Molecular genetic diagnosis of hereditary neuropathies

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This chapter is divided into two parts. The first provides a link between phenotypic characteristics and molecular genetic tests, allowing the clinician to order the appropriate genetic tests. This part will largely be presented as a decision tree (Fig. 11.1) for HMSN and a table (Table 11.1) listing characteristic and peculiar clinical features of the different forms of hereditary neuropathies and the corresponding most appropriate genetic tests.

The second part presents the different molecular genetic testing methods themselves with special emphasis on the different principles used to detect the chromosome 17p CMT1A duplication and HNPP deletion.

Ethical issues of molecular genetic testing are dealt with in a separate chapter.

Centers offering molecular genetic tests are listed in the appendix of this book.

11.1 Molecular genetic testing strategies

If the diagnosis hereditary neuropathy is suspected on the basis of typical clinical features and/or a positive family history, the following questions have to be answered before proceeding to molecular genetic tests:

- Is the disease a pure peripheral neuropathy or do patients have additional symptoms or signs? Do they have features of CNS involvement? If CNS symptoms are present, or even prominent, a broad spectrum of other neurological diseases has to be considered, which includes numerous diseases not covered in this book.

- Does the neuropathy involve the motor and sensory system (HMSN), is it a pure motor neuropathy (distal HMN) or a predominantly sensory and/or autonomic neuropathy (HSAN)? Hereditary neuropathy with liability to pressure palsy (HNPP) and hereditary neuralgic amyotrophy (HNA) can often be diagnosed on clinical grounds alone. The most important differential diagnosis of HNA is the much more common sporadic form of neuralgic amyotrophy most often manifesting as a monophasic plexopathy. At present, these diseases can only be differentiated by the family history and the usually monophasic course of the sporadic
Fig. 11.1. Ordering the appropriate molecular genetic test: a decision tree based approach