Editorial

Progress in Recognizing and Treating Polyneuropathy

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Editorial to accompany the articles:

“Polyneuropathies—etiology, diagnosis, and treatment options” by Claudia Sommer et al.

and

„Hereditary neuropathies: Clinical presentation and genetic panel diagnosis“ by Katja Eggermann et al.

in this issue of *Deutsches Ärzteblatt International*

Polyneuropathies represent a common group of diseases exhibiting a wide variety of symptoms that are encountered by treating physicians across virtually all specialties in hospitals and practices. They are disorders of the peripheral nervous system that affect—either in equal measure or to varying degrees—motor, sensory, and vegetative fibers. Although clinical presentations are often similar, i.e., distal symmetric sensorimotor symptoms, the causes vary to a considerable extent and require prompt and rigorous diagnosis in order to initiate appropriate treatment measures (1).

Progress in recent years both in our understanding of underlying pathophysiological links and in the field of diagnostic and therapeutic options has made it possible to improve classification of the clinically heterogeneous spectrum of polyneuropathy symptoms. Therefore, it is only in keeping with the times that two review articles on this topic are included in this issue of *Deutsches Ärzteblatt International* (2, 3).

Clinical pathway for the diagnosis of polyneuropathies

In the first article, Sommer et al. describe the current state of knowledge on acquired polyneuropathies based on a literature search of the last 10 years (2). As part of this, they define a clinical pathway designed to enable the most stringent and efficient diagnosis possible in routine practice. From a health economic perspective, this is both useful and welcome.

Diabetic and alcohol-induced polyneuropathies in particular are often seen in Germany and require interdisciplinary understanding and intervention. The approach proposed by Sommer et al. appears highly expedient.

However, the situation becomes more complex when dealing with rarer forms, particularly immune-mediated polyneuropathies. It is precisely for this subtype that the range of treatments—based on the results of various clinical studies—has been expanded in recent years (4). This is important, since it is inflammatory neuropathies in particular that, while less prevalent, generate higher costs for the health and welfare systems (5). Therefore, their correct identification in clinical routine is relevant:

- Acute Guillain-Barré syndrome requires rapid diagnosis in order to permit prompt therapeutic intervention, particularly to prevent a life-threatening course and improve prognosis (6).

- The chronic forms of immune-mediated polyneuropathy, on the other hand, require correct diagnosis and classification in order to ensure that the most effective treatment for the patient can be selected from a multitude of possible options (7).

Novel methods for the detection of hereditary neuropathies

Hereditary diseases have experienced a form of renaissance in recent years due to the fact that they can be more readily detected thanks to new methods. Technological advances in biomedicine are reflected in particular in the ability to determine a large number of genes, e.g., by means of next-generation sequencing, relatively inexpensively. It will become ever easier in the near future to sequence thousands of genes in one test.

This methodological advance also implies greater complexity in medical routine: It will become ever more important to define the genes to be sequenced, as well as the best point in time for their sequencing.

The majority of studies published on hereditary polyneuropathies investigated well-characterized and well-defined patient populations in which there was clear clinical suspicion of inherited disease (8). Therefore, as proposed by Eggermann et al. in their clinical pathway on the diagnosis of hereditary polyneuropathies, it is correct that individual genes should only be examined in a stepwise diagnostic work-up when there is sound clinical suspicion (3).

Broader exome sequencing, i.e., the analysis of all protein-coding regions of the genome, brings with it the problem that mutations that are not related to the clinical symptoms might also be detected, an aspect that needs to be viewed critically, particularly from an ethical perspective. Therefore, it is important to initiate gene analysis of this kind in a focused manner in the correct diagnostic sequence and at the appropriate time.

More precise prediction of clinical course required

Not only is a clear description and classification of clinical symptoms needed for all polyneuropathies, whether acquired or hereditary, but also improved clinical and paraclinical criteria that permit the clinical course in individual patients to be more accurately predicted and treatment success to be better assessed are

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required. In addition to technical advances (10), innovative study designs that integrate new clinical endpoints could help to conduct studies in more homogeneous patient populations in the future, thereby ultimately expanding the arsenal of available treatment options.

As in many areas of medicine, the individual tailoring of treatment remains the ultimate goal. A combination of the above-mentioned strategies is undoubtedly required to also achieve this goal of personalized medicine in the field of polyneuropathies. While on the one hand improved screening due to earlier polyneuropathy detection could serve to further broaden the currently known heterogeneous spectrum of these diseases, one hopes, on the other, that better surrogate markers permitting individual treatment stratification and better monitoring of treatment response will be identified. Until that time, the two clinical pathways discussed here represent the first step in the right direction.

Conflict of interest statement

Prof. Kieseier received consulting and lecture fees from Almirall.

Prof. Hartung received consulting fees and travel expense reimbursement from CSL Behring, LFB, and Octapharma.

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Cite this as:

Kieseier BC, Hartung HP: Progress in recognizing and treating polyneuropathy. *Dtsch Arztebl Int* 2018; 115: 81–2.
DOI: 10.3238/arztebl.2018.0081

CLINICAL SNAPSHOT

Rumpel-Leede Sign After Coronary Angiography

A 69-year-old man with hypertension but without diabetes mellitus presented for follow-up coronary angiography nine months after an intervention on the left main stem artery. After the procedure, which had been performed by way of the left radial artery, partial deblocking of the transradial band distal to the site of compression was followed by the appearance of petechiae in an area of previously normal skin. Petechiae distal to venous obstruction were first described by Theodor Rumpel (1909) and Carl Stockbridge Leede (1911) in patients with scarlet fever. The petechiae are due to the acute rupture of dermal capillaries. This rare, benign phenomenon is considered a sign of diminished capillary resistance and is associated with vasculopathy, thrombocytopenia, or thrombocytopenia. Longstanding diabetes mellitus and arterial hypertension are predisposing factors. In our illustrative case, the Rumpel-Leede sign arose in a hypertensive patient most likely because of platelet dysfunction under treatment with aspirin and clopidogrel after stent implantation. The petechial hemorrhages regressed within two days without any specific treatment and were no longer visible on further outpatient follow-up.

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Conflict of interest statement: The authors state that they have no conflict of interest.

Cite this as: Rattka M, Rottbauer W: Rumpel-Leede sign after coronary angiography. *Dtsch Arztebl Int* 2018; 115: 82. DOI: 10.3238/arztebl.2018.0082

Translated from the original German by Ethan Taub, M.D.