Neurofibromatosis Type 1: Clinical Diagnosis is All in the Name

When patients present with two or more of these seven criteria, be prepared to render the proper diagnosis.

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The most common neurocutaneous disorder, Neurofibromatosis Type 1 or Von Recklinghausen Disease, is most widely recognized through the appearance of café au lait spots, visible before age five, and benign cutaneous neurofibromas that become apparent before age 15. A variety of other complications, more variable in age of onset and severity, occur in one-third of patients. Neurofibromatosis Type 1 (NF1) is diagnosed when patients present with two of the seven established criteria. The mnemonic “FIBROMA” is memorable, as it appears within “NeuroFIBROMAtosis Type 1.”

Criteria for NF1

Fleshy tumors, neurofibromas are benign peripheral nerve sheath tumors made up of schwann-like cells, fibroblasts and extracellular matrix. Neurofibromas are categorized as cutaneous, subcutaneous, nodular plexiform, and diffuse plexiform. Cutaneous and subcutaneous neurofibromas, which are more superficial and may be tender or pruritic, are often surgically excised. However, nodular and diffuse plexiform tumors may cause significant pain, and surgical resection is difficult due to invasive vascular and nervous involvement.

Pigmented iris hamartomas, also known as Lisch Nodules, are evident in fewer than 10 percent of affected children under age six but in more than 90 percent of adults. Even though iris hamartomas may be visible with an ophthalmoscope, an ophthalmologist should be consulted since slit lamp examination can distinguish these lesions from iris nevi.

Bony lesions are also variable in NF1. In infancy and childhood a patient may present with sphenoid wing dysplasia, long bone bowing, pseudoarthrosis, and scoliosis.

NF1 is an autosomal dominant genetic disorder in which 50 percent of cases are familial and the other half are new mutations. Even though NF1 has variable expression, the penetrance is complete. A relative of the first degree including parents, siblings, or offspring affected by NF1 is a simple method of confirming the diagnosis when paired with one other physical finding.

MRI may detect optic gliomas, which appear as an enlargement of the optic nerve or chiasm. The tumors may originate anywhere along the visual pathway, such as the optic nerves, chiasm, and post-chiasm optic tracts. Patients may become symptomatic with progressive vision loss associated with expanding lesions. All children with NF1 should, therefore, undergo thorough ophthalmologic evaluation annually.

Macules or café au lait spots in numbers of six or more are present in 95 percent of NF1 patients. The macules must be over 5mm in greatest diameter in pre-pubertal individuals and greater than 15mm in diameter in post-pubertal patients. The macules are uniformly hyperpigmented and flat. A Woods lamp is useful to visualize lesions that may have faded in an adult or those on darker skinned individuals.

Axillary or inguinal freckling occurs in 75 percent of patients affected by NF1 and usually develops by late childhood. Freckling may also be visible in other areas of skin opposition such as the neckline or inframammary areas in women.

Neurofibromatosis Type 1 is a devastating disease and is managed symptomatically. Although many of the complications of the disease are treated with surgery, the condition requires close monitoring of patients on a regular basis.