ELSEVIER

Blood 142 (2023) 529–530

The 65th ASH Annual Meeting Abstracts

ORAL ABSTRACTS

652.MULTIPLE MYELOMA: CLINICAL AND EPIDEMIOLOGICAL

Prevalence of Peripheral Neuropathy (PN) Among Patients with Asymptomatic Monoclonal Gammopathies: A Clinical & Electrophysiological Study

Panagiotis Zis[1,2], Rodanthi Syrigou, MD[3], Stella Fanouraki[2], Maria Gavriatopoulou, MD PhD[3], Despina Fotiou, MD PhD[3], Foteini Theodorakakou, MD[3], Vasiliki Spiliopoulou, MD[3], Maria Roussou, MD[3], Ioannis Ntanasis-Stathopoulos, MD PhD[3], Panagiotis Malandrakis, MD[3], Evangelos Eleutherakis-Papaiakovou, MD[4], Magdalini Migkou, MD PhD[3], Evangelos Terpos, MDPhD[4], Meletios A. Dimopoulos, MD PhD[3], Efstathios Kastritis, MD[3]

[1] Medical School, University of Cyprus, Nicosia, Cyprus
[2] Second Department of Neurology, Attikon University Hospital, National and Kapodistrian University of Athens, School of Medicine, Haidari, Greece
[3] Department of Clinical Therapeutics, National and Kapodistrian University of Athens, School of Medicine, Athens, Greece
[4] Department of Clinical Therapeutics, National and Kapodistrian University of Athens, School of Medicine, Athens, Greece

Introduction: Asymptomatic monoclonal gammopathies (MGUS, SMM or aWM) are common among adults >50y. Peripheral neuropathy (PN) refers to any disorder of the peripheral nervous system including mononeuropathies, and symmetrical or asymmetrical polyneuropathy. PN is also common among individuals >50y. Common risk factors include diabetes, vitamin deficiencies, alcohol, renal insufficiency, hypothyroidism, autoimmune diseases and exposure to neurotoxic medication. Epidemiological studies have shown an association between monoclonal gammopathies and PN but a mechanistic link has been established only for some (anti-MAG IgM-related PN, amyloidosis, POEMS syndrome etc). However, the true prevalence of PN among patients (pts) with monoclonal gammopathies is unknown and remains challenging to associate monoclonal gammopathy with PN. The aim of our study is to establish the prevalence of PN in a large cohort of pts with asymptomatic monoclonal gammopathy and identify potential determinants.
Methods: This is an ongoing prospective, non-invasive study aiming to screen ~1500 pts with asymptomatic monoclonal gammopathies for PN. Pts under regular follow-up at the Department of Therapeutics, University of Athens, Greece are screened for neuropathic symptoms using the Michigan Neuropathy Screening Instrument (MNSI), a validated screening tool for the presence of PN that consists of 15 yes/no items. A cut off $\geq$ 4 has been proposed as a screening cut off in diabetic PN. All pts scoring $\geq$4 on MNSI and pts scoring <4 but without risk factors for PN were assessed clinically and electrophysiologically (EDX) with standard nerve conduction studies (NCS), sympathetic skin response (SSR) test and - if needed - electromyography (EMG) by a specialist. NCS protocol includes assessment of the median nerve (motor and sensory), superficial radial nerve (sensory), tibial nerve (motor) and sural nerve (sensory) conduction studies. Axonal PN was diagnosed when the sural to radial ratio (SRAR) is below 0.25 and/or the sural nerve action potential is below 6μV, demyelinating PN if the EAN/PNS criteria for demyelination are fulfilled and sympathetic dysfunction when the SSR amplitude was <500 uV.
Results: As of to date, 320 pts (42.8% males, median 67y) with asymptomatic monoclonal gammopathy have been screened; 64.3% had a diagnosis of MGUS (72.3% IgG, 14.1% IgA, 6.3% IgM, 7.3% light chain only), 23.9% had SMM and 11.8% had aWM. Among enrolled pts, 217 (68%) had no common risk factors for PN and 82 pts (25.6%) had an MNSI score $\geq$4; the commonest symptoms were cramps (48.4%), weakness (26.9%) and pain when walking (26.3%). Among pts without risk factors for PN, 42 (19.4%) had an MNSI score $\geq$ 4 and the commonest symptoms were cramps (44.7%), pain when walking (22.1%) and weakness (21.7%) (Table 1). There was no difference in the prevalence of MNSI score $\geq$4 among pts with different paraprotein types.
To date, 105 pts (41.9% males, median 66y) had EDX evaluation, of which 77 (73%) had no common risk factors for PN. Among the EDX evaluated pts, 23 (21.9%) had large fiber PN, 42 (40%) had sudomotor dysfunction and 53 (50.5%) had large fiber PN and/or sudomotor dysfunction. Among the cohort of pts without risk factors for PN, 13 (16.9%) had large fiber PN, 25 (32.5%) had sudomotor dysfunction and 34 (44.2%) had large fiber PN and/or sudomotor dysfunction. Nineteen pts that went through EDX were asymptomatic (MNSI=0), of those 4 (21.1%) had large fiber PN, 4 (21.1%) had sudomotor dysfunction and 7 (33.3%) had large fiber PN and/or sudomotor dysfunction. Only one patient, without other risk factors, had a demyelinating neuropathy while all other pts had a length-dependent axonal sensory or sensorimotor neuropathy. Pts with large fiber PN were older (73.7$\pm$11.4 vs 63$\pm$9.4, p<0.001) but no significant differences were found regarding sex, or paraprotein or light

chain type. Pts with sudomotor dysfunction were more likely to have a non-IgM monoclonal gammopathy (90.2% vs 72.6 %, p=0.029).
Conclusion: Peripheral neuropathy is common in pts with monocloncal gammopathies affecting ~20% of those without any other risk factors for PN. Although most pts with PN describe mild symptoms, both large fiber PN and sudomotor dysfunction may remain completely asymptomatic. This data provides a new insight into the prevalence of PN in pts with monoclonal gammopathies with implications for future research. The study is ongoing and updated results will be presented.

Disclosures Gavriatopoulou: *Amgen:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Janssen:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Takeda:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *GSK:* Honoraria; *X4 Pharmaceuticals:* Research Funding; *Karyopharm:* Honoraria, Research Funding; *Celgene/Genesis:* Honoraria; *Sanofi:* Honoraria. **Migkou:** *Integris Pharma:* Honoraria; *Glaxo Smith Klein:* Honoraria; *Janssen-Cilag:* Honoraria. **Terpos:** *Takeda:* Honoraria, Other: Travel expenses, Research Funding; *Sanofi:* Honoraria, Other: Travel expenses, Research Funding; *Pfizer:* Honoraria; *ASTRA/Zeneca:* Honoraria, Other: Travel Expenses; *Amgen:* Honoraria, Other: Travel Expenses, Research Funding; *BMS:* Honoraria; *Menarini/Stemline:* Honoraria; *EUSA Pharma:* Honoraria, Other: Travel expenses; *Janssen:* Honoraria, Research Funding; *GSK:* Honoraria, Research Funding. **Dimopoulos:** *Regeneron:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Menarini:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Janssen:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *GlaxoSmithKline:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *BeiGene Inc:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Bristol Myers Squibb:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Amgen:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *AbbVie:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Sanofi:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Takeda:* Honoraria, Membership on an entity's Board of Directors or advisory committees. **Kastritis:** *GSK:* Honoraria, Research Funding; *Janssen:* Honoraria, Research Funding; *Pfizer:* Honoraria, Research Funding; *Sanofi:* Honoraria.

https://doi.org/10.1182/blood-2023-180673