscript review
Arsalan Ahmed; Stydy concept and design, data collection, data analysis, manuscript writing, manuscript review
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SajidBukhari: data analysis, manuscript writing, manuscript review
UzmaBatool: data analysis, manuscript writing, manuscript review