NF1 microdeletion syndrome

Neurofibromatosis type-1 (NF1) is a genodermatosis frequently encountered in general dermatology. In many patients, the diagnosis of NF1 is made clinically based on the presence of café-au-lait macules and skinfold freckling, as well as plexiform neurofibromas detectable during early childhood. Later in life, cutaneous neurofibromas often represent important diagnostic features. NF1 is characterized by extreme clinical variability and a broad heterogeneity of NF1 gene mutations which impede genotype/phenotype correlations. Notable exceptions are NF1 microdeletions observed in 5-11 % of all NF1 patients. Patients with NF1 microdeletions frequently exhibit facial dysmorphic features and tall stature as rather specific clinical signs. Furthermore, cutaneous and subcutaneous neurofibromas present at an early age, severe global developmental delay, and cognitive disability are pathognomonic for the “NF1 microdeletion syndrome”. Importantly, NF1 microdeletions are associated with an approximately twofold higher risk for malignant peripheral nerve sheath tumors than intragenic NF1 gene mutations. The severe clinical manifestations of patients with NF1 microdeletions require early multidisciplinary clinical care and frequent tumor surveillance. Therefore, when red flag features for the “NF1 microdeletion syndrome” are present in a patient, genetic testing is necessary to confirm or exclude an NF1 microdeletion [1].

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Kehrer-Sawatzki H, Bäzner U, Krämer J, Lewerenz J, Pfeiffer C. The NF1 microdeletion syndrome: early genetic diagnosis facilitates the management of a clinically defined disease. J Dtsch Dermatol Ges. 2022 Mar 4. doi: 10.1111/ddg.14707. Epub ahead of print. PMID: 35246941.