CORRESPONDENCE

Letter to the Editor

The Neurofibromatoses

by Dr. med. Said Farschtschi, Prof. Dr. med. Victor-Felix Mautner, Dr. med. Anna Cecilia Lawson McLean, Dr. med. Dr. rer. nat. Alexander Schulz, Prof. Dr. med. Dr. med. dent. Reinhard E. Friedrich, Prof. Dr. med. Steffen K. Rosahl in issue 20/2020

Screening: The Significance of Pheochromocytoma

Loss of heterozygosity studies indicate that retinal hamartoma is a true component of neurofibromatosis (NF) type 2 and pheochromocytoma a true component of NF type 1 (1). A retrospective cohort study of NF type 1 patients from the Mayo Clinic found the age at presentation to be between age 14 years and 70 years with a pheochromocytoma size between 8 mm and 9.5 cm. In that series, metastatic or recurrent disease occurred in 7.3% of patients. Metastatic adrenal pheochromocytoma in NF1 can present at a size of 2.5 cm at the age of 17 years (2).

The American College of Medical Genetics and Genomics (ACMG) guidelines recommend considering pheochromocytoma in hypertensive NF1 patients age older than age 30 y and do not recommend biochemical or imaging screening in asymptomatic patients.

The authors of the Mayo Clinic study recommend biochemical case detection for pheochromocytoma every 3 years starting at age 10 y and also before elective surgical procedures and conception. In analogy, the screening for pheochromocytoma in patients with von Hippel Lindau disease is recommended at age 4 years, considering that there also are "asymptomatic" individuals with malignant disease (3).

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In Reply:

Many thanks for this valuable additional information on screening, regarding the significance of pheochromocytoma in neurofibromatosis. The incidence of these rare tumors stated in the literature—they have an overall population incidence of 2 to 8 per 100 000 adults (prevalence: 1 in 3000 births)—ranges from 0.1% to 7% in NF1 patients (1).

In a series by Petr and Else, mean age at diagnosis in this patient group was 42 years (2). Only 9 of the 17 patients in this cohort had hypertension, and 3 had cardiovascular crises in the context of elective surgeries. This justifies ruling out pheochromocytoma in NF1 patients before elective surgeries under general anesthetic, as indicated in the Mayo Clinic study cited by Dr. Koch.

In fact, it is currently thought that approximately one-quarter of pheochromocytomas become malignant, and metastasis has been observed as much as 20 years after removal of the primary tumor (3). This suggests that indicating screening for at-risk patients is also worthwhile, as with patients with Von Hippel–Lindau disease. On the other hand, it is worth noting that, of 850 NF1 patients who have been monitored only by the Hamburg outpatient neurofibromatosis department using whole-body MRI and follow-up since 2004, pheochromocytoma that has become malignant has so far been identified in only one patient.

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Conflict of interest statement
The authors of both discussion pieces declare that no conflict of interest exists.