ETHIOPIAN INTERNATIONAL JOURNAL OF MULTIDISCIPLINARY RESEARCH

eISSN: 2349-5715 pISSN: 2349-5707

Volume: 11, Issue 01, Jan-2024 SJIF 2019: 4.702 2020: 4.737 2021: 5.071 2022: 4.919 2023: 6.980

MAJOR TOXIC POLYNEUROPATHIES IN CLINICAL PRACTICE

Sotvoldiyev M.M

Department of Neurology, ASMI

Abstract: Polyneuropathies are diseases of the peripheral nervous system with lesions of motor, sensory or autonomic fibers which are encountered by attending physicians of almost all specialties in outpatient and clinical settings. To date, more than 100 different causes of polyneuropathies have been identified. Metabolic and toxic polyneuropathies are the most common in the group of secondary polyneuropathies. Diabetic, alcoholic, uremic, and drug-induced polyneuropathies take the leading place among these diseases. The main forms of diabetic polyneuropathy are presented. The main clinical form is distal symmetrical polyneuropathy. Clinical symptoms depend on the type of fibers involved in the pathological process - thin or thick. There is an assessment scale in points to determine the severity of diabetic polyneuropathy, which helps in clarifying the diagnosis and prognosis of the disease. The next most frequent among metabolic polyneuropathies is uremic polyneuropathy as the most frequent complication in patients suffering from chronic renal insufficiency. Risk factors of uremic polyneuropathy development, clinical picture, the course of the disease are described. Within the framework of toxic polyneuropathies, the main place is given to alcoholic polyneuropathies, chemotherapy-induced, and drug-induced. For each of these categories, clinical forms and pathophysiology of development are described. For all polyneuropathies, the main diagnostic aspects are presented. The main therapeutic approaches are shown. A separate place is given to the use of alpha-lipoic acid.

Key words: Metabolic and toxic polyneuropathies, clinical picture, risk factors, therapeutic approaches.

Polyneuropathies (PNP) are a group diseases manifested by a wide range of symptoms that are encountered by attending physicians of almost all specialties on an outpatient basis and in clinics.

These are disorders of the peripheral nervous system, in which motor, sensory and autonomic fibers are affected. Although the clinical manifestations are generally similar, the most common are distal symmetrical sensory-motor manifestations, causes very greatly and require rapid and accurate diagnosis to begin the appropriate therapeutic measures [1]. It is difficult to establish the overall prevalence of peripheral neuropathy. More than 100 different reasons ASPs have been identified, but diabetes mellitus (DM) is the most important risk factor [2]. Have been developed principles to distinguish between these different causes [5]. Differentiation between acquired and hereditary, chronic and acute, axonal and demyelinating variants of PSP helps the diagnostic process in clinical practice [7]. While in the United States there are no screening studies carried out in Sicily and Bombay showed that the prevalence of peripheral neuropathy was 7 and 2.4%, respectively [6]. The prevalence of PSP in various studies using standard protocols ranges from 0.8 to 32.5 per 1,000 (0.1–3.3%) individuals all ages [5]. When only the elderly are studied people, the prevalence of PSP ranges from 18.8 to 200 per 1,000 people (1.9–20%) [1]. There are bigdifferences in the prevalence rates of PSP reported to be associated with age of subjects, study area, and study protocol. Tests, which report a low prevalence of PSP (0.8–2.5 per 1,000), were conducted in African countries and the Middle East such as Nigeria and Saudi Arabia Arabia [4]. In these studies, only 4–11%population were over 50 years of age. On the contrary, in European countries such as Spain [2], where PSP affects 7.3 per 1,000 people, and in Albania [6], where PSP affects 32.5 per 1,000 people, about 30% are people over 50 years old. The development of PSP is associated with various diseases

eISSN: 2349-5715 pISSN: 2349-5707
Volume: 11, Issue 01, Jan-2024 SJIF 2019: 4.702 2020: 4.737 2021: 5.071 2022: 4.919 2023: 6.980

and factors. Because PSP is likely to be a multifactorial disease, it is not entirely appropriate to attribute its development to just one factor. These factors should be considered as components of the cause, and not as one sufficient reason. For example, not everyone patients with diabetes or alcoholism will develop PNPs, therefore multiple (known and unknown) component causes likely contribute to the development of the disease [9]. In clinical practice it is often one factor or disease, such as diabetes or alcohol abuse, is considered to be the underlying (sufficient) cause of PSP in humansNeuropathies are one of the most common manifestations of diabetes. Diabetic neuropathy (DN) leads to significant disability and morbidity, causes severe pain, loss of mobility and increases the risk of non-healing ulcers and amputations [2]. DM causes the development of several types of neuropathy [2], the most common is distal symmetric sensorimotor polyneuropathy. Researchers found that the prevalence distal symmetrical PSP (DSPN) is detected in 10–34% of patients with type 1 diabetes and in 8–25% with type 2 diabetes type [6]. It should be noted that the prevalence The DAI, including patients with asymptomatic disease, is likely even higher: 54% of patients with type 1 diabetes and 45% with type 2 diabetes [3]. Prediabetes is also common etiology of DSPN [2]. Severity of neuropathy is interconnected with the duration of the disease, age patient, metabolic control, the presence of arterial hypertension and hyperlipidemia, as well as smoking, alcohol abuse. At the onset of the disease, small unmyelinated fibers are affected, which leads to loss of pain and temperature sensitivity and the appearance of neuropathic pain [2]. Approximately 30–50% of patients with DN experience neuropathic pain [3], which most often manifests itself as spontaneous burning pain in the feet. Patients experience symptoms of large lesions sensory fibers, including loss of general sensation and imbalance due to loss of proprioceptive sensitivity [8]. As diabetic PSP progresses, the process involves large and small nerve fibers with distribution symptoms proximally according to the “sock” type. Speed progression of the disease depends on the duration of hyperglycemia, age, the presence of hypertension and hyperlipidemia [2]. Signs of vegetative neuropathy in the form of hypohidrosis, dry skin, vasomotor disorders and decreased temperature of the feet. Paresis usually mildly expressed, but in some cases distal sensory neuropathy is combined with proximal weakness and atrophy . The main clinical symptoms depend on the type of fibers involved in the pathological process - thin and/or thick. Diabetic PSP is diagnosed based on the presence of distal symmetrical sensory symptoms and a targeted neurological examination confirming the presence of sensory, motor and reflex changes in the distal symmetrical type [6]. Due to the fact that the earliest and most characteristic manifestation of diabetic PSP is a decrease in the threshold of vibration sensitivity, it is advisable to evaluate it annually using biotensiometer or graduated tuning fork with a frequency of 128 Hz. Study of tactile sensitivity carried out using hair monofilaments weighing. 10 g, while avoiding areas of hyperkeratosis and ulceration. In addition, it is necessary to carry out a complete neurological examination, lectroneuromyography (ENMG), laboratory tests to exclude other treatable causes of neuropathy, such as kidney failure, vitamin deficiency B12 and low thyroid function [1]. The severity of neuropathy can be measured in points, which helps in clarifying the diagnosis and prognosis diseases [2].

Alcohol is the next most common cause causing the development of PSP [4]. Neuropathy caused by chronic alcohol abuse, maybe associated with damage to large and/or small (including autonomic) nerve fibers and is quite heterogeneous according to its clinicopathological characteristics [6]. The earliest known description of neurological symptoms associated with alcohol intake was noted Letts in 1787, who described paralysis that was more pronounced in the legs than in the arms [7]. A. Mygland studied the frequency of alcohol-related PSP in the Norwegian population [8]. Based on the base data from 192 PSP diagnoses made in the country Between June 1994 and October 1999, the prevalence of alcohol-related PSP was 12.2 per 100,000, which is 10% of all PNP in the region. A

eISSN: 2349-5715 pISSN: 2349-5707
Volume: 11, Issue 01, Jan-2024 SJIF 2019: 4.702 2020: 4.737 2021: 5.071 2022: 4.919 2023: 6.980

study conducted in Taiwan by K. Linc et al. to study the etiology of 520 cases in 8.7% of this group population revealed alcohol-induced neuropathy [59]. J. Verghese et al. studied the causes of PSP in elderly people over 65 (n = 402) [6]. Alcohol-related ADL represents a decreasing proportion cases with age, since it was detected in 6.1% persons aged 65–75 years, in 1.4% of persons aged 75–84 years and none of those aged 85 years or older. According to Russian studies, latent asymptomatic forms of PSP are found in 97–100% of patients alcoholism [6]. Several risk factors are associated with the development of alcohol-related PSP [4], but it is unclear which one plays a role main role in its development [5]. Alcoholic PUP is more common more common in frequent drinkers and chronic drinkers than in occasional drinkers [16]. G. Vittadini et al. (n = 296) was Duration of alcohol abuse has been found to be one of the most important risk factors peripheral PSP, showing that subjective symptoms developed after a relatively short duration of abuse (1–5 years), but were severe PSP – after more than 10 years of alcohol abuse [15]. Alcoholic PSP is more common in women compared to men . Family history of alcohol abuse may be a factor risk of developing alcoholic PSP. Thus, A. Ammendola et al. have shown that a large proportion of those who abuse alcoholic drinkers and those with PSP had a family history of alcoholism than those without PSP [10]. Connection between chronic liver dysfunction and neuropathy was noted by several authors [11], but other works did not find any significant association between liver dysfunction and PSP [12]. A risk factor for the development of alcoholic PSP is considered malnutrition. The available literature indicates that alcoholic PSP can occur in the absence of nutritional deficiencies and that neither the prevalence nor severity of alcohol-related PSP is associated with nutritional status [56, 73]. Other publications attribute a certain role in the development of alcoholic PSP to thiamine deficiency [14]. The main pathogenetic mechanisms for the development of alcoholic PSP are considered to be direct toxicity.The effect of ethanol and its metabolites and deficiency of B vitamins associated with malnutrition and/or malabsorption disorders (malabsorption syndrome). Taking into account the main pathophysiological mechanism, toxic alcoholic ANP is isolated (result direct effects of toxic metabolites of alcohol), thiamine-deficient alcoholic ANP and mixed form [14]. For toxic (actually alcoholic) ANP characterized mainly by damage to thin fibers. Chronic gradual progression is noted [9]. The lower extremities are almost always affected to a greater extent than the upper ones, distally. Usually, patients experience selective loss of pain or temperature sensitivity, including paresthesia, numbness [13]. Toxic PSP begins with painful, burning pain or paresthesia in the feet and legs in the absence of paresis and normal tendon reflexes [4]. As it progresses, there is a decrease or loss of Achilles reflexes, approximately in half of the cases the knees weaken and fall out reflexes and even less often – tendon reflexes from the upper extremities. Over a sufficiently long period. The disease is accompanied by weakness and atrophy of the proximal parts of the legs and muscles of the hands. Sensitive disorders are often combined with autonomic-vascular changes [13]. Thiamine-deficient PSP is characterized by acute or subacute development of neurological symptoms (within a month), but long-term progression is also possible (more than a year). Lower extremities are affected in almost 100% of cases, and the upper limbs more than 50%. Initial manifestations may be not only numbness of the distal legs, but also their weakness. Movement disorders often dominate above sensory and are represented by peripheral inferior paraparesis or tetraparesis. In the thiamine-dependent form of alcoholic PSP not only superficial, but also deep sensitivity is impaired, manifested by sensitive syndrome ataxia. Autonomic disorders are often absent or mildly expressed [14]. A mixed form of alcoholic PSP develops in cases where comorbid nutritional deficiencies substances in the context of alcoholic PNP may increase the risk of its development or PSP associated with thiamine deficiency is often superimposed on PSP caused by the toxic effects of alcohol or its metabolites, as well as characterized by a combination of motor and sensory disorders

eISSN: 2349-5715 pISSN: 2349-5707

Volume: 11, Issue 01, Jan-2024 SJIF 2019: 4.702 2020: 4.737 2021: 5.071 2022: 4.919 2023: 6.980

[15]. So the most common types metabolic and toxic neuropathies - mixed (both motor and sensory), symmetrical, distal and predominantly sensory polyneuropathy. Diabetes, prediabetes, alcohol consumption, B12 deficiency, hereditary conditions, chemotherapy, chronic kidney disease and paraproteinemia are the most common causes of distal symmetrical polyneuropathy. However, even after appropriate testing cause of distal symmetrical polyneuropathy is unknown (idiopathic). Clinical history and examination are the most important components of the PNP assessment. Further laboratory tests are necessary in the presence of an atypical clinical picture and course diseases. Electrodiagnostic testing plays an important role in the characterization of neuropathies. Metabolic and toxic ANPs are associated with a significant impact on patients' quality of life. It is one of the most important indicators. The most significant factors influencing on the quality of life of these patients are identified complications that progress during the course of the disease. It is now widely accepted that the goals of therappatients with chronic diseases are in improving not only survival, but also quality life.

Literature:

1.Kieseier B.C., Hartung H.P. Progress in Recognizing and Treating Polyneuropathy. Dtsch Arztebl Int. 2018;115(6):81–82. https://doi.org/ 10.3238/arztebl.2018.0081.

2. Grantz M., Huan M.C. Unusual peripheral neuropathies. Part I: extrinsic causes. Semin Neurol. 2010;30(4):387–395. https://doi. org/10.1055/s-0030-1267282.

3. Grantz M. Unusual peripheral neuropathies. Part II: intrinsic reactive causes. Semin Neurol. 2010;30(4):396–404. https://doi. org/10.1055/s-0030-1267283.

4. Grantz M. Unusual peripheral neuropathies. Part III: intrinsic inherited causes. Semin Neurol. 2010;30(4):405–415. https://doi. org/10.1055/s-0030-1267284.

5. Burns T.M., Mauermann M.L. The evaluation of polyneuropathies. Neurology. 2011;76(7 Suppl.):6–13. https://doi.org/10.1212/ WNL.0b013e31820c3622.

6. England J.D., Gronseth G.S., Franklin G., Carter G.T., Kinsella L.J., Cohe J.A. et al. Practice Parameter: evaluation of distal symmetric polyneuropathy: role of autonomic testing, nerve biopsy, and skin biopsy (an evidencebased review). Report of the American Academy of Neurology, American Association of Neuromuscular and Electrodiagnostic Medicine, and American Academy of Physical Medicine and Rehabilitation. Neurology. 2009;72(2):177–184. https://doi.org/10.1212/01. wnl.0000336345.70511.0f.

7. Hanewinckel R., van Oijen M., Ikram M.A., van Doorn P.A. The epidemiology and risk factors of chronic polyneuropathy. Eur J Epidemiol. 2016;31(1):5–20. https://doi.org/10.1007/s10654-015-0094-6.

8. Bharucha N.E., Bharucha A.E., Bharucha E.P. Prevalence of peripheral neuropathy in the Parsi community of Bombay. Neurology. 1991;41(8):1315–1317. https://doi.org/10.1212/wnl.41.8.1315.

9. Savettieri G., Rocca W.A., Salemi G., Meneghini F., Grigoletto F., Morgante L. et al. Prevalence of diabetic neuropathy with somatic symptoms: a door-to-door survey in two Sicilian municipalities. Sicilian Neuro-Epidemiologic Study (SNES) Group. Neurology. 1993;43(6):1115– 1120. https://doi.org/10.1212/wnl.43.6.1115. 10. Cruz M.E., Schoenberg B.S., Ruales J., Barberis P., Proano J., Bossano F. et al. Pilot study to detect neurologic disease in Ecuador among a population

eISSN: 2349-5715 pISSN: 2349-5707

Volume: 11, Issue 01, Jan-2024 SJIF 2019: 4.702 2020: 4.737 2021: 5.071 2022: 4.919 2023: 6.980

with a high prevalence of endemic goiter. Neuroepidemiology. 1985;4(2):108–116. https://doi.org/10.1159/000110221.

11. Osuntokun B.O., Adeuja A.O., Schoenberg B.S., Bademosi O., Nottidge V.A., Olumide A.O. et al. Neurological disorders in Nigerian Africans: a community-based study. Acta Neurol Scand. 1987;75(1):13–21. https:// doi.org/10.1111/j.1600-0404.1987.tb07883.x.

12. Cruz Gutierrez-del-Olmo M., Schoenberg B.S., Portera-Sanchez A. Prevalence of neurological diseases in Madrid, Spain. Neuroepidemiology. 1989;8(1):43–47. https://doi.org/10.1159/000110164.

13. Longe A.C., Osuntokun B.O. Prevalence of neurological disorders in Udo, a rural community in southern Nigeria. Trop Geogr Med. 1989;41(1):36– 40. Available at: https://pubmed.ncbi.nlm.nih.gov/2763344.

14. Al Rajeh S., Bademosi O., Ismail H., Awada A., Dawodu A., Al-Freihi H. et al. A community survey of neurological disorders in Saudi Arabia: the Thugbah study. Neuroepidemiology. 1993;12(3):164–178. https://doi.org/ 10.1159/000110316.

15. Kandil M.R., Darwish E.S., Khedr E.M., Sabry M.M., Abdulah M.A. A community-based epidemiological study of peripheral neuropathies in Assiut, Egypt. Neurol Res. 2012;34(10):960–966. https://doi.org/ 10.1179/1743132812Y.0000000099.

16. Kruja J., Beghi E., Zerbi D., Dobi D., Kuqo A., Zekja I. et al. High prevalence of major neurological disorders in two Albanian communities: results of a door-to-door survey. Neuroepidemiology. 2012;38(3):138–147. https:// doi.org/10.1159/000336348.