JMSCR Vol||06||Issue||03||Page1248-1250||March 2018

www.jmscr.igmpublication.org
Impact Factor 6.379
Index Copernicus Value: 71.58
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v6i3.204

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Type 1 Diabetes mellitus and Neurofibromatosis 1 : A Rare Association (Case report)

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Abstract

Neurofibromatosis type 1 is a genetic disorder with abnormalities of the nervous tissue, bones, skin and soft tissues .It allows the growth of tumors along the nerves of bone, skin and brain. It is rarely associated with diabetes mellitus. We reported a case with neurofibromatosis type 1 and type 1 diabetes mellitus.

Keywords: *Neurofibromatosis type 1 .diabetes mellitus*

Introduction

Neurofibromatosis type 1(NF1) is a genetic relatively common disorder characterized by changes in skin color and the growth of tumors on the nerves of the skin, brain, bone and other body parts . Its severity as well as specific features varies from one individual to another.(1) It belongs to a group of related genetic conditions called the RAS opathies caused by mutations in genes of the Ras-MAPK pathway leading to profound effects on growth and development.(2)It is caused by mutations in the NF 1gene and is inherited as an autosomal dominant manner. In about 50% of cases, it is inherited from an affected parent. Other cases result from a new mutation, with no family history of NF1.(3)

NF1 occurs with an estimated incidence of 1 : 2,500 - 3,000 individuals independent of ethnicity, gender or race.(4)Von Recklinghausen was the first one who described it in 1882, but clinical diagnostic criteria were established in 1987 and revised in 1997 by the National Institutes of Health Consensus Development Conference.(5)Patients with NF1 show an increased incidence of tumors arising from neural crest such as neuro fibromas, Leiomyomas and

ganglio neuromas. It has been also related to small bowel adenocarcinoma, as well as pancreatic endocrine malignant tumors.[6]

The diagnosis of NF1 is made if two or more of the following criteria present :[1]Six or more café-aulait spots more than 5mm in the greatest diameter in prepubertal individuals[2],two or more neuro fibroma of any type or one plexi form neuro fibroma,[3]axillary or inguinal freckling,[4] bone abnormalities including sphenoid dysplasia or tibial pseudarthrosis,[5] two or more Lisch nodules, [6] Optic glioma, or[7] a parent, sibling, or child who had NF1.[7]

Case Report

A 5-year-old girl was admitted to the department of pediatrics of Ibn Sina College General Hospital, Jedda ,Saudi Arabia, with a history of fever, vomiting with abdominal pain, and disturbed level of consciousness .She was the second kid of consanguineous parents. Her perinatal history was uneventful. Family history for NF1 was positive for her brother. By examination, weight was 13 kg (below5 ^{pe}rcentile), height was 110 cm (below 5thpercentile), head circumference 50 cm, blood pressure was normal and pulse rate was 120 bum She was presented by diabetic ketoacidosis with urgent treatment in PICU by intravenous fluids and insulin. Skin examination revealed multiple (10) more than 5mm café-au-laitpatches in the upper limb, back, trunk and face (which is unusual site for the spots) varied in size the largest one is 7.8 mm. One of these patches is hairy 5.5 mm india meter. There was axillary freckling on both sides. In addition, there was soft non tender hepatomegaly (12 cm span).

Laboratory investigations revealed a blood glucose level of 540 mg/ld.;HbA1c10.7% with glycosuria and ketonuria. Severe metabolic acidosis was present;ph7.06 Paco2 15.5 mmHg, HCO 7.9 mmol/l. Liver, renal ,thyroid function tests as well as serum electrolytes were normal. The patient was diagnosed with NF1 and type 1diabetes mellitus. Insulin treatment was started with intravenous fluids for 3 days. She was firstly diagnosed as diabetic at that time. Abdominal ultrasound and MRI were normal.

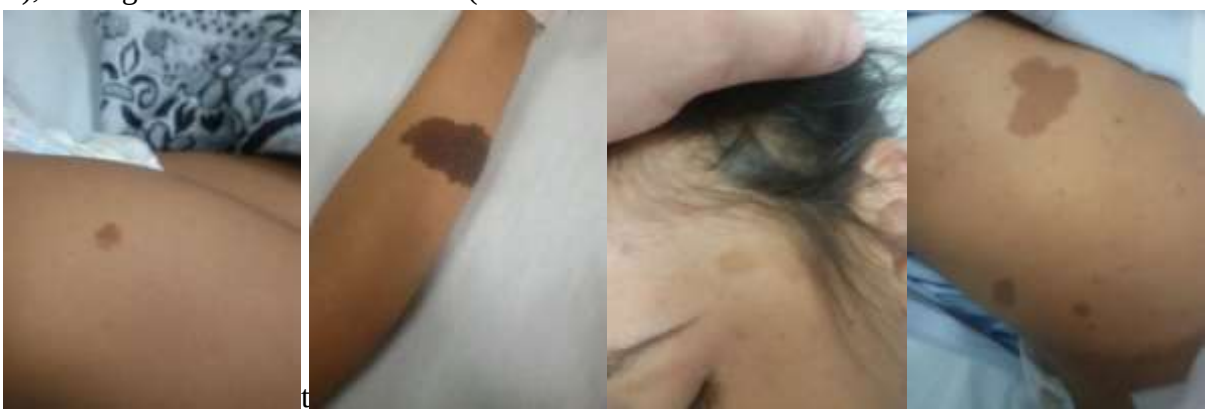

Figure 1: multiplecafé-au-lait patches more than 5 mm in the upper limb and face vary in size the largest one is7.8 mm.One of them is hairy with 5.5 mm in diameter.

Discussion

NF1 gene is mapped to chromosome 17q11.2. 50% of the patients are due to de novo gene mutation (8).We diagnosed our case by finding 10 café-au-lait spots more than5 mm in the greatest diameter with axillary freckling in both sides in addition; there was positive family history in her brother. No other clinical features of NF1,antibodies or somatostatinoma were detected.

Only few reports clarify the association between NF1 and other autoimmune diseases as systemic lupus erythromatosus, mixed connective tissue disease, rheumatoid arthritis, glomerulo nephritis, aswell as bullous pemphigoid and vitiligo.[5,9]Diabetes mellitus is rarely seen in children with NF1. It is attributed to the presence of duodenal somatostatinoma[10]which is a very rare neuroendocrine tumor(1:40 million)arises

from the pancreas or the gastrointestinal tract[12] .It is characterized by excessive secretion of somatostatin hormone by tumor cells of D-cell origin and associated with diabetes mellitus(95%) ,gall stone , weight loss, steatorrhea and achlorhydria.[13,14]Only one case of duodenal somatostatinoma reported in a patient with NF1 removed by open local excision.[11]Only 3 children with diabetes mellitus associated with NF1 cases have been reported. The first case reported by Zaka-ur-Rab and Chopra.[10]in 9-year-old boy known to have NF1 since birth and diabetes mellitus. The second case was reported by Kamoun et al.[15]in 15-year-old boy with positive family history for NF1,and positive glutamic acid decarboxylase (GAD) antibodies only.The third case reported byOzhan al 2013[6]in a 9 year old boy without finding of antibodies or soamtostatinoma.

Conclusion

Association of NF 1 and diabetes mellitus is not only very rare but also unexplained till now. This raises the necessity for proper identification of possible pancreatic antibodies to help for accurate diagnosis. Furthermore, new diagnostic modalitiesare essential forearly detection of duodenal carcinoid or somatostatinoma.

Declaration of Conflicting Interest

The authors declare that they have no competing interests.

Funding

Funding was not received from another sources.

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