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An Interesting Case of Vasculitic Myeloneuropathy

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ABSTRACT: 13-year-old female right-handed, studying 7th std. Presented with itching and multiple [1]non-healing ulcers over all 4 limbs more in the lower limbs for 1 month. She has difficulty in walking in the form of difficulty in clearing the ground. Mainly due to flail foot/foot drop. H/o difficulty in holding the chappels. Along this patient having stfifness of all four limb except distal aspect of left lowe limb. This weakness not associated with thinning of limb and without any twitching sensation/O numbness, paresthesia and burning sensation over both foot on sole and dorsum of foot and right lateral aspect of leg possibility of [2]neuropathic pain. She has deformity of left upper limb in form partial clawing of left hand. She is also having numbness and paresthesia on left middle 2 finger and medial aspect of forearm and hand, without any bowel bladder involvement, without any history of cognitive impairment, No history of loss of consciousness, seizure, headache no history suggestive of features of raised ICT. O/e HMF -Normal, Cranial nerves - normal, Spinomotor: Tone is increased all 4 limbs except right foot. Sensory symptoms -graded sensory loss on in distribution of B/L in ulnar nerve distribution and right sciatic nerve. Cerebellar sign: Rhomerg sign positive. Timed vibration reduced below the ASIS. Joint position, vibration sense impaired in both lower limb
Planter: Left planter extensor, right planter not elicitableOther systemic examination normal. Neuroimaging was normal. NCS revealed axonal neuropathy. HPE also revealed axonal neuropathy.

I. INTRODUCTION:

Myeloneuropathy is an interesting presentationand often poses a diagnostic challenge. A variety of nutritional, toxic, metabolic, infective, vasculitic, autoimmune, inflammatory, and paraneoplastic disorders can present with[3] myeloneuropathy. Deficiencies of vitamin B12, folic acid, copper, and vitamin E may lead to myeloneuropathy with a clinical picture of subacute combined degeneration of the spinal cord. Among infective causes, chikungunya virus has been shown to produce a syndrome similar to myeloneuropathy. Vacuolar myelopathy seen in human immunodeficiency virus (HIV) infection is clinically very similar to subacute combined degeneration. A paraneoplastic myeloneuropathy, an immune-mediated disorder associated with an underlying malignancy, may rarely be seen with breast cancer. Tropical spastic paraparesis, a chronic noncompressive myelopathy, has frequently been reported from South India. Establishing the correct diagnosis of myeloneuropathy is important because compressive myelopathies may pose diagnostic confusion. Magnetic resonance imaging (MRI) in subacute combined degeneration of the spinal cord typically reveals characteristic signal changes on T2-weighted images of the cervical spinal cord. Once the presence of myeloneuropathy is established, all these patients should be subjected to a battery of tests. Blood levels of vitamin B12, folic acid, vitamins A, D, E, and K, along with levels of iron, methylmalonic acid, homocysteine, and calcium should be assessed. The pattern of neurologic involvement and results obtained from a battery of biochemical tests, neurophysiological work up often help in establishing the correct diagnosis.

CHIEF COMPLAINTS:

13 yr/adolescent girl, Rt handed, studying 7th standard, hailing from Tirunelveli presented withMultiple ulcers over both legs x 1 month. Numbness and paresthesias of right footx10days difficulty in walking x 10 days. Numbness and paresthesias of left little and ring finger along with Clawingof left medial 2 fingers x 1 week

She was apparently normal 1 month back, then she developed itching of **both LL, UL**, along with **Reddish, erythematous papular lesions** which gradually expanded in size not a/w lace like patternA week later these lesions converted to **multiple painful ulcers** over the both LL, mainly on dorsum of foot and ankle. For the last 10 days she has swelling and pain of the left foot. H/o vague discomfort in the back of Rt thigh. No h/o fever, myalgia, joint pains, Raynaud's phenomenon, blackening of toe or fingers. After 2 weeks she started havingsevereparesthesias, pins and needles sensation, burning, shooting pain and numbness of of**Rt LL over sole, dorsum and lateral side of leg**andalso**Lt little and ring finger with medial side of hand which was p**rogressive and increasing in severity. H/O Cotton wool like sensation on walking present. She had difficultyinto differentiate hot and cold sensation in

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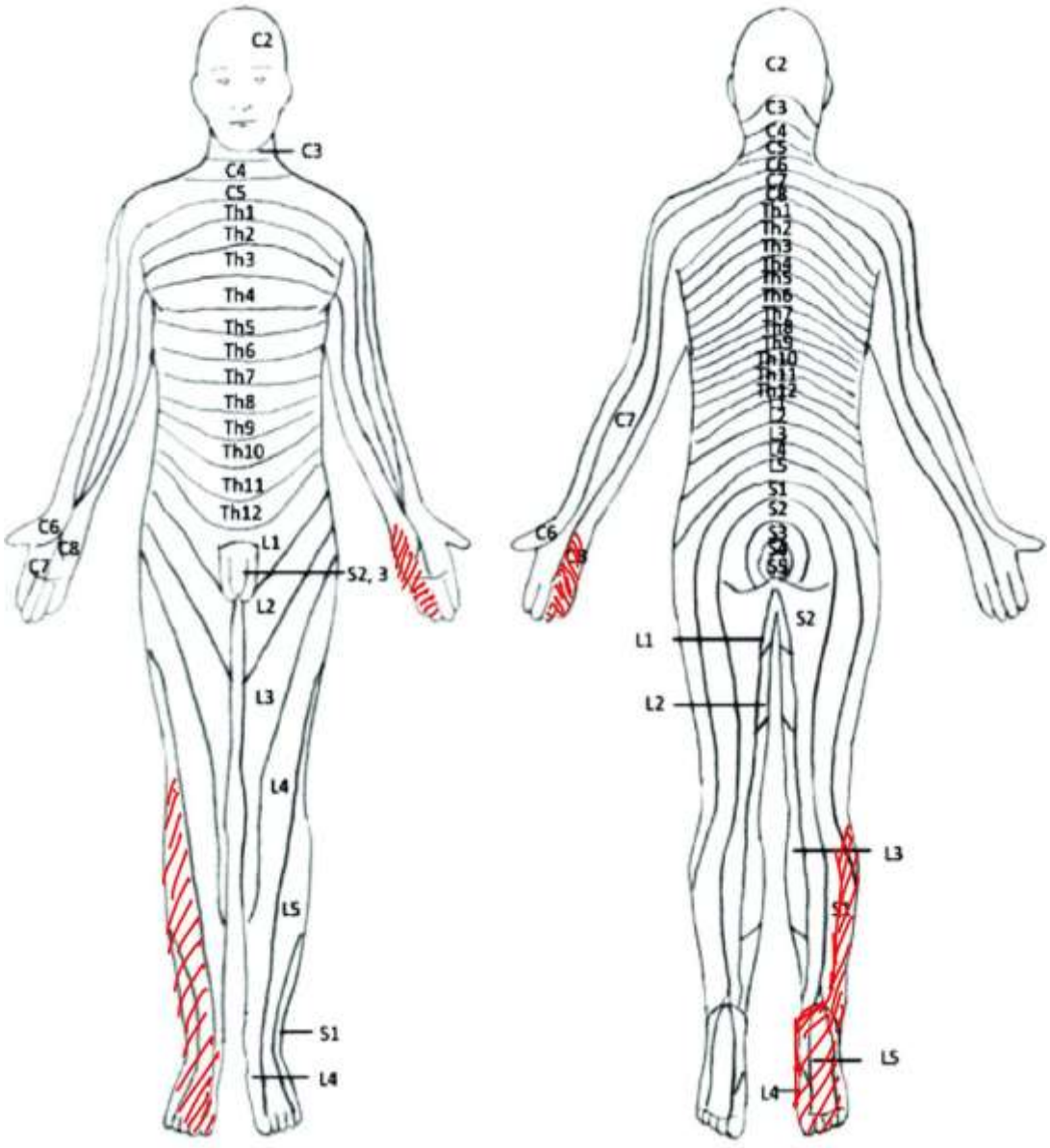
these areas. No h/o increased/decreased sweating, nail changes or hair loss.
No h/o wash basin phenomenon, lhermitte's sign, band like senasation or girdle pain
After 3 days, difficulty in walking is rapidly progressive, mainly of **Right LL**, in the form of unable to clear the foot from the ground a/w stamping of Rt foot.
Unable to grip the chappal with slipping which she is unaware off a/wflailness of foot
Not a/w difficulty in getting up. No weakness of left lower limb.

Weakness of **left upper limb** in the form of, [4]clawing of medial 2 fingers with slippage of water through fingers while face washing. No difficulty in reaching higher shelf.
No weakness of Rt upper limb

PAST HISTORY:
Cervical lymphadenitis at 5 yrs, proven to be TB by FNAC, 6 months of ATT. No other significant past medical or surgical history



Lt Upper limb
1. C8 Root
2. Lower trunk

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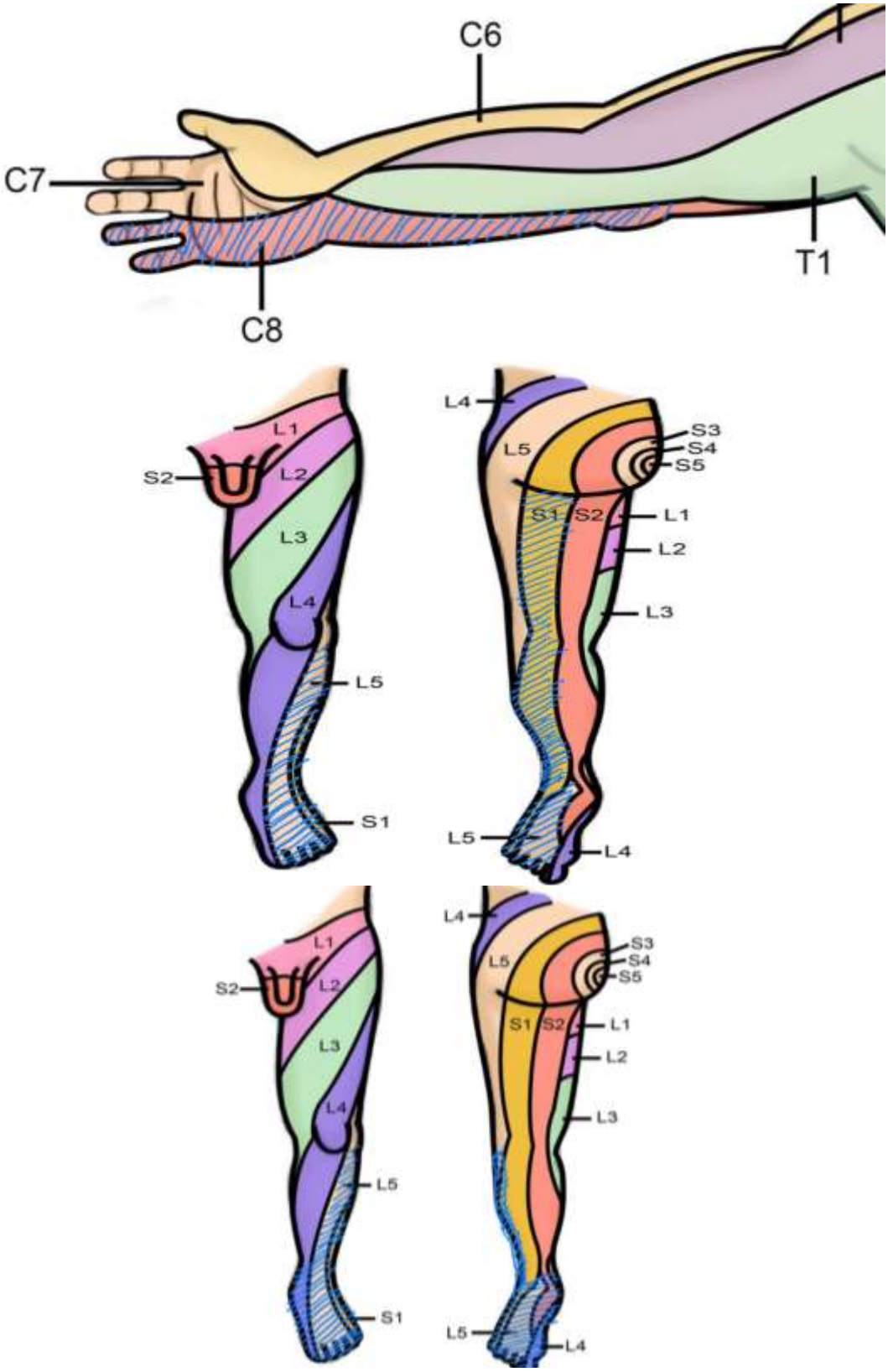
3. Medial cord
4. Ulnar nerve



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1. L5, S1 Root
2. Lower lumbosacral Plexus

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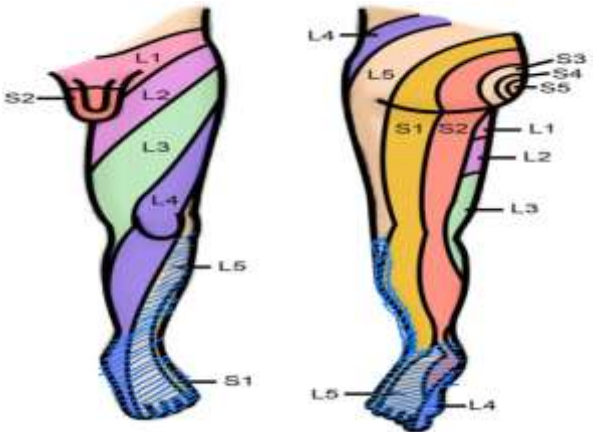
2. Lower lumbosacral Plexus



Purpose of presenting the case:

Patient presented with multiple individual nerve involvement. B/L ulnar andRt sciatic nerve were involved suggestive of mononeuritis multiplex.

Patient also has spinal cord involvement in the form of in
creased tone in all four limbs, Brisk DTR with left ankle clonus and extensor left plantar.
Multilplevasculitic ulcers over both lower limbs present.

Hb	14.5 gm%
TLC	21,200 cells/cmm
N/L/E	64%/20%/16%
AEC	3000 cells/cmm
MCV	72.4 fl
MCH	28.2 pg
PLTC	2.01 lakh/cmm
LFT	WNL
Protein (albumin+globulin)	7(4+3) g/dl
RBS	97 mg/dl
S Creatinine	0.8 mg/dl
B Urea	19 mg/dl
Na, k, ca	139, 4.1, 8.6
Urine protein	120

ESR	35 mm/hr
CRP	Positive
RA Factor (latex agglu)	Negative
Anti CCP	Negative
ANA (ELISA)	Negative
HIV I & II	Non reactive
HBsAg	Non reactive
HCV	Non reactive
SARS CoV-19 PCR DNA	Negative
Vit B12	720 pg/ml
Vit E	10 mcg/ml

Blood and urine culture sensitivity- no growth

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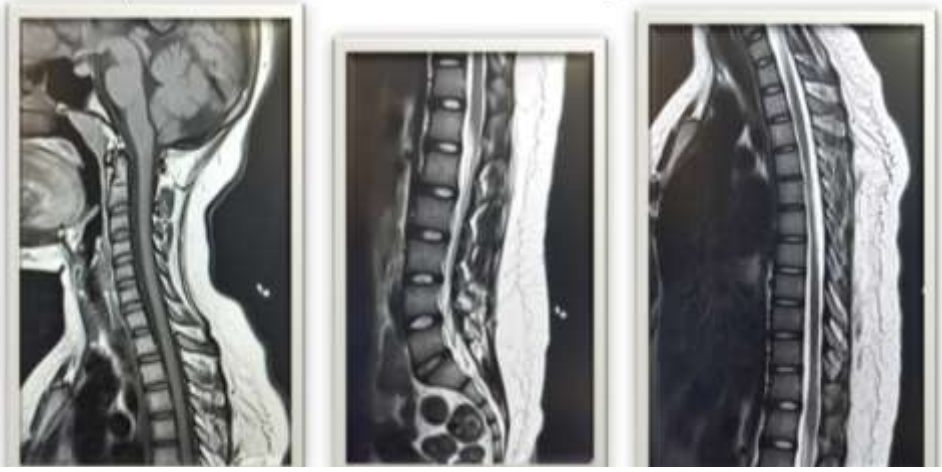
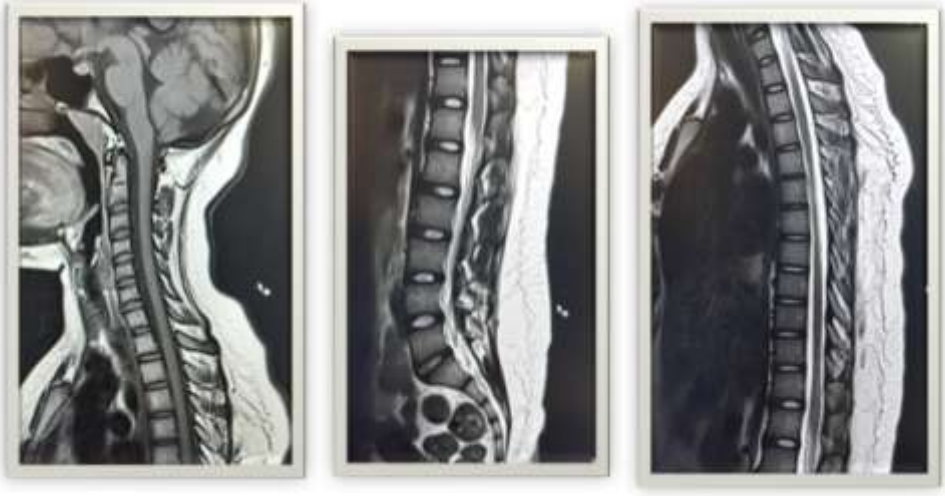
TSH	5.4 mIU/L
Slit skin smear for M leprae	Negative
VDRL	Negative
ACE levels	24 nmol/ml (< 40 normal)
24 hr urinary protein	6 mg/dl (<10 normal)
Urine microalbumin	24 mg (normal <30)
Bone marrow aspiration	Awaited

MRI spine with Brain screening



MRI spine with Brain screening



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SERUM	Anti-SARS-CoV-2 Total Antibodies (C.L.I.A.)	9.12	S/Co	0.00 - 0.99
Anti SARS CoV2 antibody screening is only for sero-surveillance and not for diagnosis of SARS CoV2 infection. *Note :- The referring doctor/healthcare provider will work with you to determine how best to care for you based on the test results along with other factors of your medical history, including any previous symptoms, possible exposure to COVID-19, and the location of places you have recently traveled.*				
	Anti SARS-CoV2 IgG Antibody (CLIA)	8.37	S/co	Non Reactive: < 1.0 Reactive: > 1.01

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	Anti SARS-CoV2 IgG Antibody (CLIA)	8.37	S/co	Non Reactive: < 1.0 Reactive: > 1.01

A/c Status : P Ref By : TVMCH Report Status : Final

Test Name	Results	Units	Bio. Ref. Interval
ANTI NEUTROPHIL CYTOPLASMIC ANTIBODIES (ANCA)* (IFA)			
p-ANCA*	Negative		
c-ANCA*	Negative		
Titre*	1:20		

ENA Profile

EXTRACTABLE NUCLEAR ANTIGENS (ENA)/ANTI NUCLEAR ANTIBODIES (ANA), QUALITATIVE PROFILE* (LIA)

U1-nRNP/Sm*	Negative
Sm*	Negative
SS-A*	Negative
Ro- 52*	Negative
SS-B/La*	Negative
Scl - 70*	Negative
PM-Scl*	Negative
Jo - 1*	Negative
CENP-B*	Negative
PCNA*	Negative
ds-DNA*	Negative
Nucleosomes*	Negative
Histones*	Negative
Rib- P Protein*	Negative
AMA- M2*	Negative

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CSF analysis

Cell count	Acellular
Protein	25 mg/dl
Glucose	72 mg/dl
Globulin	Negative
Chloride	104 mEq/L
ADA	4
Gram and AFB stain	No organism
C/S	No Growth
CSF CBNAAT	MTB Not detected

13 yr /adolescent girl, Rt handed,studying 7th standard , hailing from Tirunelveli presented with

LAB FEATURES

- 1.ESR,CRP and RA factor are elevated in most patients
- 2.CSS:Evaluation is remarkable for eosinophilia and antineutrophil cytoplasmic antibodies (ANCAs),primarily myeloperoxidase(MPO) or p-ANCA, because of its perinuclear staining pattern.Thesep-ANCA antibodies are present in as many as two-thirds of patients.
- 3.PAN: As many as onethird of cases are associated with hepatitis B antigenemia.In addition hepatitis C and HIV infection have also been reported with PAN.Abdominalangiograms can reveal avasculitic aneurysm.Tenpercent to 20% have anti-MPO/p-ANCA antibodies
- 4.GAN: Evaluation is remarkable for the presence of antineutrophil antibodies directed against proteinase3(c-ANCA).The specificity of c-ANCA for GAN is 98% and the sensitivity is 95%
- 5.MPA:Laboratory evaluation usually demonstrates the use of p-ANCA,although c-ANCAs can also occasionally be detected.

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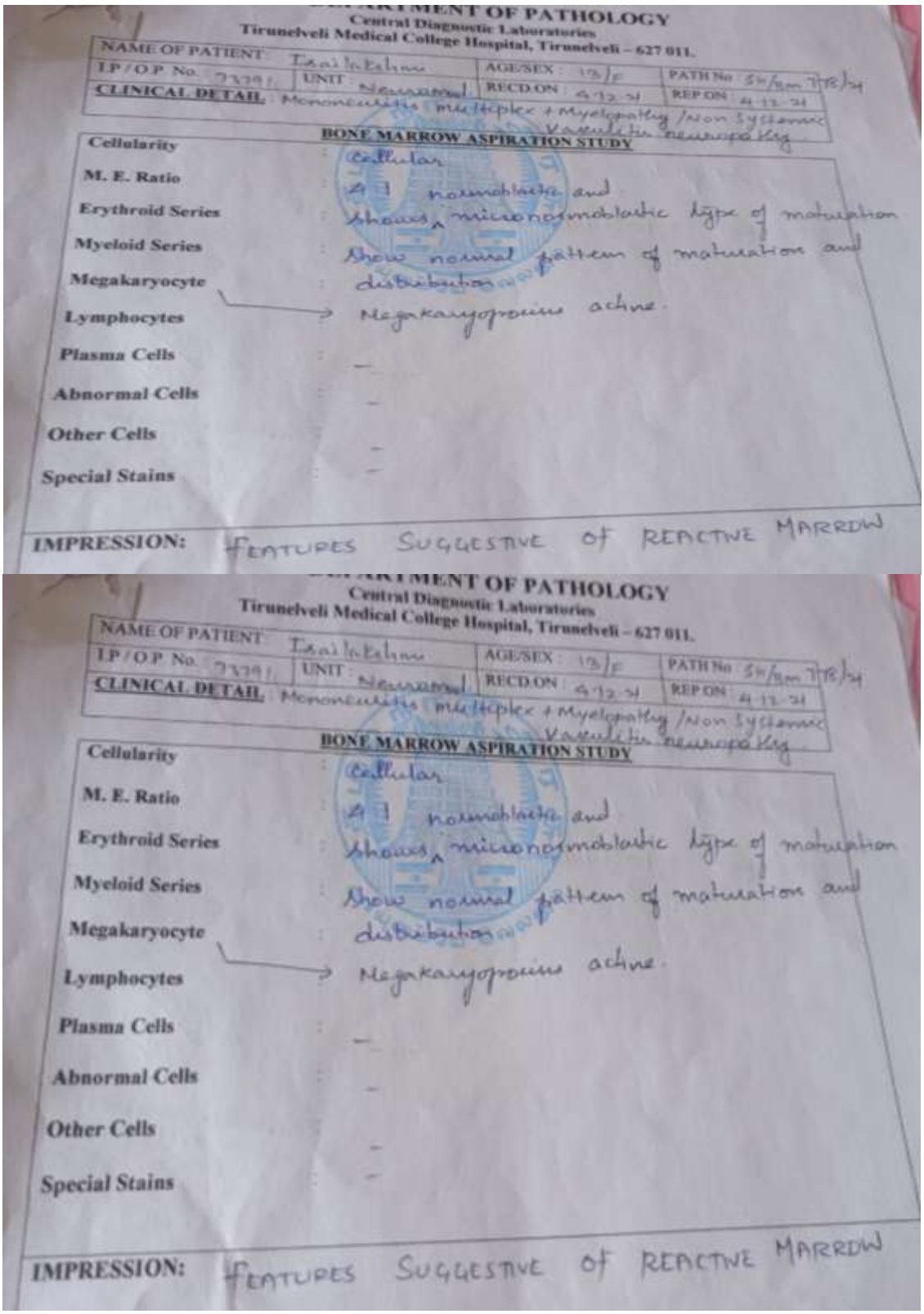

DEPARTMENT OF PATHOLOGY
Central Diagnostic Laboratories
Tirunelveli Medical College Hospital, Tirunelveli – 627 011.

NAME OF PATIENT: Isaiakshmi		AGE/SEX: 13/F	PATH No: SH/Gen 778/21
I.P / O.P No: 73791	UNIT: Neuro med	RECD ON: 4.12.21	REP ON: 4.12.21
CLINICAL DETAIL: Mononeuritis multiplex + Myelopathy / Non Systemic Vasculitic neuropathy			

BONE MARROW ASPIRATION STUDY

Cellularity	Cellular
M. E. Ratio	2:1 normoblastic and
Erythroid Series	shows micronormoblastic type of maturation
Myeloid Series	Show normal pattern of maturation and
Megakaryocyte	distribution
Lymphocytes	Megakaryopoiesis active.
Plasma Cells	–
Abnormal Cells	–
Other Cells	–
Special Stains	–

IMPRESSION: FEATURES SUGGESTIVE OF REACTIVE MARROW

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UHID:	EXT21018415	**Referring Hospital:**	Dr.Saravanan, Tirunelveli Medical College, Palayamkottai, Tirunelveli, Tamil Nadu 627011
MRD No :		**Referring Dept:**	
Patient Name:	**Miss. ISAI LAKSHMI**	**Sample Collection Date:**	02/12/2021 04:24 PM
Age :	13 years	**Lab Reference No:**	X-4961/2021
Gender:	Female	**Report Generated Date:**	08/12/2021 12:51 PM
Ward Name/Collection Centre:	Biopsy Room	**Lab Name:**	Neuropathology

Sample Details : H-2112020037 (Muscle)

MUSCLE BIOPSY IN FORMALIN (FOR OUTSIDE HOSPITALS ONLY)

Nature Of Specimen:
Received 2 bottles :
1) Muscle : Received a muscle biopsy measuring 0.8x0.6x0.5cm. Rest kept-A1
2) Nerve : Received 3 nerve segments measuring 0.5cm, 0.5cm and 1cm in length. With small tiny grey brown tissue pieces measuring 0.3x0.2x0.2cm. Rest kept-B1
Grossed by Dr.Aditi (3/12/2021)

Histopathology Report:
Muscle biopsy shows preserved fascicular architecture with mild variation in fibre size with few hypertrophic and scaphoid angulated atrophic fibres. No active myopathic features are noted. No increased endomysial fibrosis noted. There is no evidence of vasculitis.

Nerve biopsy shows foci of neovascularisation in the epineurium. No transmural inflammation or fibrinoid necrosis noted. Endoneurium shows acute axonal breakdown with formation of myelin ovoids. There is severe reduction in the nerve fibre density.
K-pal stain for myelin shows marked non-uniform, severe loss of myelinated fibres with acute myelin breakdown and minimal axonal regeneration.
Cresyl Violet stain is negative for metachromatic granules.
Immunohistochemistry : LCA immunostain for inflammation is negative

Final Impression:
1) **Muscle biopsy**- Mild neurogenic atrophy with no evidence of vasculitis, Right peroneus brevis
2) **Nerve biopsy**- Acute axonal degeneration, Right superficial peroneal nerve
Note : Vasculitis cannot be excluded. Finding of acute axonal degeneration supports an immune mediated etiology.

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II. DISCUSSION:

Neuropathy can bethe first manifestation of [5]vasculitis as in our case. Extensive diagnostic pathway is necessary to confirm or to exclude the diagnosis

Ahigh index of suspicion is essential for making the diagnosisbased on the clinical features

[6] Mononeuritis multiplex is a painful, asymmetric, asynchronous sensory and motor peripheral neuropathy invoving simultaneous or sequential damage to two or more noncontigous peripheral nerves. Our patient fits in for this diagnosis. [7]ANA Profile was done in which all autoantibodies were negative. Hence the possibility of systemic vasculitis is ruled out. Among the[8]NON SYSTEMIC VASCULITIC NEUROPATHY there are 4 types. 1. nsvn-subtypes like wartenberg migratory sensory neuropathy and post surgical inflammatory neuropathy. 2[9]. DM related3. Non DM related 4. Localised cutaneous /neuropathic vasculitis, cutaneous PAN. Other skin-nerve vasculitis overlap with NSVN clinically. NSVN is without systemic involvement and it has a subacute presentation with progressive distal predominant, asymmetric multifocal and painful axonal neuropathy associated with disabling paresis. Diagnosis of probable NSVN is made in patients lacking biopsy proof but with clinical features typical of vasculitic neuropathy. Diagnosis of definite vasculitic neuropathy is made as per the[10] consensuscriteria which states that vessel wall inflammation should be accompanied by vascular damage. Five predictors of pathologically definite vasculitic neuropathy are: 1. vascular deposits of IgM, C3 or fibrinogen by direct immunoflurosence, haemosiderin deposits, asymmetric nerve fiber loss, prominent active axonal degeneration, myofiber necrosis, regeneration or infarcts in peroneus brevis muscle biopsy

Regarding mononeuritis multiplex:

Proximal and Distal Asymmetric

The presence of significant asymmetry in a patient with prominent distal weakness suggests a mononeuritis multiplex, which is defined by damage to at least two named peripheral nerves, most often not at entrapment sites.

The most common mechanism is vasculitis, inflammatory destruction of the vasa nervorum, and resultant ischemic nerve injury. The clinical course is usually acute or stuttering, with significant pain and sensory and motor deficits in discrete peripheral nerve distributions. Over time, mononeuritismultiplex may affect so many nerves that the pattern becomes symmetric, a pattern referred to as confluent mononeuritis multiplex. Even when only one nerve is involved, the conditions that predispose patients to mononeuritis multiplex should be considered if no evidence of trauma is present, the involved nerve is not susceptible to entrapment, or the injury is not at the common entrapment site (Mononeuritis multiplex may occur in isolation (nonsystemicvasculitic neuropathy) or may occur as a manifestation of eosinophilic granulomatosis with polyangiitis, granulomatosis with polyangiitis, microscopic polyangiitis, or polyarteritis nodosa. Other systemic inflammatory disorders, such asrheumatoid arthritis, Sjögren syndrome, and systemic lupus erythematosus (SLE) can predispose patients to mononeuritis multiplex. .

Other causes of multiple mononeuropathies include lymphoma, diabetes, hepatitis, or human immunodeficiency virus (HIV). Multifocal acquired demyelinating sensory and motor neuropathy (MADSAM) is a rare variant of

KEY POINTS

- Injuries to nerve roots andmixed nerves, both of whichcontain both sensory andmotorcomponents, maypresent with pain or sensorysymptoms withoutweakness.
- Chronic inflammatorydemyelinatingpolyradiculoneuropathyprogresses for more than8 weeks after symptomonset. Unlike acuteinflammatory demyelinatingpolyradiculoneuropathy, it isgenerally not associatedwith dysautonomia, weakness of cranialmuscles, or dyspnea.
- Mononeuritis multiplexaffects named nerves butnot necessarily at thecommon entrapment sites.

III. CONCLUSION:

Neuropathy can be a first manifestation of vasculitis. High index of suspicion is needed to diagnose and treat them effectively so that the morbidity is reduced.

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