A 45-Year Old Man With Cutaneous and Subcutaneous Masses of Varying Size

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PHOTO-QUIZ

The patient was 45 years old. His physical examination showed disseminated cutaneous and subcutaneous masses of varying size and café-au-lait spots (Figures 1A-B). The patient had Lisch nodules (iris hamartomas). A neurologic examination showed no abnormalities. Axial T1-weighted magnetic resonance imaging of the brain and orbits showed no abnormalities. An abdominal ultrasonography demonstrated normal kidneys, adrenal glands, spleen and liver. He had no history of diabetes mellitus, hypertension, or any other remarkable diseases. The family history was unremarkable. He was followed by a good outcome.

What is the most probable diagnosis?

Figures 1A, B: Disseminated cutaneous and subcutaneous masses of varying size and café-au-lait spots
ANSWER to PHOTO-QUIZ

Neurofibromatosis type 1 (NF-1)

Neurofibromatosis is neurocutaneous, and the common autosomal dominant disorder, occurring in approximately 1 per 3000 people. There are two distinct forms of neurofibromatosis: type I and type II. Café-au-lait hyperpigmented macules, iris hamartomas (iris Lisch nodules) and neurofibromas are characteristic of neurofibromatosis-1 (NF1). The Hospital Ethical Committee approved the human study. We obtained a written informed consent from the patient.

NF1 is a common autosomal dominant disease characterized by formation of benign and malignant tumors. NF 1, also known as von Recklinghausen disease, is characterized by changes in pigmentation and the growth of tumours along nerves on the skin and other parts of the body. It is caused by a defect in a tumour-suppressing gene on chromosome 17q11.2. Normally the gene produces neurofibromin, a protein that regulates cellular proliferation. With the gene mutation, the lack of neurofibromin results in overgrowth of cells from neural crest areas in both the central nervous system (causing Schwann cell tumours on virtually every nerve) and on the skin. All people who inherit a copy of the mutated gene are affected. As the pattern of inheritance is autosomal dominant, only 1 copy of the defective gene is needed to cause the condition. However, it is not necessary to have an affected parent. About 30–50% of patients have a new mutation.

The diagnosis of neurofibromatosis type 1 is based on clinical findings. The patient should have 2 or more of the following: 6 or more café-au-lait spots of ≥ 1.5 cm in postpubertal individuals or ≥ 0.5 cm in prepubertal individuals; 2 or more neurofibromas of any type or 1 or more plexiform neurofibroma; and freckling in the underarms and groin 1. Our patient had multiple neurofibromas of varying size and café-au-lait spots (Figures 1A-B). The axial T1-weighted magnetic resonance imaging showed no abnormalities. A neurologic examination showed no abnormalities. He did not have any abnormalities of internal organs.

The differential diagnosis includes benign café-au-lait pigmentation (present in up to 10% of the general population), multiple lipomas, and sporadic schwannomas, gliomas and meningiomas in the central nervous system. Most people with mild neurofibromatosis have little disability. On the other hand, NF 1 is often associated with orthopedic disorders, especially scoliosis, which is the most common skeletal manifestation of NF-1. Children with NF1 demonstrated the characteristic downward shift in IQ, poor visuospatial constructual skills, and inattention. Early diagnosis and treatment may be the best way to improve outcomes. Our patient did not have any of these abnormalities.

The condition can have a serious psychological impact because the accumulation of skin nodules can be quite disfiguring. Surgical excision and laser treatment of the neurofibromas are possible, but neither treatment is universally effective. Gliomas of the optic nerve are found in up to 15% of pediatric patients with neurofibromatosis type 1. Best detected using magnetic resonance imaging, these gliomas are symptomatic in about 50% of patients at diagnosis. The high prevalence of gliomas of the optic nerve that are asymptomatic may, however, be biased by referral patterns. Indeed, in patients with neurofibromatosis type 1, the threshold of risk for optic nevre glioma is low. Our patient had Lisch nodules (iris hamartomas), but he had no glioma of the optic nerve.

Physicians who identify patients with neurofibromatosis type 1 should refer them early to facilities where appropriate evaluation and monitoring of lesions can be carried out. Early detection and monitoring may help to prevent disability and death. Morbidity, due to complications of NF1, occurs mainly in adults but occasionally in children.

REFERENCES


