

CASE REPORT

CLASSICAL DIAGNOSTIC RADIOLOGICAL FEATURES OF VON RECKLINGHAUSEN'S NEUROFIBROMATOSIS IN A NIGERIAN ADULT

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ABSTRACT

Neurofibromatosis type 1 (NF-1, Von Recklinghausen disease or peripheral NF) is a rare autosomal dominant disorder with varied clinical manifestations involving the skin, nerves and bones. It is the most common of the neurocutaneous syndromes, with variable pathological and clinical expression. Approximately half of all cases result from spontaneous mutations of the NF1 gene. The genetic defect affects chromosome 17q12 and results in decreased production of neurofibromin. The estimated worldwide incidence is put at 1 in 3500. The diagnosis of NF-1 is usually based on the seven diagnostic criteria by the National Institute of Health and the diagnosis made when there are two or more of these features. Imaging modalities like plain radiographs and Computed tomography play major roles in the diagnosis of NF-1. Knowledge of the characteristic radiologic findings, as well as their clinical significance is critical in correctly interpreting neuroimaging studies in this patient population, and appropriately guiding management decisions. The patient presented is a 29-year old female who had presented with right orbital and periorbital masses, lisch nodules, multiple scalp and body nodules, cranial bony defect and complex kyphoscoliosis. She had three of the seven classical diagnostic features of NF-1 which were confirmed on imaging.

INTRODUCTION

Neurofibromatosis (NF) is an autosomal dominant disorder which manifest as a neurocutaneous syndrome.¹ Neurocutaneous syndromes encompass a group of disorders that affect the embryonic ectodermal plate, which includes the central and peripheral

nervous systems, as well as the related skin. There are 2 distinct types - Neurofibromatosis 1 (NF-1, Von Recklinghausen disease or peripheral NF) and Neurofibromatosis-2 (NF-2 or central NF).¹ For many years, these two conditions were regarded as one entity until 1822 when Wishart described NF-2.² NF-1 was also fully differentiated from NF-2 in the late nineteenth century by von Recklinghausen.³

NF-1 has a worldwide prevalence of 1 in 2500-3500 live births, while NF-2 has a prevalence of 1 in 210,000 births.^{1,4} The manifestations of NF-1 result from a mutation in or deletion of the NF-1 gene, which is located on chromosome 17 while the deleted NF-2 gene is located on chromosome 21. The gene product, neurofibromin serves as a tumour suppressor, decreased production of this protein results in the myriad of clinical features.^{1,5}

KEYWORDS: Classical features, Von Recklinghausen's neurofibromatosis, radiological

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Von Recklinghausen described NF-I in details in a case report published in 1882^{3,4} but because of the varied presentations and pleiotropic nature of the disease, formal diagnostic criteria were not established until 1987 by the National Institutes of Health Consensus Development Conference.⁶ Imaging modalities for the diagnosis of NF-1 include plain radiograph, contrast enhanced computed tomography, magnetic resonance imaging and nuclear imaging. Understanding the characteristic imaging findings, as well as their clinical significance, is critical in correctly interpreting neuroimaging studies and appropriately guiding management decisions.

This patient is presented because of the presence of the classical features of Neurofibromatosis type 1 seen on plain radiograph and computed tomography.

CASE REPORT

A 29-year old female presented with a 20-year history of progressive orbital and periorbital swelling, inability to see with the right eye as well as abnormal posturing. Multiple nodules and pigmented spots were noticed on her body at birth.

She was short statured with severe kyphoscoliosis. She had generalized multiple "café au lait" spots and nodules. Lisch nodules were also found in the iris. A right periorbital fleshy mass consistent with a plexiform neurofibroma was seen involving the right upper eyelid and lateral periorbital region which showed intermittent contractions. There was also proptosis of the right eye with a persistent medial gaze. A soft tissue mass measuring 20cm x 14cm was seen in the occipital region with underlying bony defect.

Patient was conscious and alert. The pupils were 4mm bilaterally and reactive to light. There was right ophthalmoplegia and left 6th cranial nerve palsy. Other cranial nerves and long tracts were grossly intact. There was no known

family history suggestive of a similar illness.

A diagnosis of type 1 neurofibromatosis with right orbital and periorbital masses, multiple scalp and body nodules, cranial bony defect and complex kyphoscoliosis was made.

RADIOLOGIC FINDINGS

A lateral skull radiograph (figure 1) showed macrocrania with a large defect in the occipital bone and soft tissue mass protruding from it.

The axial cranial computerized tomography (CT) image (figure 2) confirmed the bony defect in the occipital bone as well as thinning of the right greater wing of sphenoid with absence of the postero-superior wall of the right orbit in keeping with a bare orbit. A right pencephalic cyst was seen to communicate with the occipital horn of the right lateral ventricle (figure 3).

The coronal CT images (figure 4) showed brain tissue herniating into the orbit with subsequent proptosis of the right globe. It also shows a soft tissue mass in the right periorbital region in keeping with a plexiform neurofibroma.

Thoracolumbar spine radiographs (figures 5a and 5b)– the lateral view showed severe kyphosis of the thoracic spine with sharp angulation involving the lower thoracic and upper lumbar spine. The anteroposterior view showed marked scoliosis of the thoracic and lumbar spine with concavity to the right and associated crowding of the rib as well as a shift of the heart to the right due to the severe kyphoscoliosis. The patient was scheduled for staged surgery with the plastic surgery and ophthalmology teams but she did not show up for surgery.



Figure 1: Lateral radiograph of the skull showing bony defect in the occipital bone with a soft tissue mass protruding from it.

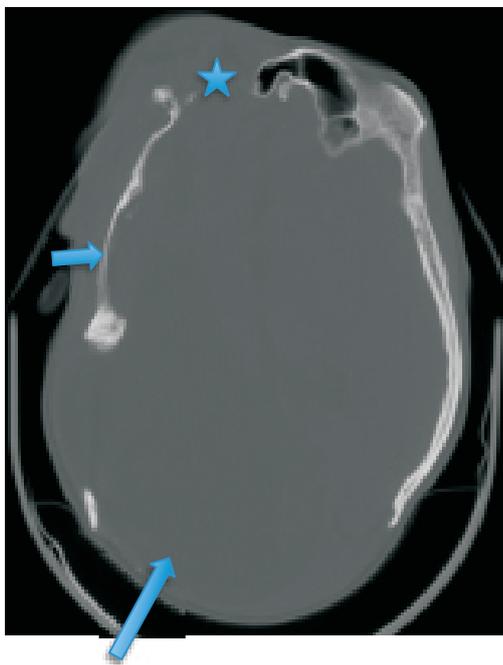


Figure 2: Axial cranial CT image showing the bony defect in the occipital bone (long arrow) as well as thinning of the right greater wing of sphenoid (short arrow) and absence of the superior wall of the right orbit (star).



Figure 3: Axial cranial CT image showing a porencephalic cyst (arrow) communicating with the occipital horn of the right lateral ventricle.

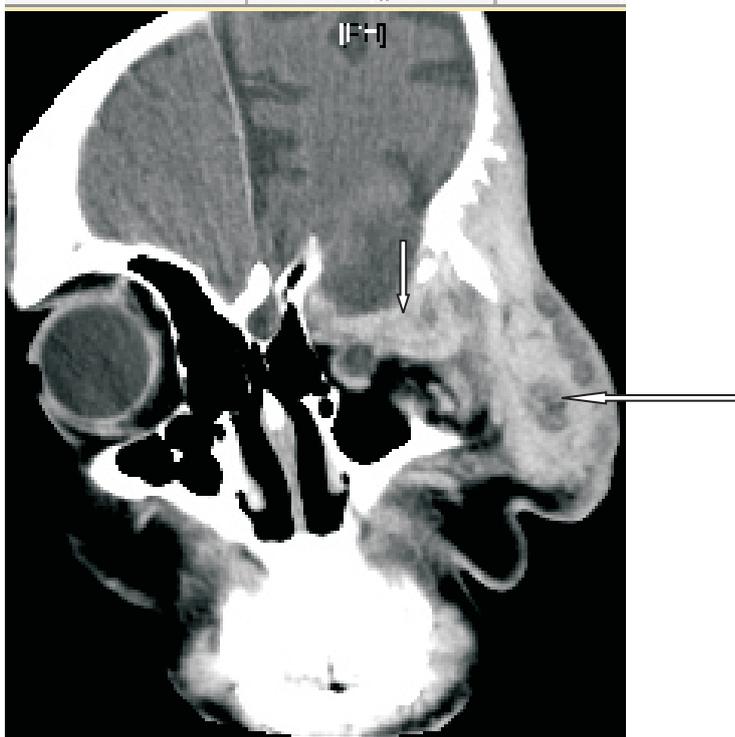


Figure 4: Contrast enhanced coronal CT showing the bony defect at the roof of the right orbit with herniation of the brain tissue into the orbit (short arrow) and displacement of the ipsilateral globe. It also shows a soft tissue mass in the right periorbital region (long arrow) in keeping with a plexiform neurofibroma.

5a



5b



Figure 5a and 5b: Lateral and anteroposterior radiographs of the thoracolumbar spine showing severe kyphoscoliosis of the thoracolumbar spine with concavity to the right and associated crowding of the rib as well as a shift of the heart to the right.

DISCUSSION

Neurofibromatosis type 1 (NF-1) is a neuroectodermal and mesodermal dysplasia characterized by a triad of pigmented cutaneous lesions, multiple soft tissue elevated tumours and various osseous manifestations of the axial and appendicular skeletons^{1,7} all of which are present in the patient presented. The diagnosis of NF-1 is usually based on the diagnostic criteria established by the National Institute of Health.² There are 7 criteria which include the presence of six or more café-au-lait spots, axillary or inguinal freckles, two or more typical neurofibromas or one plexiform neurofibroma, optic nerve glioma, two or more iris hamartomas, sphenoid dysplasia or typical long-bone abnormalities and similar history in first-degree relative. Diagnosis is made when there are two or more of these features.⁶

The hall mark of the disease is however the presence of the peripheral neurofibromas.⁵ Three subtypes exist- cutaneous (café au lait spots), subcutaneous (fibroma molluscum) and plexiform neurofibromas (elephantiasis neuromatosa).⁸

Plexiform neurofibromas, which are generally larger, more diffuse, and locally invasive, are seen in more than one fourth of patients with NF-1 and specific for the disease.⁸ They differ from focal cutaneous neurofibromas in that they arise from multiple nerve fascicles and tend to grow along the length of a nerve. These lesions typically present at birth but may continue to appear through late adolescence and early adulthood.⁸ They occur in 30% of patients with NF-1. They undergo malignant transformation in 10% of cases.^{7,8}

Confusion of NF-2 with NF-1 is very unlikely because only 1-2% of NF-2 patients have six or more café au lait patches and Lisch nodules are rare in NF-2.^{8,9} The presence of a schwannoma, which is the hall mark for NF-2 in a patient who does not fulfil NIH criteria for NF-1 makes NF-1 extremely unlikely, while the presence of multiple neurofibromas makes NF-2 very unlikely.^{1,9}

The incidence of NF-1 is independent of ethnicity, race and gender with approximately half of affected individuals representing the first case in the family as a result of a new genetic event or mutation.⁵ This case presented is a female with no known history in the family.

Ocular manifestations include optic nerve glioma which may produce blurred vision, transient blindness and scotomas. Iris hamartoma (Lisch nodules) may be present.⁵ This case presented had visual abnormality.

Skull deformity due to sphenoid wing dysplasia leads to pulsating exophthalmos as the temporal lobe herniates into the orbit. A defect in the superior orbital wall is also a recognized finding.^{10,11} These were present in this patient.

Kyphoscoliosis and atlantoaxial subluxation affect 10% to 26% of patients with NF-1. The severe form occurs in fewer than 10% of patients and may be complicated by paraplegia and respiratory compromise.^{1,12} The neurological sequelae are usually the consequence of pressure on peripheral and spinal nerves and the spinal cord. This patient had severe kyphoscoliosis but no neurological sign.

Abnormalities in growth are a common feature of NF-1.⁵ Large head size is present in half of patients and is not associated with any intracranial or endocrinologic

pathology. Short stature is also common and is not usually associated with hormonal dysfunction.⁵ The patient presented was short statured with macrocrania.

Approximately 2% of individuals with NF-1 develop bowing of the long bones, particularly the tibia. Repeated fracture and failure to heal can result in a pseudoarthrosis (false joint).¹³ Focal gigantism or local overgrowth of both skeletal and soft tissue may also occur.⁵ None of these was found in the patient presented.

Many of these signs do not appear until late childhood or adolescence, and thus confirming the diagnosis which is often delayed despite a suspicion of NF-1.² This patient presented had 3 of the 7 criteria – (1) more than six café-au-lait spots (2) sphenoid dysplasia and (3) one plexiform neurofibroma.

Plain films may detect a variety of subtle and not so subtle bony abnormalities associated with NF-1. It may show growth disturbance, (i.e. hyperplastic bones, "streaky" appearance to the medullary cavity, skull asymmetry, or sphenoid dysplasia) bowing deformities, or pseudoarthrosis of long bones.^{5,11} The patient presented had skull asymmetry and sphenoid dysplasia.

Typical CT findings in persons with type 1 neurofibromatosis include the detection of optic glioma and herniation of brain tissue into the orbit through the orbital wall defects as seen in this case presented. Findings in the chest will include small well-defined subcutaneous neurofibromas, focal thoracic scoliosis, vertebral scalloping, enlarged neural foramina, and characteristic rib notching from adjacent neurofibromas. Dural ectasia, meningocoeles, and dumbbell-shaped masses may be detected around the spinal canal.^{8,9}

MRI of the brain and the spine may be helpful in these patients especially in the diagnosis of the neurogenic tumours.¹² This was not done in this patient because of financial restraint.

Gallium-67 scintigraphy may be used as a screening tool for patients with NF-1, especially patients with a large plexiform neurofibroma when there is concern about 1 or more areas having undergone malignant transformation.¹⁴ This investigation, though helpful is not locally available.

The current management of NF-1 focuses on genetic counseling and symptomatic treatment of specific complications.¹⁵

CONCLUSION: The 29-year-old female presented is an example of the rare cases of NF-1 with multiple classical diagnostic features.

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