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Case Report Open Access

Language Delay Revealing a Kabuki Syndrome: Case Report and Literature Review

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Abstract

Kabuki Syndrome (Kabuki make-up syndrome: KMS), first described in Japan in 1981, is a rare syndrome of unknown cause, characterized by the combination of morphological facial variations , mental retardation (intellectual disability) and various malformations. We report a case of Kabuki syndrome revealed by a language delay.

Keywords: Kabuki syndrome; Clinical manifestations; Language delay; Malformations

Introduction

Kabuki Syndrome (Kabuki make-up syndrome: KMS), first described in Japan in 1981, simultaneously by Kuroki et al. [1] and by Niikawa et al. [2]. First called Niikawa-Kuroki syndrome, it will be later renamed the Kabuki make-up syndrome, because of facial features suggestive masks and Kabuki makeup in the Japanese ancient theater. Its incidence is estimated at one in 32 000 birth in Japan. It's a rare syndrome of unknown cause characterized by the combination of morphological facial variations, growth retardation, skeletal abnormalities, mental retardation (intellectual disability) and abnormal dermatoglyphics. To these signs, are variably added other possible defects and a wide range of pathologies, hardly sparing any organ. We report a case of Kabuki syndrome: a boy of 9 years and 6 months, who visited the Child Psychiatry Department for consultation in Avicenne Military Hospital for language delay. The objective of our study is to report the case of a rare syndrome and often unrecognized and to describe its different clinical manifestations and laboratory as well as the most reported forms of revelation through a literature review.

Case Presentation

A 9 years and 6 months old child, with a male phenotypic sex, comes from a consanguineous marriage (the parents are first cousin), who visited the Child Psychiatry Department for consultation in Avicenne Military Hospital for language delay. He didn't have a medical family history, but he had a personnel history as a neonatal distress and neonatal hypotonia with a refusal of feedings and crises of crying. The child psychiatric interview revealed a delay in psychomotor acquisitions: the child could not walk until the age of 4 years and the language was limited to a few words. On physical examination, the child has dysmorphic face (Figure 1) with eversion of the lower eyelid, long palpebral fissures, arches eyebrows, long eyelashes, flattened tip of the nose, prominent ears, and abnormal dentition. On the hands, the fingers' pulps are protruding with raised center. The child has failure to thrive: height: 115cm (-3 Standard Deviation), with a normal weight: 28 kg . The child had not microcephaly (cranial perimeter: 53 cm). The clavicles were in place and skeletal X-rays didn't show any anomalies. The hernia openings were free and the examination of external genitalia didn't show any anomalies. Psychomotor tests showed an overall delay of psychomotor acquisitions, his mental age was 4 years. The speech and language therapy assessment showed a very limited stock of words with a failure in understanding instructions (language of a 4 year old child) .The cognitive tests showed a moderate intellectual disability. Genetic counseling suspected Kabuki Syndrome and the Genetic karyotyping to metaphase stage was normal, with a normal karyotype 46, XY chromosomes.

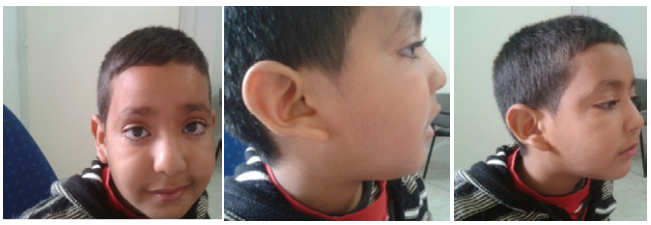

Figure 1: Dysmorphic faces of an Experimental Child.

The results of the performed investigation searched for all body systems congenital malformation revealed an inter ventricular communication and atrial septal of 4 mm in echocardiography. The ENT examination showed a cleft palate with a frenulum treated surgically, hearing loss of 30% at the audiogram. Abdominal ultrasound didn't reveal any urological malformations. The ophthalmic tests were normal, including strabismus or nystagmus. The brain MRI showed a kink outside an enlargement of the right temporal horn. The child had no history of seizures and EEG was normal. The immunological balance, seeking an autoimmune pathology, was negative. Currently the patient has a multidisciplinary management (child psychiatry, speech therapy and psychomotor rehabilitation and adapted schooling).

Discussion

The diagnosis of Kabuki make-up syndrome (KMS) is based on five cardinal clinical signs: facial dysmorphia, growth retardation, skeletal abnormalities, mental retardation and abnormal dermatoglyphics. To these signs, are variably added other possible defects and a wide range of pathologies, hardly sparing any organ. The characteristic craniofacial dysmorphia is present in 100% of the cases and gives the patient a highly evocative appearance with elongated palpebral fissures with eversion of the lateral part of the lower 1/3 of the eyelid, large arched eyebrows with sparse outer 1/3 or notch, short columella with flattened nasal tip; large prominent ears and horn; a cleft lip or palate or arched palate. The teeth are dysplastic, poorly located, spaced or absent and often tapered upper incisors [2-4]. With a low hairline at the back of the neck .The

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growth retardation is usually postnatal [4] He settled in the first year of life and increases with age, compounded by early feeding difficulties. Musculoskeletal abnormalities present in 88% of cases [4], are varied, they include brachydactyly type 5, brachymesophalangy, clinodactyly of the 5th finger, scoliosis, joints hyperlaxity and dislocation. The microcephaly is inconstant. Dermatoglyphic abnormalities are typically reported with persistent fetal volar pads, they are part of the cardinal signs. Mental retardation is variable , generally moderate [5-7]. Psychomotor acquisitions are delayed due to very frequent sensory deficits, especially hearing [3,4,6] and hypotonia [3,4]. A hearing loss is common in 30-40% of the cases, sensorineural origin or secondary to chronic otitis media due to the craniofacial malformation or due to a susceptibility to infections.

In our case, the diagnosis was based on the facial anomalies characteristic of KMS, abnormal dermatophytes, cleft palate, growth retardation, mental retardation, and associated heart defects.

Associated malformations are potentially numerous and varied. They concern: the heart in 50% of the cases [8]. This is most often of septal defects, coarctation of the aorta are found in 25% of cases, it may also include mitral stenosis, aortic or pulmonary, tetralogy of Fallot or abnormal pulmonary venous return [9,10]. The diaphragmatic hernia [4,11,12] is present in 3-8% of cases. Renal abnormalities: renal hypoplasia or renal dysplasia or urinary tract dysplasia, dual system with ureteral duplicated, with or without ureterocele, megaureter are also described [3,4,13]. The association of extrahepatic biliary atresia has been reported sporadically, as a possible neonatal sclerosing cholangitis or congenital hepatic fibrosis [3,4,14,15]. Several publications mention the significant frequency of anorectal anomalies (imperforation or fistula) [16,17]. The central nervous system is not spared. Many anomalies have been described (microcephaly, arachnoid cysts, hydrocephalus with stenosis of the aqueduct, posterior cranial fossa abnormalities, polymicrogyria) [18,19]. The presence of epilepsy is often reported and concerns 10 to 40% of patients. Immune dysfunctions are also common. Most often, these are various autoimmune manifestations: [20,21] hematologic (thrombocytopenia, anemia, neutropenia), celiac disease, insulin dependent diabetes, vitiligo, and, rarely, autoimmune dysthyrodism. Deficits of humoral immunity with hypo gamma globulin are also reported in this context [22] favoring recurrent infections. Endocrine disorders are multiple, deficiency in growth hormone [23] is frequent, and it is to seek when we have short stature smaller than - 3DS and recurrent hypoglycemia [24]. The occurrence of early puberty [25,26] is found in 25-43% of cases. Thyroid disorders (hypo- or hyperthyroidism) and the LH deficiency are possible but uncommon.

The causes of the syndrome remain unknown for now. Multiple intrafamily observations [27] suggest a genetic origin and a dominant inheritance with variable expressivity. However most of the reported cases are sporadic. The identified chromosomal abnormalities are numerous. They can be gonosomal (mosaic 45X-47XXX , X ring) [28,29], multiple autosomal (trisomy 10p, deletion or duplication in 2q37 [30,31]). The multiple rearrangements of 8p22-8p23,1 duplication region, triplication, paracentric inversion are frequently reported in the literature [32,33], but comparative genomic hybridization techniques have not only confirmed this [34] approach. Recently, the possible role of gene C20orf 133, located 20p12-1 region deleted in a patient, was mentioned. [35] Other regions of the genome are potentially involved [36], but the authors insist on the genetic heterogeneity of the syndrome.

The mode of revelation of this syndrome is very variable, it may be hypotonia, feeding difficulties, recurrent infections, growth retardation or obesity. Language delay in the KMS has been reported by several authors, and it is linked in some cases with deafness; other authors suggest a neurological origin of the delay, while in several cases the delay is associated with the presence of a cleft lip and palate, neonatal hypotonia or mental retardation. [37]. It's necessary to complete the clinical approach with an assessment, which will include, at first, karyotyping, heart and abdominal ultrasound, an ENT examination, AEP and scan of the temporal bones, ophthalmologic examination and skeletal X-rays. Depending on the patient's age and clinical guidelines, other explorations will be considered (psychomotor assessment and psychometric assessment tests, Dynamic Dosing GH front of a short stature, looking for an autoimmune pathology and exploration humoral immunity, odonto stomatological balance sheet). Using a pediatric geneticist and a center of competence is needed when it is possible, since it allows the confirmation of the diagnosis, identification of the cases identified and the appropriate implementation of new molecular biology techniques. The management of its anomalies is mainly symptomatic.

Conclusion

Kabuki syndrome is not related only to Asian populations and it is probably still frequently unknown. [3] The diagnosis is based mainly on the clinical picture. The mode of KMS revelations are highly variable as well as the associated malformations. The outcome of these patients can be better understood through the multiplication of identified and tracked cases. The management adapted to each case is needed to improve the course and prognosis of these patients.

References

1. Kuroki Y, Suzuki Y, Chyo H, Hata A, Matsui I (1981) A new malformation syndrome of long palpebral fissures, large ears, depressed nasal tip, and skeletal anomalies associated with postnatal dwarfism and mental retardation. J Pediatr 99: 570–573.
2. Niikawa N, Matsuura N, Fukushima Y, Ohsawa T, Kajii T(1981) Kabuki make-up syndrome: A syndrome of mental retardation, unusual facies, large and protuding ears, and postnatal growth deficiency. J Pediatr 99: 565–569.
3. Kenneth LJ (1994) Kabuki syndrome in Smith's recognizable patterns of human malformation. San Diego Elsevier: 118-119 .
4. Wessels MW, Brooks AS, Hoogeboom J, Niermeijer MF, Willems PJ (2002) Kabuki syndrome: A review study of three hundred patients. Clin Dysmorphol 11: 95–102.
5. Spano G, Campus G, Bortone A, Lai V, Lugie PF (2008) Oral features in Kabuki make-up syndrome. Eur J Paediatr Dent 9: 149–152.
6. Vaux KK, Jones KL, Jones MC, Schelley S, Hudgins L (2005) Developmental outcome in Kabuki syndrome. Am J Med Gent A 132: 263–264.
7. Fareed M, Afzal M (2014) Estimating the inbreeding depression on cognitive behavior: a population based study of child cohort. PLoS ONE 9: e109585.
8. Santiago J , Muszlak M, Goulois E, Ranaivoarivony V (2010) Syndrome de Kabuki en milieu tropical chez un nourrisson hospitalisé pour diarrhée et stagnation pondérale . Archives de pédiatrie 17: 588–593.
9. Mc Mahon CJ, Reardon W (2006) The spectrum of congenital cardiac malformations encountered in six children with Kabuki syndrome. Cardiol Young 16: 30–33.
10. Moral S, Zuccarino F, Loma Osorio P (2009) Double aortic arch: An unreported anomaly with Kabuki syndrome. Pediatr Cardiol 30: 82–84.
11. Hinnichs B, Gramss B, Meineche P (2002) Defective clavicles in Kabuki syndrome. Genet Couns 13: 477–479.
12. van Haelst MM, Brooks AS, Hoogeboom J, Wessels MW, Tibboel D, et al. (2000) Unexpected life-threatening complications in Kabuki syndrome. Am J Med Genet 94: 170–173.
13. Iwama Y, Sugiama S, Kaiga K, Eguchi M, Furukawa T et al. (1987) Kabuki make-up syndrome associated with megaureter. Acta Paediatr Jpn 29: 182–185.

14. Mac Gaughran JM, Donnai D, Clayton SJ (2000) Biliary atresia in Kabuki syndrome. Am J Med Genet 91: 157–158.

15. Nobili V, Marcellini M, Devito R, Capolino R, Viola L et al. (2004) Hepatic fibrosis in Kabuki syndrome. Am J Med Genet A 124: 209–212.

16. Kokitsu-Nakata NM, Vendramini S, Guion AML (1999) Lower lip pits and anorectal anomalies in Kabuki syndrome. Am J Med Genet 86: 282–284.

17. Matsumura M, Yamada R, Kitani Y (1992) Anorectal anomalies associated with Kabuki make-up syndrome. J Pediatr Surg 227: 1600–1602.

18. Kara B, Kayserili H, Imer M, Caliskan M, Ozmen M (2006) Quadri geminal cistern arachnoid cyst in a patient with Kabuki syndrome. Pediatr Neurol 34: 478–480.

19. Di Gennaro G, Condolluci C, Casali C (1999) Epilepsy and polymicrogyria in Kabuki make-up (Niikawa-Kuroki) syndrome. Pediatr Neurol 21: 566–568.

20. Fujishiro M, Ogihara T, Tsukuda K (2003) A case showing an association between type 1 diabetes mellitus and Kabuki syndrome. Diabetes Res Clin Pract 60: 25–31.

21. Hoffman JD, Ciprero KL, Sullivan KE, Kaplan PB, McDonald-McGinn DM, et al. (2005) Immune abnormalities are a frequent manifestation of Kabuki syndrome. Am J Med Gent A 135: 278–281.

22. Zannolli R, Buoni S, Macucci F, Salvucci S, Plebani A, et al. (2007) Kabuki syndrome with trichrome vitiligo, ectodermal defect and hypogammaglobulinemia A and G. Brain Dev 29: 373–376.

23. Mazzanti L, Tamburrino F, Bergamaschi R, Scarano E, Montanari F, et al. (2009) Developmental syndromes: Growth hormone deficiency and treatment. Endocr Dev 14: 114–134.

24. Kapoor RR, James C, Hussain K (2009) Hyperinsulinism in developmental syndromes. Endocr Dev 2009 14: 95–113.

25. Francesschini P, Vardeu MP, Guala A, Franceschini D, Testa A, et al. (1993) Lower lip plits and complete idiopathic precocious puberty in a patient with Kabuki make-up (Niikawa-Kuroki) syndrome. Am J Med Genet 47: 423–425.

26. White SM, Thompson EM, Kidd A, Savarirayan R, Turner A, et al. (2004) Growth, behavior, and clinical findings in 27 patients with Kabuki syndrome. Am J Med Genet A 127: 118–127.

27. Hou JW (2004) Variable expressivity in a family with Kabuki make-up (Niikawa-Kuroki) syndrome. Chang Gung Med J 27: 307–311.

28. Chen CP, Lin SP, Tsai FJ, Chern SR, Wang W, et al. (2008) Kabuki syndrome in a girl with mosaic 45. X/ 47. XXX and aortic coarctation. Fertil Steril 89. 1826e5-1826e7.

29. Rodriguez L, Diego AD, Lorda S I, Gallardo FL, Martínez FML et al. (2008) A small and active ring X chromosome in a female with features of Kabuki syndrome. Am J Med Genet A 146: 2816–2821.

30. Utine GE, Alanay Y, Atkas D, Aktas D, Tuncbilek E, et al. (2008) Kabuki syndrome and trisomy 10p. Genet Couns 19: 291–300.

31. Cusco I, del Campo M, Vilaedell M, González E, Gener B, et al. (2008) Array-CGH in patients with Kabuki-like phenotype: Identification of two patients with complex rearrangements including 2q37 deletions and no other recurrent aberrations. BMC Med Genet 9: 27.

32. Kimberley KW, Morris CA, Hobart HH (2006) BAC-FISH refutes report of an 8p22-8p23.1 inversion or duplication in 8 patients with Kabuki syndrome. BMC Med Genet 7: 46.

33. Milunsky JM, Huang XL (2003) Unmasking Kabuki syndrome: Chromosome 8p22-8p23.1 duplication revealed by comparative genomic hybridization and BAC-FISH. Clin Genet 64: 509–516.

34. Shieh JT, Hudgins L, Cherry AM, Shen Z, Hoyme HE, et al. (2006) Triplication of 8p22-8p23 in patient with features similar to Kabuki syndrome. Am J Med Genet A 140: 170–173.

35. Maas NM, Van de Plutte T, Melotte C, Francis A, Schrander SCT, et al. (2007) The C20orf133 gene is disrupted in a patient with Kabuki syndrome. J Med Genet 44: 562–569.

36. Kuniba H, Yoshiura KI, Kondoh T, Ohashi H, Kurosawa K, et al. (2009) Molecular karyotyping in 17 patients and mutation screening in 41 patients with Kabuki syndrome. J Hum Genet 54: 304–309.

37. Nuray Bayar Muluk Selen Gündüz, Kıvanç Ayas, et al. (2009) Evaluation for language and speech development in Kabuki make-up syndrome: A case report. Int J Pediatr Otorhi 73: 1837–1840.