

Case Report on Nitrofurantoin Induced Peripheral Neuropathy

Dr. Medidhi Adithya¹, Dr. Bomma Surya Teja², Dr. Saba Kauser³, Dr. Rana Fatima⁴

¹Junior Resident, Department of General Medicine, Prathima institute of medical sciences.

²Junior Resident, Department of General Medicine, Prathima institute of medical sciences.

³PHARM. D, Prathima institute of Medical Sciences

⁴MD, DNB, Nephrology, Professor, Prathima Institute of Medical Sciences

Abstract: *Background:* It is the synthetic antimicrobial and its antibacterial spectrum is broad and is particularly effective against *Escherichia coli* and *Klebsiella* and *Enterobacter* species, hence its use for the treatment of urinary tract infections. Nitrofurantoin neuropathy has a characteristic morphology as demonstrated in the case. Skin biopsy helps to confirm the diagnosis and plays an important role in the management of these patients. *Case Report:* A 45 Years female patient was admitted with complaints of difficulty in walking, difficulty in eating, difficulty of getting up from squatting position, slurring of speech since 15 days. *Discussion:* Punch biopsies were performed with a 3 - mm disposable circular punch) after the injection of lidocaine hydrochloride, 2%, under an aseptic technique. The morphology of nerve fibers was observed. *Conclusion:* Skin biopsy helps to confirm the diagnosis and plays an important role in the management of patients. Nitrofurantoin neuropathy has a characteristic morphology as demonstrated in the case. Skin biopsy helps to confirm the diagnosis and plays an important role in the management.

Keywords: Nitrofurantoin neuropathy, skin biopsy, urinary tract infections, nerve fibers morphology, difficulty in walking

1. Background

Nitrofurantoin was first introduced in 1952. It is the synthetic antimicrobial and its antibacterial spectrum is broad and is particularly effective against *Escherichia coli* and *Klebsiella* and *Enterobacter* species, hence its use for the treatment of urinary tract infections. Nitrofurantoin is excreted and concentrated in the urine. In the presence of impaired renal function, the urine levels fall below the therapeutic range while the serum levels increase into the toxic range. Thus, its efficacy is limited in the setting of renal impairment, with an associated greater risk of toxic effects and adverse reactions. Nitrofurantoin is an overall relatively safe drug. Primary adverse effects are predominantly gastrointestinal tract symptoms with nausea, emesis, and anorexia. Peripheral neuropathy is a less - recognized adverse reaction. The first case of peripheral neuropathy attributable to nitrofurantoin was reported by de Fine Olivarius in 1956. Since then, many more cases and reviews have been published, although these were mainly reported in the 1960s through 1980s. Typically, nitrofurantoin neuropathy manifests as length - dependent sensorimotor polyneuropathy. The glove and stocking pattern of sensory symptoms were accompanied by varying degrees of motor weakness in the same pattern of distribution, with muscle atrophy of the intrinsic muscles in severe cases. Only 2 cases with perineum disturbance have been reported. Most patients had moderate to severe abnormal sensory and motor conduction on NCS and axonal degeneration on sural nerve biopsy

Skin biopsy is a useful investigation to confirm the diagnosis of small - fiber neuropathy. Length - dependent small - fiber neuropathy demonstrates the typical proximal - distal gradient of INFD density, confirming the length - dependent loss of cutaneous innervation. Conversely, ganglionopathy or non-length - dependent small - fiber neuropathy in patients with

hyperesthesias reveals a distinct pattern of epidermal denervation. The morphologic changes of clustering of swelling of nerve fibers in the papillary dermis are most unusual. This morphologic feature is not unique to nitrofurantoin and has also been observed in ganglionopathy¹⁰ and small - fiber neuropathy secondary to Sjögren syndrome. The mechanisms for the predilection for the nerve fibers, in particular small - caliber fibers, in the papillary dermis are unknown. Nitrofurantoin interferes with pyruvate oxidation by competing with thiamine pyrophosphate. However, neurotoxic neuropathies from other causes (eg, vitamin B6 excess) are not associated with such nerve fiber changes on skin biopsy.

Nitrofurantoin neuropathy may present with a wide spectrum of manifestations, more commonly large - fiber sensorimotor neuropathy and small - fiber neuropathy. Non-length - dependent neuropathy/ganglionopathy is rarely described in neurotoxic neuropathy. Nitrofurantoin neuropathy has a characteristic morphology as demonstrated in these case. Skin biopsy helps to confirm the diagnosis and plays an important role in the management of these patients.

2. Case Report

A 45 Years female patient was admitted with complaints of difficulty in walking, difficulty in eating, difficulty of getting up from squatting position, slurring of speech since 15 days. Her medical history includes Hypertension since 4 years on amlodipine 10 mg, r since 3 years on Rosuvastatin Aspirin and clopidogrel 20 mg, chronic kidney disease since 6 months on dialysis from one month. Four months back following which she was on Nitrofurantoin 100 mg per oral once a day for urinary tract infection for 6 weeks into therapy. On physical examination symptoms worsened sunburn like sensation which were pronounced in thighs, shoulders, necks

Volume 13 Issue 5, May 2024

Fully Refereed | Open Access | Double Blind Peer Reviewed Journal

www.ijsr.net

and generalised dysesthesias with prickly heat her symptoms persisted despite discontinuation of Nitrofurantoin. Neurological examination revealed preserved muscle strength & tendon reflexes in all extremities. Results from extensive investigations including Haematological profile, Thyroid function test, serum electrolytes were all unremarkable. Blood urea - 1115.6 mg/L (16 to 38 mg/L), serum creatinine - 6.10mg/dL (1.20 mg/dL). A Skin biopsy shows a thin epidermis with orthokeratosis and intact basal layer. The underlying dermis shows fibrosis and collagenisation with focal perivascular lymphocytic infiltrate. The subcutis is unremarkable. A skin biopsy revealed INFD that was within the normal limits. There were morphologic abnormalities, with clustered terminal nerve fiber swellings and collagenisation of the dermis with mild inflammatory infiltrate.

3. Discussion

Punch biopsies were performed with a 3 - mm disposable circular punch (Acupunch; Acuderm) after the injection of lidocaine hydrochloride, 2%, under an aseptic technique. Biopsy specimens were obtained from the lateral aspect of the following sites: the upper thigh (10 cm below the greater trochanter), the distal thigh (10 cm above the patella), and at the ankle (10 cm above the lateral malleolus). Specimens were fixed in Zamboni solution, and free - floating 50 - µm sections were immune stained with the panaxonal marker protein gene product 9.5 (ubiquitin hydrolase; ABD Serotec). For each biopsy, at least 3 sections were read. The epidermal fibers were identified, counted, and documented as the number of intraepidermal nerve fibers per millimeter of epidermis. The morphology of nerve fibers was observed. Technical details have previously been described.

4. Conclusion

Nitrofurantoin neuropathy has a characteristic morphology as demonstrated in the case. Skin biopsy helps to confirm the diagnosis and plays an important role in the management of patients. Nitrofurantoin neuropathy has a characteristic morphology as demonstrated in the case. Skin biopsy helps to confirm the diagnosis and plays an important role in the management

Health care professionals need to be aware that using nitrofurantoin might have adverse effects, such as peripheral neuropathy

References

- [1] McCarthy BG, Hsieh ST, Stocks A, et al. Cutaneous innervation in sensory neuropathies: evaluation by skin biopsy. *Neurology*.1995; 45 (10): 1848 - 18557477980
- [2] Morris JS. Nitrofurantoin and peripheral neuropathy with megaloblastic anaemia. *J Neurol Neurosurg Psychiatry*.1966; 29 (3): 224 - 2284287116
- [3] Sachs J, Geer T, Noell P, Kunin CM. Effect of renal function on urinary recovery of orally administered nitrofurantoin. *N Engl J Med*.1968; 278 (19): 1032 - 10355644963
- [4] Olivarius B. Polyneuropathy during treatment with nitrofuraxuin. *Ugeskr Laeger*.1956; 118: 753 - 755de Fine14274088
- [5] Yiannikas C, Pollard JD, McLeod JG. Nitrofurantoin neuropathy. *Aust N Z J Med*.1981; 11 (4): 400 - 4056272676
- [6] Toole JF, Parrish ML. Nitrofurantoin polyneuropathy. *Neurology*.1973; 23 (5): 554 - 5594349239
- [7] Kammire LD, Donofrio PD. Nitrofurantoin neuropathy: a forgotten adverse effect. *Obstet Gynecol*.2007; 110 (2, pt 2): 510 - 51217666646
- [8] Mendell JR, Sahenk Z. Clinical practice: painful sensory neuropathy. *N Engl J Med*.2003; 348 (13): 1243 - 125512660389
- [9] Gorson KC, Herrmann DN, Thiagarajan R, et al. Non - length dependent small fibre neuropathy/ganglionopathy. *J Neurol Neurosurg Psychiatry*.2008; 79 (2): 163 - 16917911181
- [10] Lauria G, Sghirlanzoni A, Lombardi R, Pareyson D. Epidermal nerve fiber density in sensory ganglionopathies: clinical and neurophysiologic correlations. *Muscle Nerve*.2001; 24 (8): 1034 - 103911439378
- [11] Chai J, Herrmann DN, Stanton M, Barbano RL, Logigian EL. Painful small - fiber neuropathy in Sjogren syndrome. *Neurology*.2005; 65 (6): 925 - 92716186536
- [12] Argov Z, Mastaglia FL. Drug - induced peripheral neuropathies. *Br Med J*.1979; 1 (6164): 663 - 666219931
- [13] Lauria G, Morbin M, Lombardi R, et al. Axonal swellings predict the degeneration of epidermal nerve fibers in painful neuropathies. *Neurology*.2003; 61 (5): 631 - 63612963753
- [14] Dabby R, Gilad R, Sadeh M, Lampl Y, Waternberg N. Acute steroid responsive small - fiber sensory neuropathy: a new entity? *J Peripher Nerv Syst*.2006; 11 (1): 47 - 5216519781
- [15] Appleyard S, Saraswati R, Gorard DA. Autoimmune hepatitis triggered by nitrofurantoin: a case series. *J Med Case Reports*.2010; 4: 31120863377