## A multidisciplinary approach in neurofibromatosis 1

We read the Review on neurofibromatosis type 1 (NF1) by Angela Hirbe and David Gutmann[1] with great interest. Although Hirbe and Gutmann precisely described the genetic, phenotypic, and skin features, their focus is on the less frequent clinical manifestations including dysplastic abnormalities of the central and peripheral nervous system, changes to musculoskeletal and respiratory systems, and the occurrence of CNS and non-CNS tumours. Cardiac and peripheral vascular disorders are also possible clinical complications in NF1 that require specific discussion.[2] Our experience shows that vascular complications in NF1 can occur in different sites and can evolve rapidly, with patients developing new aneurysms, even after endovascular treatment. Cardiovascular abnormalities are often underestimated because a diagnosis is usually made only in patients with specific clinical manifestations. Echocardiograph data suggest that up to 27% of patients with NF1 have cardiac involvement, with a half of patients having pulmonary artery stenosis.[3]

NF1-related vasculopathy includes renal and cerebral artery stenosis, aortic coarctation, and arteriovenous malformations. The pathogenesis, clinical features, and natural history of these anomalies remain poorly understood; however, impaired NF1 gene function in vascular endothelial cells has been shown to increase proliferation and growth.[1-3] Vasculopathy usually affects the arterial system, leading to cerebrovascular disease (eg, narrowed or ectatic blood vessels, vascular stenosis, aneurysm, or moyamoya disease) or renal artery stenosis. Stenotic lesions are the most common and are caused mostly by intimal proliferation with resulting luminal obstruction; the renal artery is the most frequent site involved, and renovascular hypertension is the most common clinical presentation.[4]

Investigators have noted intimal thickening, thinning of the media, and parietal dilatation in small vessels of patients with NF1.[5,6] Many other vessels such as the aorta, and intercostal, subclavian, brachial, radial, and vertebral arteries can be affected by aneurysmal dilatations.[4,6-8] Lumbar arteries are rarely involved, with only one case described.[9] Patients with NF1 can have aneurysms, but the synchronous involvement of two different circulatory regions is not yet known.[8] However, the real incidence of these abnormalities is indeed unknown because many lesions are undetected.

Traditional surgery with arterial clipping and aneurysmal excision is the only available option for treatment; in patients with NF1, complications are of major concern because of the fragility of the dysplastic vessels. Endovascular treatments, such as coil transarterial embolisation or percutaneous stent-graft placement, are sometimes considered preferable when it is mandatory to maintain an efficient blood flow in the regions perfused by the treated vessel; these are less invasive and have low intra-operative and post-operative mortality.[10]

Clinicians must be aware of the diverse clinical features, particularly with vascular complication and recurrence, of NF1. Prompt diagnosis is needed to provide optimum care, and serial diagnostic procedures are needed to increase awareness, to avoid early and late adverse events, and to prevent deleterious outcomes.

We declare no competing interests.

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We read with great interest the Review about neurofibromatosis type 1 (NF1) by Angela Hirbe and David Gutmann.[1] Although the Review has much neuro-oncological detail, we would like to make some comments about the outlined diagnostic approach, on the basis of our clinical experience.

The diagnostic criteria for NF1 were drawn up in 1988 at the National Institute of Health Consensus Conference.[2] Since then, understanding of the disease has improved. Over the past 26 years, the gene for NF1 has been discovered, observations have been made of further clinical features such as choroidal hamartomas, unidentified bright objects, anaemic nevi, glomus tumours, and juvenile xanthogranulomas,[3-5] and histological and molecular assessments of freckles have revealed that they do not differ