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Bohring-Opitz syndrome in Libya

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Introduction

Finding a diagnosis for rare syndromes usually carry a high risk of mal diagnosis, but the availability of genetic tests enables us even in the under developed countries (medically) to reach a definite diagnosis. Bohring-Opitz syndrome is a malformation syndrome characterized by severe intrauterine growth retardation, poor feeding, profound mental retardation, trigonocephaly, prominent metopic suture, exophthalmoses, nevus flammeus of the face, up slanting palpebral fissures, hirsutism, and flexion of the elbows and wrists with deviation of the wrists and metacarpophalangeal joints. Bohring and others (1) presented four unrelated cases of a syndrome resembling Opitz trigonocephaly (C) syndrome, also the authors identified two cases in the literature, formerly reported as having C syndrome (2, 3), Addor et al. (2) reported a 6-year old girl with C-trigonocephaly syndrome and diaphragmatic hernia. Also, Bohring and co-workers (4) reported four additional unrelated cases of Bohring-Opitz syndrome, Pierron and others (5) reported a patient with Bohring-Opitz syndrome. Hoischen and co-workers (6) reported seven unrelated patients with Bohring-Opitz syndrome due to de novo heterozygous mutations in the ASXL1 gene. Magini and colleagues (7) reported two unrelated patients with Bohring-Opitz syndrome confirmed by molecular analysis.

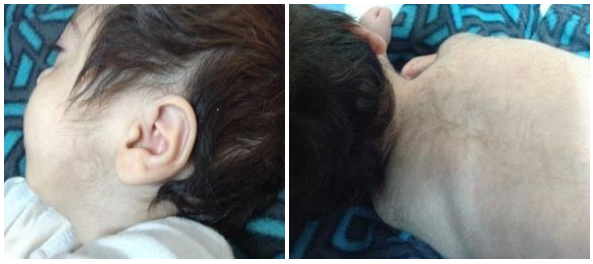
Materials and methods

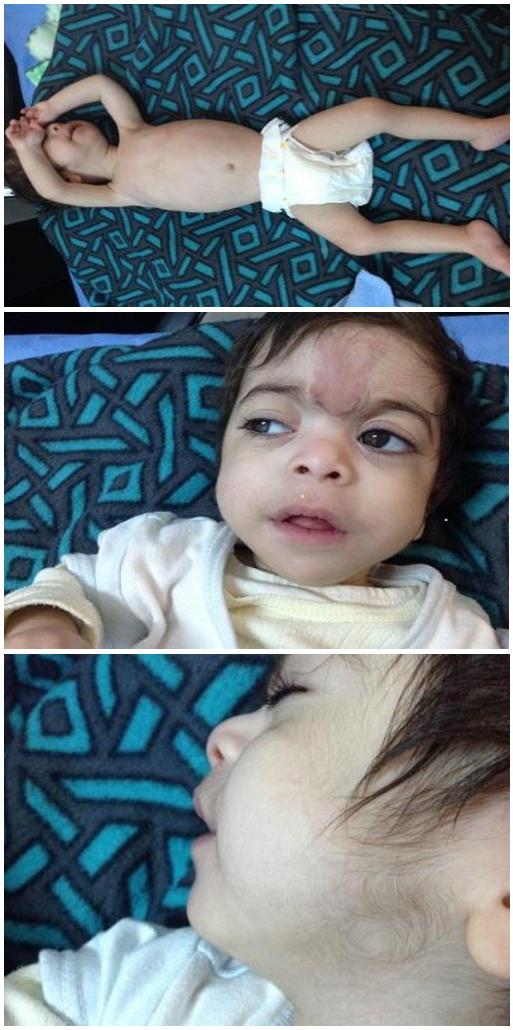
Cases: Mohammed is 1.3 years old presented to me since two months because of global developmental delay and failure to thrive. After uneventful normal pregnancy he was delivered by c/s with no pre or post natal complications, the father and mother are medium class family, non-consanguineous, this child is their first baby, his birth weight was 2.3 kg and the child is fed artificially but have poor sucking, global developmental delay, vaccinated up to date.

Examination

Microcephaly (41 cm), trigonocephaly, high arched palate, prominent eyes and hypoplastic supraorbital ridges, upslanting palpebral fissures, depressed nasal bridge and anteverted nares, facial nevus flammeus, lowest, posteriorly angulated ears, hirsutism , failure to thrive weight (5.5 kg) less than 5 percentile for age, height (65 cm) less than 5 percentile, and severe developmental delay; he is only able to turn his head from one side to other not able to control head, sit or stand, not able to reach objects by hands and socially he is not interested in surrounding, no language development is attained, hearing is defected.

Neurologically: conscious not oriented to surrounding, cranial nerves is normal except for eighth nerve defect, severely hypotonic, with power over three in all limbs with normal reflexes.





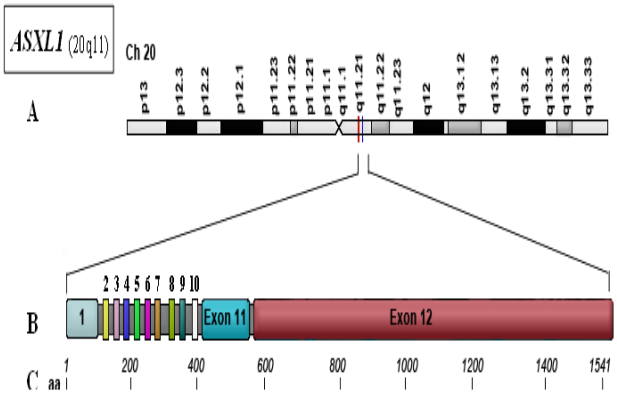
Radiological: Normal limbs without any dislocation of any joint, spine also normal, brain MRI normal, kidneys are directed strangely more out ward than normal largely distended urinary bladder and colon, azygous vein in the lungs, and he has gastroesophageal reflux.

Molecular genetics and laboratory testing: Done by the help of Ali Omar Askar hospital by Biocientia company and proved the heterozygous pathogenic mutation in ASXL1 gene (nonsense mutation: c: 1210 C > T) (14) the test done by DNA sequencing, with the clinical picture and documentation of gene mutation the diagnosis of Bohring-Opitz syndrome is done. Metabolic screen includes electrolytes, heamatological parameters, hormonal assessment, amino acids, organic acids, mucoolysaccride screen, oligosacc-haride screen all are normal.

Discussion

With few exceptions, Bohring-Opitz syndrome occurs as a sporadic disorder. The ASXL1 gene is present in the long arm of chromosome number 20 and involved in the maintenance of both activation and silencing of the HOX genes, which are involved in body patterning, as well as in chromatin remodeling, although the patients did not have any specific homeotic transformations.

ASXL1 is widely expressed at low level in heart, brain, skeletal muscle, placenta, pancreas, spleen, prostate, small intestine, colon, peripheral blood, leukocytes, bone marrow and fetal liver. Highly expressed in testes in our case there is no evidence of upper limb deformity or radial dislocation also no ulnar deviation of he hands with prominent eyes that appears as exophalmus (criteria of C–trigonocephay), this raise the question about the diagnosis is Bohring Opitz syndrome or it may be new variant of this syndrome.



Most of the cases are sporadic mutations but family counseling is still needed because of the reported few familial cases. No evidence of any heamatological abnormalities in the reported cases of this syndrome or in our case too. In conclusion, Bohring Opitz syndrome is characterized by intrauterine retardation with children delivered under weight, hypotonic, classical dysmorphism, poor weight gain and severe psychomotor delay. Most of the cases are sporadic mutations but family counseling is still needed because of the reported few familial cases.

References

1. Bohring A, Silengo M, Lerone M, Superneau DW, Spaich C, Braddock SR, Poss A and Opitz JM. Severe end of Opitz trigonocephaly (C) syndrome or new syndrome? Am J Med Genet. 1999, 85: 438-446.
2. Addor MC, Stefanutti D, Farron F, Meinecke P, Lacombe D, Sarlangue J, Prescia G and Schorderet DFC. Trigonocephaly syndrome with diaphragmatic hernia. Genet Counsel. 1995, 6: 113-120.
3. Oberklaid F and Danks DM. The Opitz trigonocephaly syndrome: a case report. Am J Dis Child. 1975, 129: 1348-1349.
4. Bohring A, Oudesluijs GG, Grange DK, Zampino G and Thierry P. New cases of Bohring-Opitz syndrome, update, and critical review of the literature. Am J Med Genet. 2006, 140A: 1257-1263.
5. Pierron S, Richelme C, Triolo V, Mas JC, Griffet J, Karmous-Benailly H, Quere M, Kaname T, Lambert JC and Giuliano F. Evolution of a patient with Bohring-Opitz syndrome. Am J Med Genet. 2009, 149A: 1754-1757.
6. Hoischen A, van Bon BWM, Rodriguez-Santiago B, Gilissen C, Vissers LM, de Vries P, Janssen I, van Lier B, Hastings R, Smithson SF, Newbury-Ecob R and Kjaergaard S. De novo nonsense mutations in ASXL1 cause Bohring-Opitz syndrome. Nature Genet. 2011, 43: 729-731.
7. Magini P, Della Monica M, Uzielli MLG, Mongelli P, Scarselli G, Gambineri E, Scarano G and Seri M. Two novel patients with Bohring-Opitz syndrome caused by de novo ASXL1 mutations. Am J Med Genet. 2012, 158A: 917-921.
8. Brunner HG, van Tintelen JP and de Boer RJ. Bohring syndrome. Am J Med Genet. 2000, 92: 366-368.
9. Greenhalgh KL, Newbury-Ecob RA, Lunt PW, Dolling CL, Hargreaves H and Smithson SF. Siblings with Bohring-Opitz syndrome. Clin Dysmorph. 2003, 12: 15-19.
10. Kaname T, Yanagi K, Chinen Y, Makita Y, Okamoto N, Maehara H, Owan I, Kanaya F, Kubota Y, Oike Y, Yamamoto T, Kurosawa K, Fukushima Y, Bohring A, Opitz JM, Yoshiura K, Niikawa N and Naritomi K. Mutations in CD96, a member of the immunoglobulin superfamily, cause a form of the C (Opitz trigonocephaly) syndrome. Am J Hum Genet. 2007, 81: 835-841.
11. Lindor NM, Ramin KD, Kleinberg F and Bite U. Severe end of Opitz trigonocephaly C syndrome. Am J Med Genet. 2000, 92: 361-362.
12. Nakane T, Kubota T, Fukushima Y, Hata Y, Ishii J and Komiyama A. Opitz trigonocephaly (C)-like syndrome, or Bohring-Opitz syndrome: another example. Am J Med Genet. 2000, 92: 361-362.
13. Osaki M, Makita Y, Miura J, Abe N, Noguchi S and Miyamoto A. A Japanese boy with apparent Bohring-Opitz or 'C-like' syndrome. Am J Med Genet. 2006, 140A: 897-899.
14. Laboratorium genoomdiagnostitiek, center for human genetics, Biocientia Gmbh, Konrad-Adenaur-str.17 Germany.