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Refractory Hypertension Due to Pheochromocytoma in A Type I Neutrofibromatosis: Single Case Report

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2. Key words

Mesh terms; Neurofibromatosis type 1; Hypertension; Pheochromocytoma

1. Abstract

1.1. Background: Neurofibromatosis type I (NFI) is a common genodermatosis, with an incidence of 1 new case to 3000-3500 live births. Described in 1882, it occurs from gene mutations of the encoding protein called neurofibrinin. NF1 patients are at increased risk for neoplasms. **Aims:** We report a case of a patient with neurofibromatosis with a recent diagnosis of pheochromocytoma (PHEO), due to the rarity of this association. 1.2. Case Report: Fourty-sex years old female patient with NF1 and hypertension since the age of 25, developing difficulty in controlling blood pressure levels. During the investigation, a left adrenal mass was identified in tomography, with a hyper capturing pattern on the scintigraphy. After preparation, adrenalectomy was performed. Conclusions: Thirty percent of patients with NF1 develop hypertension, usually primary. A lower percentage may be secondary, usually due to renovascular causes. About 1% of cases hypertension is caused by PHEO. It's a rare neoplasm that occurs between 20 and 50 years of age, with no gender predilection. Refractory hypertension, associated with paroxysms of headache, intense sweating and palpitations suggests PHEO. The treatment is surgical. Long-term follow-up of NF1 patients is common in dermatological practice. With the presentation of this rare association, we call attention to the adequate follow-up of these patients the presents with hypertension.

3. Background

"Neurofibromatosis is a common autosomal dominant genodermatosis of high penetrance, initially described by von Reckinghausen in 1882. Among its subtypes, type I neurofibromatosis (NFI) is the most frequent, with an approximate incidence of 1new case for 3000 to 3500 live births. Mutations of the gene encoding the neurofibrinin protein, located on the short arm of chromosome 11, locus 11.2[1], are identified. The main clinical features are brown-milk stains, ephelides typically located in the axilla and inguinal region (Crowe's sing), cutaneous and subcutaneous neurofibromas, Lisch nodules (iris hamartomas), optic gliomas and plexiform neuromas[1]. These findings are included in the diagnostic criteria defined by the National Institute of Health Consensus Conference in 1988. Classically, patients are followed by dermatologists because of their exuberant cutaneous findings. Although the therapeutic perspective is poor, follow-up gains importance in anticipating possible malignant transformations. Among them, sarcomatous transformation of plexiform neuromas, suspected by the rapid tumor growth associated with local pain, is the main concern. This phenomenon occurs in about 3 to 5% of patients and is emphasized in the literature [1]. However, several other neoplasms have an increased incidence. These can be both benign and malignant. Mention may be made of acoustic neuroma, meningiomas, neuroblastoma, thyroid carcinoma, pheochromocytoma (OGF), skin neoplasms including melanoma [2].

4. Aims

We report a case of a patient with NFI and recent diagnosis of OES, due to the rarity of this association, seeking to call attention to the importance of the follow-up of these patients.

5. Case Report

A 46-year-old female patient with NF1 **(Figure 1, 2 and 3)** was being followed in our outpatient dermatology clinic. She was diagnosed with high blood pressure when she was 25-years-old, but recently cardiology was having trouble to control her tension levels despite optimum anti-hypertensive drug combination. In

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this context, during investigation, she presented a left adrenal mass on a CT-exam. **(Figure 4)** An addition scintigraphy showed hypercaptation in the upper region above the left kidney. With a probable diagnosis of PHEO, she was hospitalized to terminate investigation, clinical compensation and surgical treatment. Video laparoscopic adrenalectomy was performed, without complications. Patient is still being followed, now with 6 months post treatment, with no evidence of recurrence of the disease, requiring no more anti-hypertensive treatment.

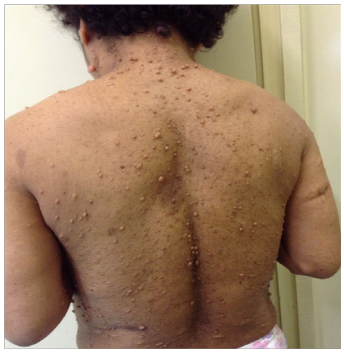


Figure 1: Multiple cutaneous neurofibromas on her back.

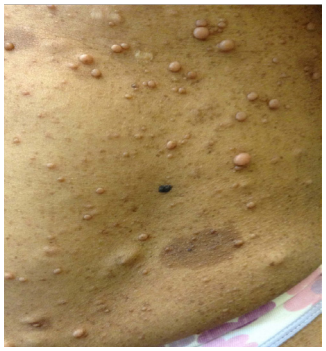


Figure 2: An example of a *Café au Lait* (brown-milk) spot, along with neurofibromas.

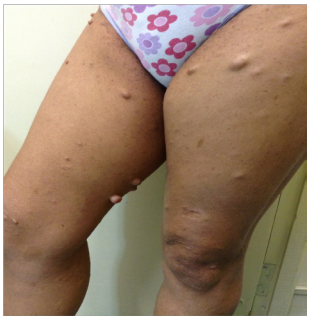
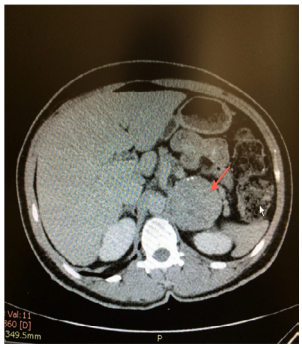


Figure 3: Multiple cutaneous neurofibromas on her legs.



Picture 4: A mass in the topography of the left adrenal gland, evidenced by the CT examination.

6. Discussion

NFI is known to be a disease whose management requires a multidisciplinary team, being fundamental its knowledge in several areas, even at the primary care level, in view of its significant prevalence[1]. However, in general, the patients are at least accompanied by the dermatologist because of the exuberance of the cutaneous lesions. The importance of follow-up, since effective treatment is not available, lies mainly in the higher incidence of tumors, including malignant behavior ones. A cohort of 448 patients with NFI, with a follow-up of 5705 patients / year, found a 2.7-fold higher risk of malignant neoplasia in relation to the general population. It is postulated that the mutation involved inactivate NF1 genes with tumor suppressor activity, possibly explaining the increased frequency of neoplasias [2].

About 30% of NFI patients develop hypertension, and it is therefore essential that these patients have their blood pressure checked. Most cases are primary or essential, but in a lower percentage it may be secondary to a renovascular component and, even more uncommonly, can be justified by the presence of PHEO (about 1% of cases) [3].

PHEO corresponds to a rare neoplasm of chromaffin cells, with prevalence in the general population of about 2 to 8 cases: 1,000,000. It affects patients between 20 and 50 years of age, and there is no predilection for sex. Ninety percent of the cases are benign, unilateral, located in the adrenal gland [4,5]. About 10% of them are family members associated with dominant autosomal disorders, such as NF1. Tuberous sclerosis, Stuge-Weber syndrome and Carney syndrome are also of dermatological importance [5].

Refractory hypertension associated with paroxysms of headache, intense sweating and palpitations suggest FEO [4]. Diagnosis involves the measurement of serum and urinary metanephrines and catecholamines, as well as magnetic resonance imaging or scintigraphy for localization of the tumor. Surgical excision is the appropriate treatment and, in general, it is via laparoscopic surgery after adequate preoperative preparation [4,5].

Screening for PHEO in patients with NF1 is generally recommended at the onset of hypertension [6,7]. However, a study in patients with these two conditions showed that, in most cases, there was no change in blood pressure. Thus, the suspicion of PHEO should not be restricted to the onset of hypertension, but also to other signs and symptoms that may indicate the presumption of this diagnosis [4]. However, the plan to screen only symptomatic patients has led to an underestimation of the prevalence in these individuals. Thus, screening for PHEO in patients with NF1 is recommended for all patients over 40 years of age through

the quantitative analysis of metanephrines and imaging tests such as CT or RM [8]. Additional examinations before pregnancy and any surgeries are also recommended, although there is still a need to determine the cost-benefit of this strategy [9].

7. Conclusions

Among genodermatoses, NF1 is the most common, so the care of these patients is common in the dermatological practice. In addition, the survival of its patients is close to the general population, in such a way that these patients will be followed in the long term. We report this case due to the rarity of this association with PHEO, and the need for adequate follow-up of these patients.

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