Phenotypic Analysis of A Case of ‘3MC Syndrome’ with Review of Literature

Soma Rani Roy¹,∗ and Md. Sazzad Kader²

¹Resident Surgeon and Head of Oculoplasty & Ocular Oncology, Chittagong Eye Infirmary, Bangladesh
²Senior Assistant Surgeon, Chittagong Eye Infirmary, Bangladesh
∗Corresponding author: dr.somaroy2020@gmail.com

Abstract. 3MC syndrome is a very rare entity. It’s prevalence is unknown but most cases are reported from Middle East. First case was reported in 1978 and named as Michel syndrome and recently with other three syndromes together these syndromes are named as 3 MC syndrome. All are autosomal recessive disorder and reported from both consanguineous and non-consanguineous parents. Here we phenotypically analyzed a case presented with the features of blepharophimosis syndrome associated with craniosynostosis suggestive of Mischel syndrome which is a part of ‘3 MC syndrome’.

Keywords: Blepharophimosis, epicanthus inversus, telecanthus, craniosynostosis, short 5th finger.

INTRODUCTION

The 3MC syndrome includes 4 rare autosomal recessive disorders which designated earlier as Carnevale, Mingarelli, Malpuech (MIM 248340), and Michaels (MIM 257920) syndromes. Among these, Michel’s or ocuopalato-skeletal syndrome was first reported by, Michel et al. in 1978 [1]. All these syndromes are rare autosomal recessive in inheritance and reported from both consanguineous and non-consanguineous healthy parents. Facial dysmorphism is the main features of these syndromes and these are hypertelorism, telecanthus, blepharophimosis, blepharoptosis, and highly placed arched eyebrows and found in 70 to 95% cases. Cleft palate and lip, cognitive impairment, hearing difficulty and defective postnatal growth can found in 40 to 68% cases. Skeletal disorders like craniosynostosis, radioulnar synostosis and systemic anomalies like genital and vesicorenal are associated in 20–30% cases. Some rare features of anterior segment defects, cardiac anomaly, caudal appendages, umbilical hernia diastasis recti may also found [2]. Though the prevalence of 3MC syndrome is unknown, literature search showed the most affected people reside in Middle East [3].

Here we report a case of 3MC syndrome who presented with the features of blepharophimosis syndrome and craniosynostosis which are predominant feature of Michel syndrome. From best of our knowledge this is the first documented case from Bangladesh.

CASE REPORT

A seven years old girl presented at Orbit & Oculoplastic clinic with the complaints of drooping of right upper lid since birth. She was the first and only baby of a healthy first-degree consanguineous parents who was delivered by cesarean section. Her birth weight was 3200 gm with a normal APGAR score. She had no history of post-natal oxygen inhalation or other illness nor any perinatal illness history of mother but had history of some delay in mile stone of development.

Her general examination revealed short height in comparison to same age girl and weight was 39 kg which above the 95th percentile that is overweight for her age. She had flat occiput and frontal bone with overriding of fronto-parital suture with brachycephaly skull; high arched palate; short broad hand with short 5th finger; broad feet with a gap between great and second toes; normal sized low set ears with hearing difficulty (Figures 1 and 2). She also had mild mental retardation. Her facial examination showed, bilateral ptosis with more in right eye (palpebral fissure height 4 and 7 mm), shallow orbit with mild pseudoptosis, telecanthus (Intercanthal distance 38 mm and
Soma Rani Roy and Md. Sazzad Kader

Figure 1. Facial features. (A) Bilateral ptosis, epicanthus, telecanthus, hypertelorism, sparsed hair in eyebrow. (B) High arched palate. (C) Brachycephaly, flat occiput and frontal bone, malar and mandibular hypoplasia, low set ear.

Figure 2. Limb abnormalities. (A) Short broad hand with short 5th figure. (B) Short feet with wide gap between great toe and second toe.

Her best corrected visual acuity was 6/9 in both eyes with wet refraction of $-0.75 \times 90^\circ$ in right eye and $-0.50 \times 90^\circ$ in left eye with normal ocular structure in both anterior and posterior segment. She was primarily diagnosed as Michel syndrome and according to literature review she was finally diagnosed as 3MC syndrome. Spectacles was prescribed and counseled for bilateral ptosis surgery. Parent were unwilling to do ptosis surgery and she was kept in regular follow up of 6 months interval.

**DISCUSSION**

The first reported case were 4 sibling (3 male, 1 female) from a normal, non-consanguineous parent by Michel in 1978 [1] and De L Paz in 1991 [4]. They had features of blepharophimosis, blepharotosis, epicanthus inversus (BBE); hypertelorism; anterior segment defect of eye; cleft lip and cleft palate; skeletal defect; deafness and mild mental retardation. In 1990 Cunniff [5] also reported one case of Michel syndrome and according to literature review she was finally diagnosed as 3MC syndrome. Spectacle was prescribed and counseled for bilateral ptosis surgery. Parent were unwilling to do ptosis surgery and she was kept in regular follow up of 6 months interval.

1994 by Guion et al. [6]. In 1989 Carnevale et al., reported 2 cases from a consanguineous parent with BBE; large low set ears; convergent squint; abdominal muscle agenesis (partial); cryptorchidism; hip dislocation and developmental delay [7]. Mingarelli et al. in 1996 described similar oculo-facial-skeletal-abdominal abnormality associated with hearing difficulty with normal shaped ear but normal intelligence [7]. In 1983 Malpuech et al. and subsequently Reardon et al. in 2001, Kerstjens-Frederikse et al. in 2005 reported some cases associated with urogenital anomalies; caudal appendages along with hypertelorism, ptosis, epicanthus, prenatal growth deficiency and mild mental retardation which were mention as Malpuech syndrome [7–9]. These overlapping phenotype (Table 1) were reviewed by Titomanlio et al. in 2005 and they explained that all these syndromes are not separate disorders rather than a single recessive spectrum. They also proposed the name of ‘3 MC syndrome’ (Malpuech-Mischel-Mingarelli-Carnevale syndrome) [7]. All these reported syndromes are from both consanguineous and non-consanguineous parents.

Our reported case was from a normal consanguineous healthy parent. She had typical BBE, telecanthus, hypertelorism which is present in 70 to 90% cases of 3MC syndrome but highly arched eyebrow was absent. She had skull bone deformities, malar hypoplasia, sparse lateral eyebrow as reported by Guion-Almeida et al. [6] in a case of Michel syndrome and this case was from a consanguineous parent which is similar to present case. Any radio-ulnar synostosis, abdominal diastasis and systemic problem like vesico-renal or genital abnormality which are mostly found in Carnevale and Malpuech syndrome was absent in our case [7–9]. Patient had low set ears, hearing difficulty; short 5th figure and mild mental retardation which are features of most Michel syndrome. In our patient, cleft lip and palate was absent which is found in 40–68% cases but it was also absent in cases reported by De la Paz et al. 1991 [4] Cunniff and Jones 1990 [5].

Literature search showed most patients of 3MC syndromes are from Middle East though the prevalence has not yet known [3]. All these syndrome has most common presentation of blepharophimosis, blepharotosis, epicanthus inversus which in together is called blepharophimosis syndrome and autosomal dominant in inheritance. But these syndromes are autosomal recessive in inheritance and reported from both consanguineous and non-consanguineous parents. Genetic analysis showed these disorders are caused by mutation in mostly 3 genes and these are mannose-binding lectin-associated serine protease (MASP1), COLEC11 or COLEC10 genes [2, 10, 11]. Up to 2020, total 46 ‘3 MC’ patients from 34 families are reported to have the mutation of above mentioned genes and were from consanguineous parents [4]. Most patients (26 patients) had mutation in (MASP 1) gene [3]. Mutation of these gene causes production of defective corresponding protein resulting in defective cell migration at early stage of
embryonal development. When cell migration is impaired it interferes with the ontogenesis of tissue and organ resulting in various abnormalities [2].

Here we analyzed the phenotypic features of our patient and due to unavailability of genetic test, we were unable do this. Our analysis showed most features are from Michel syndrome. As all 4 syndromes in combination are expressed as 3 MC syndrome [OMIM 265050], ours is also a case of 3MC syndrome from a normal consanguineous Bangladeshi parent and from best of our knowledge is the first case from Bangladesh.

CONCLUSION

3 MC syndrome is rare disease and phenotypic features analysis will help ophthalmologist for proper management and referral where genetic test are limited or not available.

CONFLICT OF INTEREST

The authors declared no conflict of interest.

FUNDING

None.

REFERENCES


