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A CASE OF BILATERAL ANOPHTALMIA COMBINED WITH UNILATERAL CLEFT LIPS AND CLEFT PALATE

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ABSTRACT

Anophthalmia (complete absence of eyes) and microphthalmia (small eyes) are two of the more common of the severe, disabling congenital anomalies of the eye. Many infants with anophthalmia or microphthalmia will have a coexisting defect involving non-eye structures or other eye structures. Pathogenesis of anophthalmia/microphthalmia is a complex interplay of single gene mutation, chromosomal anomalies, and environmental factors. We reported a one week old male who was born of a full-term by normal spontaneous delivery at 37 weeks of amenorhea from non-consanguineous parents (25 years & 18 years) and was their firstborn. The mother of the baby smoked and chewed tobacco, consumed alcohol, and use decoction and herbal medicine. The ophtalmological examination showed a bilateral empty orbits with an inflamed

palpebral conjunctiva and purulent secretions. Besides, the baby presented a clift lips associated with clift palate. The main etiology of this deformity was not known because neither antenatal nor postnatal screenings were performed in order to elucidate the causes. We adressed some suggestions to avoid the repetition of this preventable malformation.

KEY WORDS: Anophtalmie, cleft lips, cleft palate, smoking, herbal medicine.

INTRODUCTION

Anophthalmia (complete absence of eyes) and microphthalmia (small eyes) are two of the more common of the severe, disabling congenital anomalies of the eye. Many infants with anophthalmia or microphthalmia will have a coexisting defect involving non-eye structures orother eye structures. Diagnosis of anophtlamia is usually clinical, following a complete ophthalmological examination.[1] Pathogenesis of anophthalmia/microphthalmia is a complex interplay of single gene mutation, chromosomal anomalies, and environmental factors.[2] The best estimates of the birth prevalence of microphthalmia and anophthalmia from well maintained population based registers are 14 and 3 per 100 000 births, respectively.[3] Anopthalmia with contralateral cleft lip and palate is an extremely rare anomaly.[4]

Objective: To report a rare case of newborn male presented bilateral anophthalmia and right unilateral cleft lip and palate.

OBSERVATION

A one week old male who was born of a full-term by normal spontaneous delivery at 37 weeks of amenorhea from non-consanguineous parents (25 years & 18 years) and was their firstborn. He was brought by his parents for consultation at pediatric service of University Clinic Center Befelatanana. The chief complaints reported by his parents were the absence of reaction to illumination of the eyes with bilateral suppurating palpebral conjunctiva. The housewife mother had an antenatal history of leucorrhea, burning sensation of the micturation pushing her to use decoction and herbal medecine intake throughout the pregnancy. Moreover, she is a smoking mother evaluated about 2 packages a week. She did 3 prenatal cares, received three doses of antitetanic vaccine and an iron and folic acid supplementation since the third month of pregnancy. None of antenatal screnings were performed such as blood test and obstetrical ultrasound. A part from decoction and herbal medecine, she had no history of drug consumption nor exposure to X-ray. Physical examination revealed a subicteric baby with a good peripheric and axial tonicity, in quadriflexion and vigorous. His

cranial circumferences measured 33 cm, the fontanelle was planar, permeable at about 2 fingers wide. He measured 50cm, weighed 2,700 Kg, 36,9°C of temperature. The ophtalmo-logical examination showed a bilateral empty orbits with an inflammed palpebral conjunctiva and purulent secretions. Besides, the baby presented a clift lips associated with clift palate (1a, 1b). During a permeability testing of the choan, the catheter passed without difficulty confirming the presence of cleft palate. The remaining clinical examination was normal, we didn't find any other abnormalities either. So, we posed a bilateral anophtalmia, cleft lift and cleft palate accompanied with conjunctivitis as diagnosis. We prescribed an eye wash with Ringer lactate twice a day and Rifamycin eye drops 6 times a day during 10 days period as treatment. In addition, we recommended a D vitamine 1200UI per day and an exclusive maternal breastfeeding. A further medical screening within 10 days was planed but the parents of the baby did not come back.

Figure 1a and 1b: bilateral anophtalmia combined with cleft lips and palate.

DISCUSSION

Anophthalmia (complete absence of eyes) and microphthalmia (small eyes) are two of the more common of the severe, disabling congenital anomalies of the eye. The association of anopthalmia with cleft lips and palate are repoted to be a rare disease We report a case of a baby presenting a bilateral anophtalmia, right unilateral cleft lift and palate accompanied with bilateral conjunctivitis.

Many cases of anophtalmia have been reported. Meliha H et al reported a first case of anophtalmia in a female child delivered at University Clinic Center Tuzla in Bosnie

Herzegovine.[5] Faten and al reported a rare case of newborn male presented with right anophthalmia and left unilateral complete cleft lip and palate, facial clefting and choanal atresia. They named it as an anophtalmia plus syndrome.[6] Our patient presented a right cleft lips with cleft palate but the anophtalmia was bilateral and there was no choanal atresia. Ozcelik et al reported a 4 year old baby with unilateral complete right cleft lip and palate, absent vomer bone, right anophthalmia, left congenital nystagmus and mental-motor retardation, which are clinically features similar to Fryns anophthalmia- plus syndrome.[7] Warburg *and al*, reported a female infant with bilateral extreme microphthalmia, bilateral oblique facial clefts, bifid uvula, bilateral congenital glaucoma, bilateral lower lid colobomas, low set ears, bilateral choanal stenosis, frontal encephalocele and craniosynostosis.[8] Wiltshire et al documented in the literature a boy with bilateral extreme microphthalmia, left facial cleft, bifid uvula, cataracts with anterior segment disorganization, right choanal atresia and an abnormal nose.[9]

All the aforementioned share the presence of anophthalmia or microphthalmia. The association of anophtalmia microphtalmia with cleft lip and or palate is classified as an anophtalmia plus syndrome. Our case deserves to be categorized as an anophtalmia plus syndrome also.

Concerning the causes of anophtalmia, cleft lips and cleft palate, many theories have been suggested. Verma AS et al suggested that the exact pathogenesis of anophthalmia remains unknown Epidemiological studies have predicted two main factors causing anophthalmia and/or microphthalmia: heritable factors and environmental factors while Anophthalmia/ microphthalmia have a complex etiology with chromosomal, monogenic and environmental causes. Identified factors include gestational-acquired infections, maternal Vitamin A deficiency, exposure to x -rays, solvent misuse and thalidomide exposure.[1] The mother of our patient reported not to be exposed to any radiation nor drug consumptions across the pregnancy period. But the gestational-acquired infections were not proven for she didn’t do any serology.

Abdolreza J and al conducted a retrospective study to evaluate family history and risk factors for cleft lip and palate patients and their associated anomalies in Teheran. They concluded that Consanguineous marriage, low folic acid consumption and consanguineous marriage were strongly associated with increased risk of CL/P.[10] The parents our patient verbaly reported that they are not relative but DNA Test was not performed to prove that

affirmation.Moreover, she took folic acid drug. According to abdolreza et al, prenatal screening and genetic tests are strongly recommended to detect deformities. Nevertheless, the mother of our baby patient didn't do any screening during pre and posnatal period. Besides, she didn't return for further follow up. In Madagascar, according to National Statistical Institute, in 2012, 37% of women did not do a postnatal visit during 41 days following the birth, against 35% in 2008.[11] In addition, Mark C and al reinforced that women who receive prenatale care during the first trimester have better pregnancy outcomes than women who have little or no prenatal care.[12] Verma A S and al reported that Cleft lip and palate association with intrauterine varicella infection has not been widely reported or proven yet[1] whereas Boyer S G and al emphasized that TORCH is an acronym which stands for Toxoplasmosis, Other (Parvovirus B19, Varicella-Zoster virus infection, Syphilis, Hepatitis B), Rubella virus, Cytomegalovirus infection and Herpes Simplex virus infection is an intrauterine infection. These groups of infections are the main threats of serious congenital infection during pregnancy, which may ultimately cause fetal damage or other anomalies. In most cases, the infection can be severe enough to cause serious damage to a fetus than his/her mother. The gestational age of the fetus influenced the degree of severity.[13] Then, during the research conducted by Muhammad A Z and al to evaluate the sero-positivity of TORCH infections during pregnancy in Peshawar Pakistan region revealed that the frequency of TORCH infection during pregnancy is 6.99%. Frequency of anti Toxoplasma IgM antibodies is 2.5%, rubella 1.5%, cytomegalovirus 1.8% and Herpes simplex virus 1.1%. Their study revealed that TORCH infections require serious attention as these infections cause serious abnormalities and anomalies in children as well as to pregnant females.[14] It is stated that environmental factors such as prenatal exposures to rubella, toxoplasmosis, varicella cytomegalovirus, alcohol, thalidomide, retinoic acid[15], hydantoin, and lysergic acid diethylamide can cause an/ microphthalmia.[16] According to Mariman, environmental influences on fetal development (Mariman, 1998) such as exposure to rubella virus, may form the cause of anophtalmia.[17] Rajnish K Y, Siddhartha M, Sudipta S supported that TORCH disease can cause congenital malformations like central nervous system, resulting in neurological abnormalities, visual impairment and deafness, in addition to other malformations, such as congenital heart disease.[18] Prenatal exposure to these teratogens is preventable.[16] In our case, the mother of the baby didn't doany serology to detect the presence of TORCH during the pregnancy. If she had done the blood test, and positif, the infant deformity would have been avoided.

Williamsons and FitzPatrick identified recent genetic studies done by Williamsons and FitzPatrick in 2014 demonstrated a genetic cause in 80% of the cases with bilateral severe microphthalmia/anophthalmia while we have no clear-cut evidence to say the genetical origin of bilateral anophtalmia of our patient because their is no genetic research centre in Madagascar.[19]

As far as the usage of herbal medicine to cause deformities is concerned, an exclusive use of medicinal plants as treatment of malaria and urinary tract infections during pregnancy may pose a health risk for the mother and her unborn child.[20] The mother of our patient took herbal medicine and decoction. Being students, having no education, having low income and having tertiary education level make women more likely to use herbal medicine during pregnancy.[21] [22] [23] The other factors that make women more likely to consume herbal medicines are being primipare.[24] That fact compares to the case of the mother of our patient, she is a primipare housewife whom the education level is low. The common benefits of using herbal medicine during pregnancy include managing vomiting and nausea, reducing the risk of preeclampsia, managing urinary tract infection and common cold, and shortening of duration of labour.[25]

During 1997, Andriamialy R CL et al had conducted a retrospective study about a premature childbirth. They registered 1 394 (18,1%) premature delivery of 7 717 childbirth. The teens and the women more than 35 years-old were the most prone to develop a premature childbirth. Bisides, more than 25% of the pregnant women had a bad habit of toxic products intake such as alcohol, tobacco and decoction. Our child patient was born from a smoking and decoction user mother.[26] So, the use of herbal medicine is a common phenomenon in low and middle income countries like Madagascar. Herbal medicine has an importante place in Malagasy populations daily life either in a rural or urban areas. The women can't separate themselves from the plant. In Mahajanga, the herbalists sell the herbal medicines for the wellbeing of the people. But the enhancement of the value of herbal medicine doesn't prevent the women from picking wild or grown plants growing around their houses. RANARIJAONA H and al divided the medicinale plants into 2 groups, the curative and cosmetic medicines. The curative herbal medicines are used to treat the mother and newborn, painful menstruation, unregular menstruation cycle, miscarriage threat, stimulate lactation, maternal genital infection during antenatal and postnatal periods. The survey conducted toward medical staff at maternity hospital of Mahabibo in Mahajanga to identify the most

chief symptoms in which women are pushed to use herbal medicines highlighted that the maternal health state before and during the pregnancy, the complications of the menstruation, uterine affection, the problem of sterility, abortion, postpartum and postnatale diseases are the most reasons.[27]

Cecilie S et al conducted a quantitative, ethnobotanical study on Malian women's attitudes towards the use of medicinal plants during pregnancy. They observed that 79.9 % had used medicinal plants during pregnancy. Only 17 women (8.5 %) had received a recommendation from a traditional practitioner.[20]

It is reported that the exclusive use of medicinal plants as treatment of malaria and urinary tract infections during pregnancy may pose a health risk for the mother and her unborn child.[20] The common untoward effects of using herbal medicine in pregnancy are heartburn, premature labour, miscarriage, increase blood flow, abortion and allergic reactions.[25] Different studies revealed that using herbal medicine during the first 12 weeks and the last 12 weeks of gestation is dangerous for the fœtus.[25] Catherine A. F and al, reported the incidence and nature of herbal medicinal products' adverse events and herb–drug interactions used by some pregnant and postnatal women. They found that the use of An-Tai-Yin (Angelica sinensis) and parsley (for prevention of miscarriages) during the first trimester was associated with musculoskeletal and connective tissue congenital malformations, and eye congenital malformations in the offspring. Herbal medicinal products such as almond oil, chamomile, licorice, and raspberry leaf used during pregnancy may be associated with adverse maternal and perinatal outcomes or toxicity from contaminants.[28]

Regarding the attitude of the mother of our baby patient, she smoked and chewed tobacco evaluated about 2 packages a week. In 1990 in Germany, a multicenter allergy study surveying 5,395 postpartum women concluded that 28.6% smoked during pregnancy.[29] Dudenhausen and al noticed during their study from 2001–2002 investigating the cotinine-concentration in the urine of 323 pregnant women in the second trimester Approximately one quarter of German future mothers smoked during pregnancy.[30] The smoking mother of our patient was jobless and wastful. It is explained that indicators of socio-economic status are an independent, reliable correlate of active smoking during pregnancy. Studies from Australia and Texas, USA indicated that low socio-economic status three or more times below the poverty line combined with the absence of health insurance increase the risk for smoking

during pregnancy, regardless of ethnicity. The smoking rate among Australian women with low socio-economic position.[31] [32]

As for the side effects of tobacco, in a Dutch study from May 2012 investigating the effects of smoking on the maternal immune system by examining first-trimester decidual tissue and peripheral blood, researchers concluded that mothers smoking during pregnancy have an altered local and systemic immune system.[33] Smoking cigarettes has a tremendous negative impact on the genetic and cellular level of not only the mother but of the fetus as well. If certain genetic predispositions are present, the adverse effects of smoking during pregnancy are multiplied. Genetic and epigenetic mechanisms in combination with cytogenetic damage are believed by a 2012 study from North Carolina, USA, to play an important role in the pathogenesis of malformations and adverse outcomes associated with smoking and pregnancy.[34] Patricia F and Andrea S added that babies of smoking mothers have more deformities, lung diseases, and middle ear infections when born to mothers who smoke to start smoking when they get older.[35]

We have read the case of our baby patient that he was exposed to differents aformentioned possibles causes of his deformities. He had an high risk to develop malformations. We couldn't identify with accuracy the exact etiology of his anophtalmia, cleft lips and cleft palate because none of the screenings was performed neither in antenatal nor in postnatale. Anyway, we have some suggestions to address about this issue.

Regardless of genetic and chromosomal etiologies of anophtalmia, cleft lips and cleft palate, somes cause are preventables such environemnt, infections and toxic.

Firstly, Pregnant females should be encouraged to receive adequate nutrition, which is best achieved through consumption of a healthy, balanced diet, and to refer to guidelines on healthy eating.[36] Secondly, pregnant woman should follow properly the prenatal and the postnatal cares in order to detect and treat on ahead the eventual infections which may harm the mother and fetus. In addition, education, support and assistance are of high importance to decrease maternal and fetal morbidity and mortality by sensitising them with Smoking cessation campaigns that target the smoking future mother as well as her social network. Beyond that, stricter pharmacovigilance measures should be taken to avoid possible harm arising from current herbal medicinal product use during pregnancy and herbal medicinal

products should not be recommended during pregnancy until robust evidence of safety is available.

In conclusion, Anophthalmia (complete absence of eyes) and microphthalmia (small eyes) are two of the more common of the severe, disabling congenital anomalies of the eye. We reported a case of report a rare case of newborn male presented bilateral anophthalmia and left unilateral cleft lip and palate. The baby was born from a smoking mother, alcoholic, decoction and herbal medecine user. The exact cause of the deformity of the baby was not precised. A prevention is crucial by following properly the antenatal and postnatal cares for pregnant women.

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