East African Medical Journal Vol. 92 No. 11 November 2015
POST- AXIAL POLYDACTYLY A AND DELAYED PUBERTY IN A FEMALE AFRICAN PATIENT WITH NEUROFIBROMATOSIS TYPE 1: CASE REPORT
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POST- AXIAL POLYDACTYLY A AND DELAYED PUBERTY IN A FEMALE AFRICAN PATIENT WITH NEUROFIBROMATOSIS TYPE 1: CASE REPORT

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SUMMARY

Hand and foot polydactyly is a finding that has been rarely reported in neurofibromatosis type I. To the best of our knowledge, about eight patients have been described to date with polydactyly associated to neurofibromatosis. Here we report on a 14-year-old girl with non familial bilateral and symmetrical postaxial polydactyly, delayed puberty and neurofibromatosis type 1.The occurrence of post-axial polydactyly type A in NF1 patients appears to be not a fortuitous event, but well a possible feature of NF1 mutation.

INTRODUCTION

Neurofibromatosis type 1 (NF1) is a neurocutaneous disorder with abnormalities in various tissues derived from the neural crest. Although skeleton abnormalities are common in neurofibromatosis type 1, extremities are rarely affected and hand as well as foot polydactyly is a rare finding in this group of patients (1).

In Black race populations, post axial polydactyly, especially for the hands, is a quite common feature, with an incidence of 13.9 in 1000 live births, showing both genetic and phenotypic heterogeneity (2). Most of bilateral and symmetrical cases are known to be familial (3).

To date, about 8 patients have been reported in the literature with polydactyly associated with neurofibromatosis (4-6). We describe a girl with a non familial bilateral and symmetrical postaxial polydactyly, delayed puberty and neurofibromatosis 1.

CASE PRESENTATION

A 14 year old African female patient was referred to our clinic for multiple non-painful swelling on the face and thorax. She was the eighth of nine children born to healthy non consanguineous parents. There was no history of another family member with similar manifestations. Severe growth delay was evident, with weight 29.3 kg (-5 SD, CDC growth charts), height 139 cm (-3.8 SD). Body Mass Index was (-2.9 SD). Clinical examination revealed hundreds of soft tissue cutaneous nodules on the body, involving the face (3x4 cm) and the thorax (figure 1). Some café-au-lait spots were noted on the trunk and lower arms. We observed freckles over the back and axillary region (figure 2). The patient reported that some pigmented lesions were present at birth and some others appeared when she was four years old.

Pubic and axillary hair, as well as breast development, where absent, consistent with a delayed puberty (figure 3). A well formed extra digit, articulated to the fifth metacarpal, was present on both right and left hands, consistent with a post-axial polydactyly type A (Figure 4). There was neither syndactyly nor clinodactyly.

Observation of the spine revealed scoliosis (Figure 5). A solid (15cm x 4 cm) tumor (Figure 6) with typical microscopic appearance of a plexiform neurofibroma with multiple tortuous enlargements of cutaneous peripheral nerves was observed on the sternum (figure 7).

Figure 1
Multiple skin neurofibroma on the patient's face and thorax

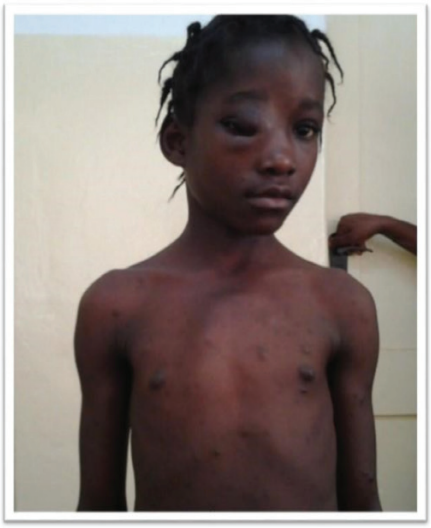


Figure 2
Freckles

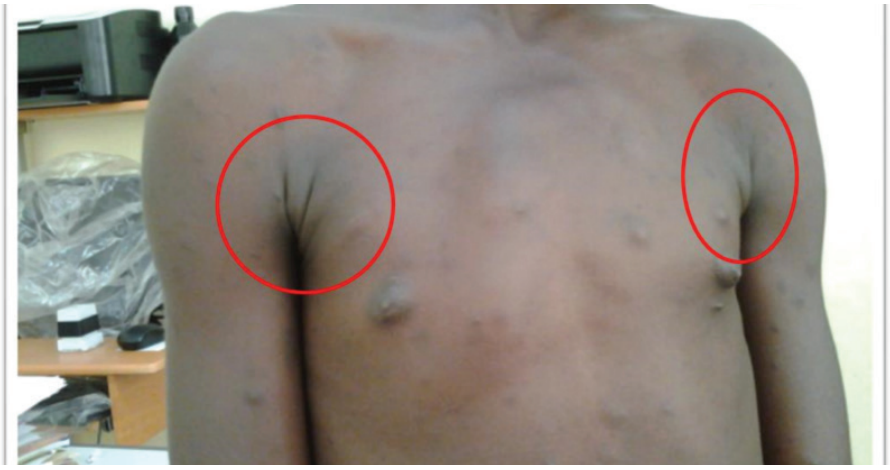
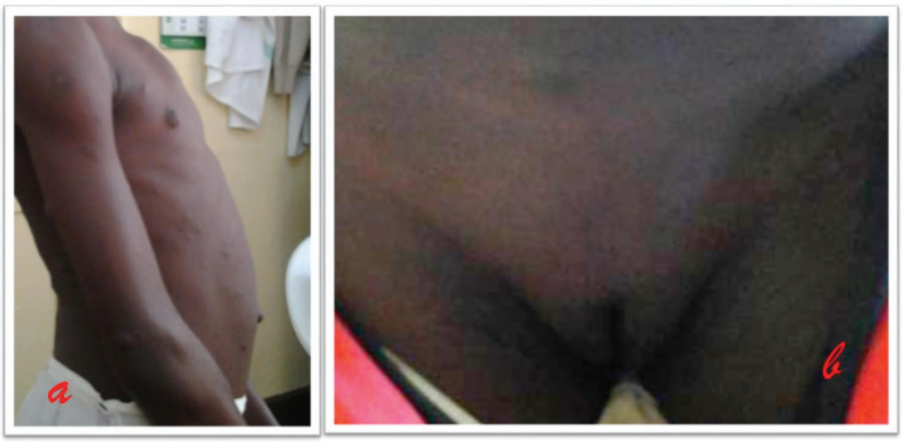


Figure 3
Delayed puberty



a) no glandular tissue b) no pubic hair at all

Figure 4
Post- axial polydactyly type

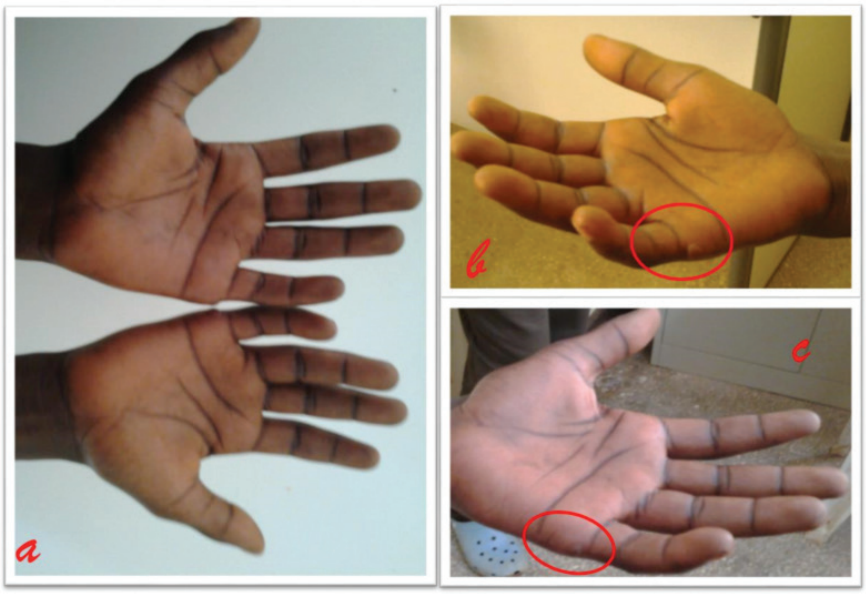


Figure 5
Scoliosis

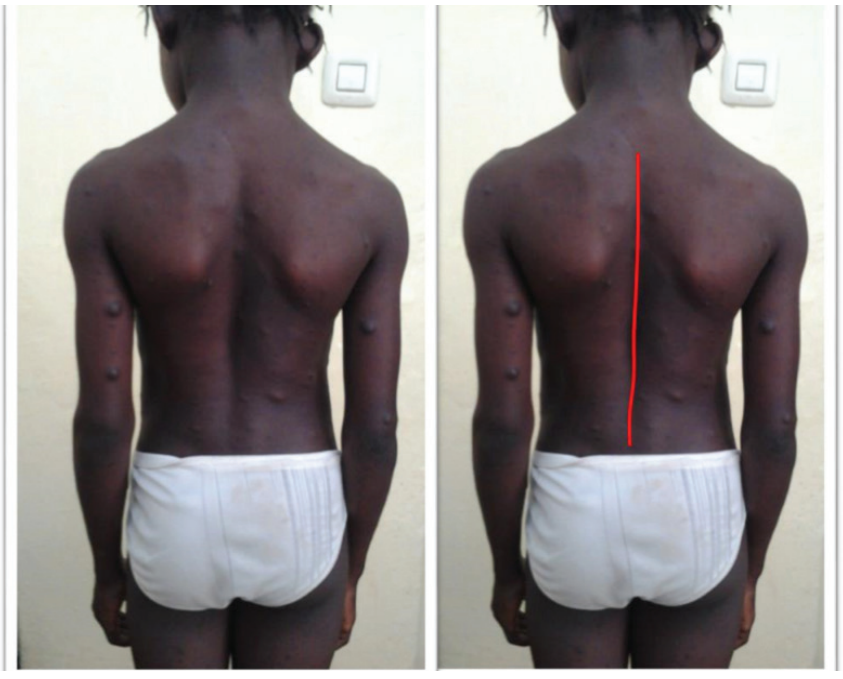


Figure 6
Neurofibroma plexiforme

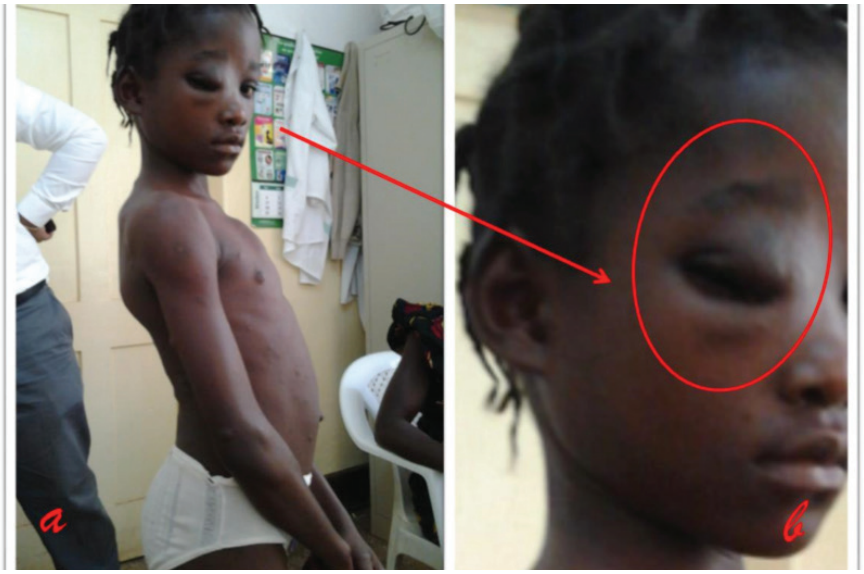


Figure 7

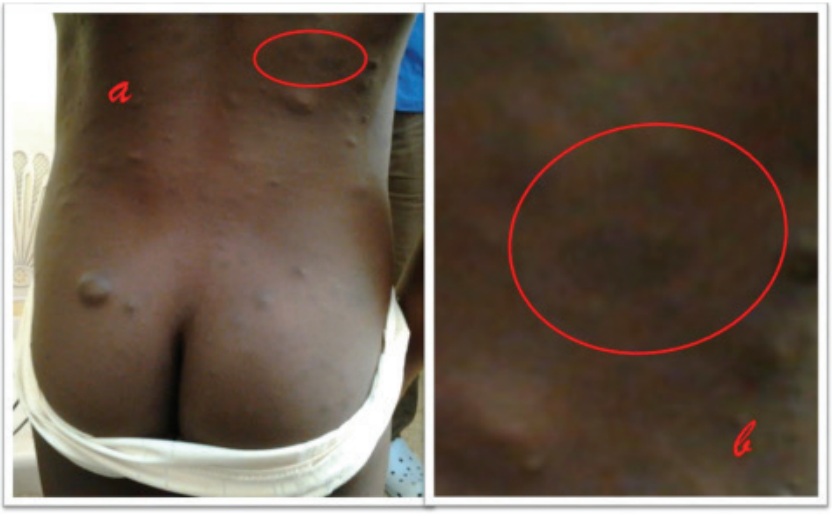
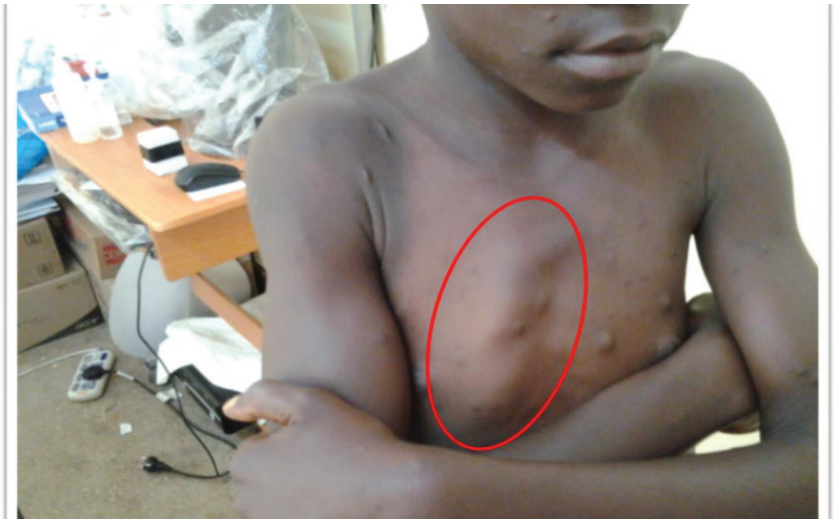


Figure 8
Tumor arising from sternum



DISCUSSION

The diagnosis of NF1 is currently based on the clinical criteria encoded by the National Institute of Health (NIH) Consensus Conference statement organized in 1988 (7). To meet the NIH diagnostic criteria for NF1, an individual should demonstrate at least 2 of the 7 features listed by Stumpf *et al*. (8). Tadini *et al*. suggest adding some laboratory data and cutaneous and extra-cutaneous signs to the classic diagnostic criteria (9). Half of all NF1 cases are familial and half are caused by new mutation (10). The development of NF1 is aconsequence of inactivation of NF1 gene. The gene, located on chromosome 17, presents one of the greatest frequencies of spontaneous mutations in the whole human genome. Gene product, acytoplasmic protein called neurofibromin, is atumor suppressor, with expression detected in various cells, mainly in melanocytes, neurons, Schwann cells and glial cells (11).

In our observation, we recorded skin café-au-lait spots, plexiform fibroma, neurofibroma nodules, freckling and scoliosis (table 1). Furthermore, the anatomopathological examination of the tumor arising from the sternum confirmed the diagnosis of neurofibroma type 1. In addition, we observed a post axial polydactyly and signs of delayed puberty with, at the age of 14 years, no glandular tissue development and no pubic hair at all (12).

Skeleton abnormalities are common in neurofibromatosis type 1, but extremities are rarely affected, with only a few reports of associated hand or foot polydactyly (1, 4, 6).

In Ruggieri *et al*. series of 135 patients with neurofibromatosis type 1, four patients (3%) had polydactyly, with one showing preaxial, two postaxial and one preaxial in association with postaxial types. Polydactyly appeared thus to be more frequent in Neurofibromatosis (3%) than in general population 0.014-0.12%, indicating that this association was likely to be non random (5).

At cellular and developmental levels, polydactyly is known to result from a failure in the control of digit number (3). GLI3 and SHH, known to modulate digit number during development, have been implicated in polydactyly (3, 13). Levy *et al*. suggested that, in developing limb, up regulation of SHH and its target GLI1, which had been observed in neurofibroma malignant lesions, could lead to disorders in anterior posterior polarity (14). It has also been suggested that ectopic activation of SHH in the anterior limb mesenchyme of NF1 embryos might result in polydactyly or other digit malformations (6).

Both Type A polydactyly and neurofibromatosis have been suggested to be inherited in an autosomal dominant mode, with marked penetrance (3). Of interest, a review of the patient's pedigree could not reveal any other member of the family in the two previous generations who had polydactyly or NF1. The non familial occurrence of both post-axial polydactyly type A and neurofibromatosisin our patient is therefore likely to lend support to the previous speculation that polydactyly in this case should not be considered as a random incident but well as anactual feature related to NF1 mutation (5, 15).

In conclusion, the occurrence of post-axial polydactyly type A in NF1 patients appears to be not a fortuitous event, but well a possible feature of NF1 mutation.

Table 1
Overview of reported patients with polydactyly and neurofibromatosis 1

	Ruggieri *et al*. (5)			Merlob *et al*. (4)	Shinawi and Patel (6)				Our patient
Year	1999	1999	1999	1999	1987	1987	1987	2007	2014
Sex	F	M	F	M	M	M	M	M	F
Age	6	8	8	11	NB*	5	Ad	7m**	14
Café au lait spot	+	+	+	+	+	+	+	+	+
Freckling	+	+	+	+	?	?	?	?	+
Dermalneurofibromas	-	+	-	+	?	?	?	?	+
Nodulaneurofibroma	-	+	+	+	?	?	+	?	+
Lisch nodules	-	-	+	+	?	?	?	?	-
Famillyhistory	-	+	+	+	+	+	+	?	-
Skeletal malformations	+	+	+	-	+	+	+	+	+
Post axial polydactyly	+	-	-	+	+	+	+	-	+
Pre axial polydactyly	-	+	+	-	-	-	-	+	-

*newborn , ** month

ACKNOWLEDGEMENTS

We are grateful to parent of the reported infant for their kind collaboration.

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