Congenital Diaphragmatic Hernia and Maternal Hypothyroidism: A Case Report

Manisha Behal[1,*], Rajeev Vinayak[2]

[1]Associate Professor, Dept. of Obstetrics & Gynaecology, [2]Associate Professor, Dept. of Pediatrics, MMU Medical College & Hospital, Kumarhatti, Solan, Himachal Pradesh

***Corresponding Author:**
Email: manishabehal30@gmail.com

Abstract

Congenital Diaphragmatic hernia is a rare entity with incidence of 1:2000-3000 live births and causes are still largely unknown. This case hints about possible relationship with maternal hypothyroidism which needs further research to confirm/refute.

Key words: Congenital diaphragmatic hernia, Hypothyroidism, Newborn

Access this article online	
Quick Response Code:	Website: www.innovativepublication.com
	DOI: 10.5958/2394-2754.2016.00032.1

Introduction

Congenital diaphragmatic hernia (CDH) has an incidence of 1: 2000–3000 live births[1,2,3,4,5] and accounts for 8% of all major congenital anomalies. The left-sided Bochdalek hernia occurs in approximately 85% of cases which have a mortality of 45-50%. Associated anomalies are present in 10-50% of patients with CDH; these anomalies confer a twofold relative risk of mortality when compared with patients with isolated CDHs.[6,7]. The etiopthogenesis of CDH in humans is unknown[8] but in animal models several teratogenic processes including exposure to chemicals have been found to induce CDH[9,10]. This case is presented as mother had high raised levels of TSH and there is resemblance of Herbicide Nitrofen (which cause CDH in experimental models) to thyroid hormone.

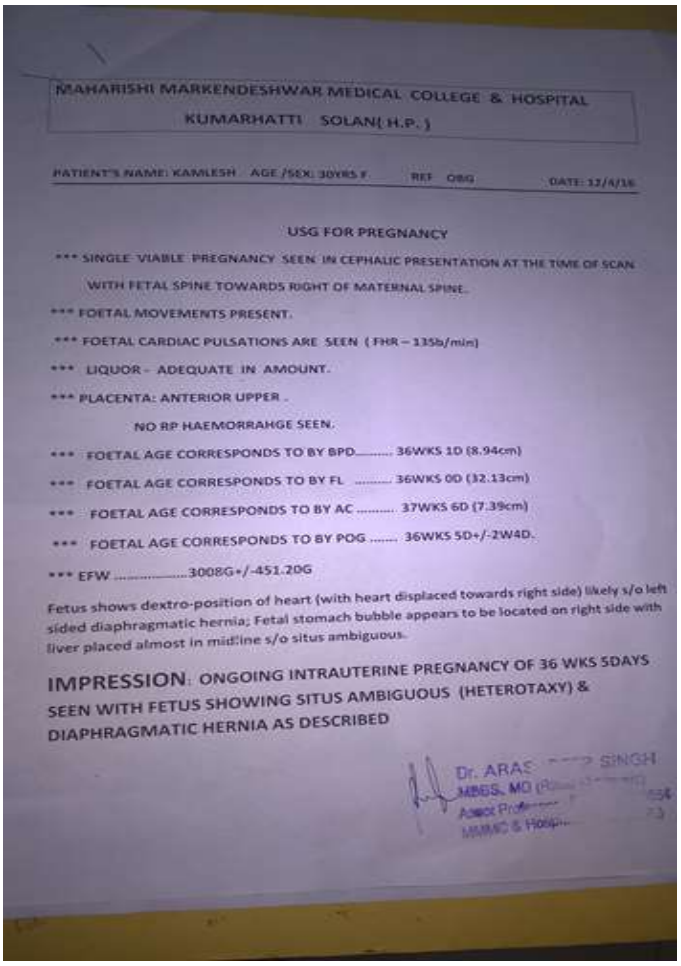
Case Report

A 30 year old female, an unbooked case was admitted on 09/04/2016 in Obstetrics and Gynecology department of our institute for safe confinement. She was of 39 weeks 5 days gestational age on admission (G3P2L2A0). She had previous two normal live children born by vaginal delivery at Civil hospital, Solan, 7 and 4 years back. Present pregnancy ANC checkups were done regularly at District hospital, Solan. She was a known case of hypothyroidism since December 2015 but was not on any medications. No h/o any other drug intake except iron/folic acid and calcium supplementation. Antenatal US done on 08/04/2016 at regional hospital Solan was normal. T3/T4/TSH done on 10/04/2016 were 0.49 ng/ml, 3.12 mcg/dl and 177.5 microIU/ml respectively. TSH done on 08/04/2016 was 170.3microIU/ml. Lipid profile showed raised TG-320.2mg/dl, Total Cholesterol 344mg/dl and LDL 232 mg/dl. HIV, HBsAg, VDRL and Anti HCV were all negative/Non-reactive. Blood group was AB Rh positive. USG done in our institution on 12/04/2016 showed Heart displaced to right side, Fetal stomach bubble located on right side with Liver placed almost in midline, likely suggestive of left side Diaphragmatic Hernia (Fig. 1).

She delivered by normal vaginal delivery on 12/04/2016 1:57 PM, a live female child. Baby had inadequate respiratory efforts after birth and was immediately intubated and given Bag and tube ventilation. Baby was shifted to NICU and patient put on Pressure limited ventilator support (Fig. 2). Baby was of 2.7 kg weight and showed no external major/minor malformations. Anthropometry was normal. X ray chest was done within ½-1 hr after birth (Fig. 3). It showed Intestinal loops in left hemi thorax with heart and trachea shifted to right. Right side lung was collapsed. No air was seen in abdomen. NG tube tip was seen in right side of chest. Diagnosis of Congenital diaphragmatic Hernia most probably Bochdalek type was made. Umblical vein catheterization was done and baby put on ionotropes and supportive treatment. VBG done showed Ph-Low, PCO2 74mmHg, PO2 33mmHg on FiO2 100%. Hb 11.3gm%, Platelets- 2.52 lacs/mm3, RFT and LFT were normal. Blood gp- A Rh positive. To rule out other associated congenital anomalies USG Abdomen, Spine and ECHO heart could not be done due to baby being on ventilator. Patient was seen by Pediatric surgeon who advised surgery after stabilization of baby. Baby expired on 12/04/2016 at 11:30 PM even after adequate ventilator and supportive management.

Some important points which arise in this case are

1. Whether Raised TSH is a co-incidental finding or is associated with CDH?
2. Was such a severe presentation and Rapid progression was correlated to Raised TSH in mother or it was due to large size hernia of Intestine, Stomach and Liver only.



MAHARISHI MARKENDESHWAR MEDICAL COLLEGE & HOSPITAL
KUMARHATTI SOLAN(H.P.)

PATIENT'S NAME: KAMLESH AGE /SEX: 30YRS F REF OBG DATE: 12/4/16

USG FOR PREGNANCY

*** SINGLE VIABLE PREGNANCY SEEN IN CEPHALIC PRESENTATION AT THE TIME OF SCAN WITH FETAL SPINE TOWARDS RIGHT OF MATERNAL SPINE.
*** FOETAL MOVEMENTS PRESENT.
*** FOETAL CARDIAC PULSATIONS ARE SEEN (FHR – 135b/min)
*** LIQUOR - ADEQUATE IN AMOUNT.
*** PLACENTA: ANTERIOR UPPER .
NO RP HAEMORRAHGE SEEN.
*** FOETAL AGE CORRESPONDS TO BY BPD..... 36WKS 1D (8.94cm)
*** FOETAL AGE CORRESPONDS TO BY FL 36WKS 0D (32.13cm)
*** FOETAL AGE CORRESPONDS TO BY AC 37WKS 6D (7.39cm)
*** FOETAL AGE CORRESPONDS TO BY POG ..... 36WKS 5D+/-2W4D.
*** EFW .....3008G+/-451.20G

Fetus shows dextro-position of heart (with heart displaced towards right side) likely s/o left sided diaphragmatic hernia; Fetal stomach bubble appears to be located on right side with liver placed almost in midline s/o situs ambiguous.

IMPRESSION: ONGOING INTRAUTERINE PREGNANCY OF 36 WKS 5DAYS SEEN WITH FETUS SHOWING SITUS AMBIGUOUS (HETEROTAXY) & DIAPHRAGMATIC HERNIA AS DESCRIBED

Dr. ARAS SINGH
MBBS, MD
Assoc Prof
MMMC & Hosp

Fig. 1:

Fig. 2:

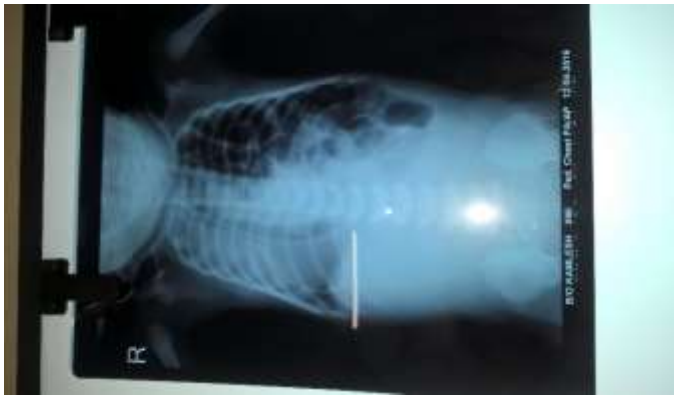


Fig. 3:

Discussion

The most commonly used teratogenic model for CDH is the nitrofen model. Nitrofen is a Protox-inhibiting herbicide of the diphenyl ether class. The teratogenic effect of nitrofen is exerted mainly during the critical period of organogenesis. There have been various studies that suggest that Nitrofen may interact with embryonic nuclear receptors for thyroid hormone[10]. The configuration of Nitrofen is very similar to that of triiodothyronine (T3) and thyroxine (T4) which are necessary for normal fetal lung development[11]. Maternal hypothyroidism has been associated with an increased risk of many birth defects in newnorns[12,13], but information on it being a causative agent in CDH is not confirmed[14]. When it was used in rats experimentally it interfered with the lung development causing lung hypoplasia and various anatomical malformations including diaphragmatic hernias [10,15,16,17.] This hypothesis links pulmonary hypoplasia and CDH with thyroid hormone status of mother while she is pregnant. Only 60-90% of exposed rat pups demonstrated CDH suggesting a "dual-hit" hypothesis, in which one insult affects the lungs and second insult affects the diaphragm development causing CDH. Other studies show direct delivery of the nitrofen compound (and not active metabolites) into the fetus through the maternal–fetal circulation, indicating direct effects of nitrofen on fetal diaphragm and lung development [10]. Recent studies have stated that nitrofen alters the retinoic acid pathway and so thyroid hormones doesn't play a part as a causative agent in CDH. Nitrofen may also cause epigenetic defects, as miR-200b expression is seen to be decreased in nitrofen caused hypoplasia of lungs[18]. Nitrofen and other teratogenic chemicals used on experimental animals inhibit retinal dehydrogenase-2 (RALDH-2), an enzyme necessary for the production of retinoic acid, thus causing vitamin A deficiency which contributes to pathogenesis of CDH.

Further studies are needed to confirm or refute these hypothesis and this makes our case an interesting one.

References

1. Langham MR Jr, Kays DW, Ledbetter DJ, Frentzen B, Sanford LL, Richards DS. Congenital diaphragmatic hernia. Epidemiology and outcome. Clin Perinatol (1996) 23:671–88.
2. Robinson PD, Fitzgerald DA. Congenital diaphragmatic hernia. Paediatr Respir Rev 2007;8:323–335.
3. Ackerman KG, Pober BR. Congenital diaphragmatic hernia and pulmonary hypoplasia: new insights from developmental biology and genetics. Am J Med Genet C Semin Med Genet 2007;145:105–108.
4. Slavotinek AM, Warmerdam B, Lin AE, Shaw GM. Population-based analysis of left- and right-sided diaphragmatic hernias demonstrates different frequencies of selected additional anomalies. Am J Med Genet A 2007;143:3127–3136.
5. Zaupa P, Kleinlein B, Hollwarth ME. Bilateral congenital diaphragmatic hernia and gastroschisis in a newborn: can low intrathoracic pressure prevent the pulmonary hypoplasia. Pediatr Surg Int 2007;23:711–713.
6. Tonks A, Wyldes M, Sommerset DA, et al. Congenital malformations of the diaphragm: findings of the West Midlands congenital anomaly register 1995 to 2000. prenatal diagnosis. 2004.24:596-604. [Medline]
7. Slavotinek AM. Single gene disorders associated with congenital diaphragmatic hernia. Am J Med Genet C Semin Med Genet 2007;145:172–183.
8. Cunnif C, Lyons Jones K, Jones MC (1990) Patterns of Malformation in children with congenital diaphragmatic defects. J Pediatr 116:258-261
9. Cullen ML, Klein MD, Philippart AI (1985) Congenital Diaphragmatic hernia. Surg Clin North Am 65:1115-1138.
10. Brown T, Manson J. Further characterization of the distribution and metabolism of nitrofen in pregnant rat. *Teratology* (1986)34:129–39.
11. DeMello DE, Davies P, Reid LM (1989) Lung growth and development. Curr Pulmonol 10:159-208.
12. Potter JD (1980) Hypothyroidism and reproductive failure. Surv Gynecol Obstetr 150:251-255.
13. Khoury M J, Becerra JE, d'Almada PJ (1989) Maternal thyroid disease and risk of birth defects in offspring: a population-based case-control study. Paediatr Perinat Epidemiol 3:402-4.
14. Albert P. Bos, Annemieke M. Pattenier, Rick E. Grobbee, Dick Lindhout, Dick Tibboel, Jan C. Molenaar, Hum Genet (1994);94:445-446.
15. Greer JJ. Current concepts on the pathogenesis and etiology of congenital diaphragmatic hernia. *Respir Physiol Neurobiol* (2013)189:232–40. doi:10.1016/j.resp.2013.04.015.

16. Stone LC, Manson JM. Effects of the herbicide 2, 4-dichlorophenyl-p-nitrophenyl ether (nitrofen) on fetal lung development in rats. *Toxicol Appl Pharmacol* (1981) 20:195–207. doi:10.1016/0300-483X(81)90051-2.
17. Costlow RD, Manson JM. The heart and diaphragm: target organs in the neonatal death induced by nitrofen (2, 4-dichlorophenyl-p-nitrophenyl ether). *Toxicology* (1981);20:209–27. Doi:10.1016/0300-483X(81)90052-4.
18. Pereira Terra P, Deden AC, Zhu F, Barb I, Jorge Correia P, Richard K. MicroRNA miR-200b rescues abnormal branching morphogenesis of nitrofen- induced hypoplastic lung explants. Canadian Association of Pediatric Surgeons 45th Annual Meeting. Charlottetown, PE: Canadian Association of Pediatric Surgeons (2013).