(International Print/Online Journal)

SJIF IMPACT FACTOR: 4.617
PUBMED-National Library of Medicine ID-101739732

ISSN (Print): 2209-2870
ISSN (Online): 2209-2862

International Journal of Medical Science and Current Research (IJMSCR)
Available online at: www.ijmscr.com
Volume2, Issue 6, Page No: 344-348
November-December 2019

Neurological manifestations of Rare Systemic Diseases

[1]Dr. Jagruti Jain, [2]Dr. Manohar Joshi, [3]Dr. Darshankumar Chandak
[1,3]Junior Resident, [2]Associate Professor
Department of Medicine, Dr. D.Y.Patil Medical College, Navi Mumbai

***Corresponding Author:**
Dr. Manohar Joshi
Associate Professor, Department of Medicine, Dr. D.Y.Patil Medical College, Navi Mumbai

Type of Publication: A Case Report
Conflicts of Interest: Nil

ABSTRACT

Introduction: Rheumatological diseases may have a varied presentation. In the present case review, we describe three cases who presented with very similar neurological complaints but were diagnosed with three distinct rheumatological conditions.

Methodology: These three patients presented to the outpatient clinic of our department. The data presented in this article were obtained from the retrospective review of their medical records.

Results: First patient complained of progressive inability to get up from squatting position, lifting her hand, swelling in all four limbs and a blackish rash in the sun exposed areas. Anti-neutrophilic antigen panel was positive for Mi-2 and a final diagnosis of dermatomyositis was made. A 57 year old male gave history of tingling numbness, hematuria and pain abdomen with vomiting. Perinuclear antineutrophil cytoplasmic and anti-MPO antibodies were positive. Kidney biopsy showed necrotizing lesions with fibroid necrosis aiding the diagnosis of microscopic polyangitis. Second patient, a 15 year old boy gave history of left knee pain and difficulty walking, following which, he developed repetitive purposeless movements. Detailed examination revealed bilateral Kayser-Fleischer rings and exaggerated deep tendon reflexes. Low serum ceruloplasmin and raised 24 hours urine copper excretion clinched the diagnosis of Wilson's disease.

Conclusions: Accurate and timely diagnosis needs a multidisciplinary approach, so that delay in treatment can be avoided.

Keywords: Rheumatoid disorders; Nervous system disorders; Vasculitis.

INTRODUCTION

Rheumatological diseases include a wide array of disorders of the joints and soft tissues and often involve multiple organ systems. The underlying disease process of a particular rheumtological disease may be such that the meninges, brain, spinal cord, cranial and peripheral nerves, and muscle may be involved. Many of these disorders have a genetic basis, many have immunological basis and in some environmental factors play a role. In addition, neurological manifestations may be the presenting complaint of these rheumatological conditions, which may delay the diagnosis. Apart from the musculo-skeletal involvement, pulmonary and renal nvolvement are common as well. In this case review, we describe three cases that presented with very similar neurological complaints but were diagnosed with three distinct rheumatological conditions.

METHODOLOGY

The three patients described in this case series presented to the outdoor clinic of the Department of D.Y.PATIL Medical College and Hospital, Navi Mumbai. Three of these cases presented mainly with difficulty in walking and one with paresthesia. We retrospectively reviewed and collected data from the medical records of the patients. The personal identifiers of the patients were not noted to maintain confidentiality and thus informed consent of the patients was not required.

CASE DESCRIPTION

Case 1

A 64 year female old patient started complaining of difficulty in getting up from squatting position about one month age, along with difficulty in gripping of chappals. Five days later, she had difficulty in getting up from supine position and also moving from side to side on bed. She also complained of difficulty in lifting her hand above her forehead or getting food to her mouth, though she could hold a glass of water with some difficulty. Currently, she has difficulty in lifting her neck from supine position and also holding her neck in sitting position (it falls in forward direction). However, she can move her neck from side to side. After few days of developing weakness, she started complaining of swelling in all four limbs, insidious in onset, non-progressive, along with dull aching pain which increased on even slight movement or on touch and relieved on taking medications from local doctor. She had no history of involuntary movements, tingling, numbness, root pain, girdle like sensation, ptosis, diplopia, squint, facial deviation, dystrophy, hoarseness of voice, wasting of tongue muscle or bowel/bladder disturbance. On further enquiry, the patient complained of rashes in the sun exposed area for past one month, which started alongside the weakness. The rash on inspection was blackish in color, not associated with redness or itching, extending from elbow to knuckles of right hand and just around the knuckles in the left hand. The patient denied any similar episodes of weakness or rash previously. The patient attained menopause about 8 years ago. A provisional diagnosis of acute onset motor flaccid quadriplegic (proximal more than distal) with no sensory/autonomic/bowel bladder involvement along with rash was made, most probably of inflammatory etiology. On examining, the patient had normal vitals. Blackish discoloration on forehead and cheeks along the nasolabial folds was present. Similar blackish discoloration on the anterior chest wall below clavicle as well as the back upto T3 level was present ('shawl sign'). Gottron's sign (hyperpigmented rashes on bony prominences especially knuckles) was present. Examination of the superficical and deep sensory system was within normal limits and deep reflexes were absent. Air entry was decreased bilaterally in the intrascapular region. Routine haematological investigations were normal. Anti-neutrophilic antigen testing panel was positive for Mi-2 which is associated with polymyositis and dermatomyositis. Based on the clinical examination and laboratory testing, final diagnosis of dermatomyositis was made. The patient was put on oral prednisolone with a marked improvement in muscle power in three weeks, followed by low dose maintenance therapy.

Case 2

57 year old male presented with complaints of tingling numbness in the extremities with glove and stocking nature, difficulty in walking, hematuria, pain in abdomen associated with vomiting and mild grade fever. No history of cold, cough, oliguria, chest pain, breathlessness, palpitations, burning micturition or constipation was given by the patient. No major illness or chronic disease was reported by the patient. On examination, the vitals and systemic examination of respiratory, cardiovascular and abdominal system were within normal limits. Power of all four limbs was 5/5, tone was normal, deep reflexes were absent and glove and stocking anesthesia was observed. Higher functional was intact, with absent joint position. Based on the clinical presentation, polyneuropathy was suspected for which cerebrospinal fluid examination and serum protein electrophoresis was ordered. Patient's erythrocyte sedimentation rate (ESR) was 95 mm/hour and C-reactive protein was 213. Perinuclear antineutrophil cytoplasmic antibody (pANCA) was positive for the patient and Electromyography and nerve conduction studies revealed asymmetric acute motor sensory axonal poly-radiculopathy. Provisional diagnosis of rapidly progressive glomerulo-nephritis was made. While methylprednisone was started, kidney biopsy, sural nerve biopsy and anti-MPO and anti-PR3 antobodies were sent, of which MPO antibodies came positive. Urinalysis revealed 24 hour urinary protein more than 200 mg/day. No evidence of monoclonal gammopathy was seen, however, distorted gamma region was seen on protein electrophoresis. CT thorax revealed mild right sided pleural effusion with subsegmental atelectasis of the underlying lung parenchyma, with fibrotic strands involving apicoposterior segment of the left upper lobe, apical segment of right upper lobe and inferior lingual. Kidney biopsy showed necrotizing vascular lesions and segmental fibrinoid necrosis in one glomerulus which is attributable to pANCA positivity. A diagnosis of microscopic polyangitis was made and

Volume 2, Issue 6; November-December 2019; Page No.344-348

the patient was treated with intravenous methylprednisolone, followed by oral doses.

Case 3

A 15 years old boy presented with pain in left knee joint and difficulty in walking for last six months, which was treated by a local doctor with symptomatic improvement. After five months of the onset of the pain, the boy developed repetitive purposeless abnormal movements of the left upper and lower limbs, which were progressive and which eventually involved all the four limbs over the next three months. Currently the patient is non-ambulatory. After numerous referrals and misdiagnosis, the patient was brought to our institute. His father reported similar progressive abnormal movements in patient's elder brother as well. On examination, his vital signs were normal, but found to have progressive dysarthria. There was no pallor, icterus or significant lymphadenopathy. His nervous system examination revealed dystonia, exaggerated deep tendon reflexes, ankle clonus and a positive Babinski's sign. His muscle power was more than 4/5 in all the limbs. The Kayser-Fleischer ring (KF ring) was visible on both sides by the naked eye, which was confirmed by an ophthalmologist by slit lamp examination. Systemic examinations did not reveal any abnormality. Complete blood count, serum electrolytes and the renal functions were normal. The total serum bilirubin was 0.6 mg/dl, the total serum protein was 6.5 gm/dl, with raised liver enzyme levels. His coagulation profile was within normal limits. His serum ceruloplasmin was low and his 24 hours urine copper excretion was increased to 175 µg (normal 24 hours urine excretion 20 – 50 µg). His urine routine and microscopic examinations were normal. Liver biopsy could not be done as the parents refused the procedure and genetic testing for mutation analysis was not done due to financial constraints. MRI brain revealed the "Face of the miniature Panda" and also revealed hyperintensities in the thalami and pons. Based on the clinical features, the diagnosis of Wilson's disease with a neurological manifestation was made. The patient was started on oral zinc (1mg/kg/dose of elemental zinc) 8 hourly and on trihexiphenidyl to control the dystonia. Avoidance of high copper containing food items like chocolates, nuts, legumes and mushrooms was advised. His dystonia reduced in intensity after two weeks of treatment.

DISCUSSION

In this case series, we described the detailed presentation and clinical findings of three patients who presented with neurological complaints and had distinct rheumatological diagnoses (Table 1). The case presented chiefly with weakness in their extremities and presented with difficulty in walking and standing up, while the third case presented with numbness and tingling sensation. In 1866, Virchow described ochronosis as the physical manifestations of homogentisic acid deposition within connective tissue, such as cartilage, ligaments, tendons. Such patients develop clinical musculoskeletal symptoms in mid-life years, described as the ochronitic arthropathy, which includes pain in the lower back, thighs, and large joints due to degenerative changes from chronic inflammation. Cervical spinal cord involvement, as seen in our patient, is uncommon and has been previously attributed to redundancy in the ligamentum flavum, resulting in cord compression. Bullough described disc herniation as an initial presenting feature. Though end-plate changes have been noted by numerous authors, they might be difficult to interpret.

Dermatomyositis is an idiopathic inflammatory myopathy with an incidence of 9.63 per million, showing a bimodal distribution at 5 to 15 and 50 to 60 years. The most frequent presentation is insidious painless proximal symmetrical weakness over 3 to 6 months. Our patient presented with classical skin manifestations like Gottron's papules, heliotrope rash and blackish rash across the anterior chest, which aided in the diagnosis and provided leads for laboratory investigation. Patients with adult-onset dermatomyosistis tend to be at a higher risk of having an underlying cancer. A Scandinavian study concluded that up to one third of patients with dermatomyositis either have cancer at diagnosis or subsequently develop it, which in most cases is a solid tumor. Steroids are the first line treatment. However, due to the lack of sufficient number of randomized-controlled trials, no consensus has been reached regarding the dose or duration of treatment. Moreover, long-term treatment is lacking which can guide the physicians towards the most effective treatment for long-term remission. Third case in this series was diagnosed with microscopic polyangitis, san ANCA-associated vasculitis. Previously published literature has reported 55%-79% of cases

Volume 2, Issue 6; November-December 2019; Page No.344-348

having neurologic symptoms, and peripheral nervous system involvement is much more common. Peripheral nervous system involvement has a burden of significant long-term damage and life quality impairment. Polyneuropathy among patients with microscopic polyangitis show a wide range (7% to 58%). This disparity in reported rates and types of polyneuropathy in these patients might be because of the varied ability to distinguish between neuropathy due to diabetes, uremia or vitamin deficiency. Furthermore, centres with standard diagnostic algorithms and diagnostic procedures and with availability of rare work-ups might identify even low-grade polyneuropathy in some cases. Previously published studies did not find a direct association with higher mortality, although recently data suggested higher mortality in patients with microscopic polyangitis with peripheral nervous system involvement.

The final case in this series was that of Wilson's disease, which is one of the few genetic disorders that can be successfully treated with pharmacological agents. Like in our case, clinical improvement with treatment is observed in the majority of the patients. However, neurological worsening may also occur, often severe and irreversible. In many cases, this deterioration occurs soon after initiation of chelators or zinc salts. It has been hypothesized that upon treatment initiation, rapid mobilization of copper from tissue with transient elevation of blood and cerebrospinal fluid levels of toxic free copper may be responsible for the neurological deterioration. Late neurological deterioration may also occur, but that is mainly associated with poor treatment compliance adherence.

CONCLUSION

This case series describe how three patients with distinct rheumatological diseases presented with neurological complaints like difficulty walking and paresthesia. All of these patients presented to us after numerous referrals and missed diagnoses. With advances in the field of neuroimmunology, pathways by which the nervous and immune systems interact can be understood in a better manner. Accurate and timely diagnosis needs a multidisciplinary approach, so that delay in treatment can be avoided

Table.1 Summary describing the three cases in this series

Diagnosis	**Presenting complaint**	**Specific finding which clinched the diagnosis**
Dermatomyosiits	Difficulty in walking and neck holding	Blackish rash on anterior chest ('shawl sign'), Gottron's sign, Anti-neutrophilic antibody positive for Mi-2
Microscopic polyangitis	Tingling and numbness, glove and stocking anesthesia	Perinuclear antineutrophil cytoplasmic antibody and anti-MPO positive

Volume 2, Issue 6; November-December 2019; Page No.344-348

Wilson's disease	Difficulty in walking, involuntary purposeless abnormal movements	Kayser-Fleischer ring, Low ceruloplasmin, high urinary copper excretion

REFERENCES

1. Goldblatt F, O'Neill SG. Clinical aspects of autoimmune rheumat- ic diseases. Lancet. 2013;382(9894):797–808
2. Kopec K, Kusz D, Wojciechowski P, Cielinski L, Laszczyca M. Orthopaedic problems in patients affected by alkaptonuria. A case report. Ortop Traumatol Rehabil. 2007;9(2):206-214.
3. Kalevski SK, Haritonov DG, Peev NA. Alcaptonuria with lumbar disc prolapse: case study and review of the literature. Spine J. 2007;7(4):495-498.
4. Galdston M, Steele JM, Dobriner K. Alkaptonuria and ochronosis with a report of three patients and metabolic studies in two. Amer J Med. 1952 Oct;13:432-52.
5. Bullough PB, Boachie-Adjei O. Atlas of spinal diseases. 1st ed. Philadelphia: JB Lippincott; 1988. p 68-75.
6. Kahveci R, Ergu¨ngo¨r MF, Gu¨naydin A, Temiz A. Alkaptonuric patient presenting with "black" disc: a case report. Acta Orthop Traumatol Turc. 2013;47(2):134-8.
7. Bendewald MJ, Wetter DA, Li X, et al. Incidence of dermatomyositis and clinically amyopathic dermatomyositis: a population-based study in Olmsted County, Minnesota. Archives of dermatology. 2010 Jan;146(1):26-30
8. Bohan A, Peter JB. Polymyositis and dermatomyositis (first of two parts). The New England journal of medicine. 1975 Feb 13;292(7):344-7.
9. Hill CL, Zhang Y, Sigurgeirsson B, et al. Frequency of specific cancer types in dermatomyositis and polymyositis: a population-based study. Lancet 2001 Jan 13;357(9250):96-100.
10. Sassi SB, Ghorbel IB, Mizouni H, et al. Microscopic polyangiitis presenting with peripheral and central neurological manifestations. Neurol Sci 2011;32:727-729.
11. Robson J, Doll H, Suppiah R, et al. Damage in the anca-associated vasculitides: long-term data from the European vasculitis study group (EUVAS) therapeutic trials. Ann Rheum Dis. 2015;74(1):177–184
12. Suppiah R, Hadden RDM, Batra R et al. Peripheral neur- opathy in ANCA-associated vasculitis: outcomes from the European Vasculitis Study Group trials. Rheumatology 2011;50:2214 22.
13. Schirmer JH, Wright MN, Vonthein R, et al. Clinical presentation and long-term outcome of 144 patients with microscopic polyangiitis in a monocentric German cohort. Rheumatology (Oxford). 2016;55(1):71–79
14. Czlonkowska, T. Litwin, M. Karlinski, K. Dziezyc, G. Chabik, M. Czerska, D-Penicillamine versus zinc sulfate as first-line therapy for Wilson's disease, Eur. J. Neurol. 21 (2014) 599–606.
15. Kim, S.J. Chung, H.W. Shin, Trientine-induced neurological deterioration in patient
16. with Wilson's disease, J. Clin. Neurosci. 20 (2013) 1398–1401.
17. W. Maselbas, G. Chabik, A. Czlonkowska, Persistence with treatment in patients with Wilson disease, Neurol. Neurochir. Pol. 44 (2010) 260–263.

Volume 2, Issue 6; November-December 2019; Page No.344-348