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REVIEW ARTICLE

The Unborn Patient: An Update on Fetal Therapy

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ABSTRACT

The traditional method of managing a malformed fetus involves either medical termination of pregnancy or postnatal management. Presently, with advancements in radiodiagnosis, almost all of the congenital malformations occurring in these unborn 'patients' can be diagnosed antenatally. With this, fetal intervention, though in its baby steps, has become a reality. The present article reviews the advancements made in fetal therapy.

Keywords: Antenatal diagnosis, Fetal therapy, Medical termination of pregnancy.

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INTRODUCTION

The human fetus has for centuries remained a medical recluse in an opaque womb. However, in the 21st century, with lot of advancements in radiodiagnostic techniques, the accurate delineation of the normal and abnormal fetal anatomy has become a reality. Today, almost all of the congenital malformations occurring in these unborn 'patients' can be diagnosed antenatally. However, knowledge about the management of these anomalies is not widely prevalent. The exact pathology of the anomaly involved, its natural course, complications and treatment options needs to be known.

It is important that surgeons familiar with the management of these lesions after birth be involved in management decisions and family counseling. Because of various reasons, many of these fetuses are unnecessarily getting terminated. Many of them are subjected to cesarean section, when not indicated. In the present article, an honest effort has been to address these issues.

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RATIONALE FOR FETAL TREATMENT: SELECTION, FEASIBILITY AND RISK

Until recently, when the various therapeutic options became available, the only dilemma was whether to abort the fetus or wait till delivery. Knowledge regarding the natural course of the disease and the pathology involved has given new insights into the management of these complex anomalies. Antenatal intervention for a few selected conditions has shown some promising results. The rest of the article would try to update regarding the current standards in fetal therapy.

Defects usually managed by Termination of Pregnancy[1]

- Anencephaly, hydranencephaly, alobar holoprosencephaly
- Severe anomalies associated with chromosomal abnormalities (e.g. trisomy 13)
- Bilateral renal agenesis
- Severe, untreatable, inherited metabolic disorders, e.g. Tay-Sachs disease
- Lethal bone dysplasias, e.g. thanatophoric dysplasia, recessive osteogenesis imperfect

Defects best corrected after Delivery at Term[1]

- Esophageal, duodenal, jejunoileal and anorectal atresias
- Meconium ileus
- Enteric cysts and duplications
- Small intact omphalocele, meningocele
- Unilateral hydronephrosis
- Craniofacial, extremity and chest wall deformities
- Cystic hygromas
- Small sacrococcygeal teratoma, mesoblastic nephroma, etc.
- Benign cysts: Ovarian, mesenteric, choledochal, etc.

In such conditions, the delivery can be planned at an appropriate place where these conditions can be handled effectively.

Defects that may influence the Mode of Delivery[1]

Elective cesarean section rather than a trial at vaginal delivery may be needed in the following conditions:

- Conjoined twins
- Giant ruptured omphalocele
- Severe hydrocephalus
- Large or ruptured meningomyelocele
- Large cervical teratoma/cystic hygromas, SCT
- Malformations requiring preterm delivery in the presence of inadequate labor or fetal distress

Defects that may require Induced Preterm Delivery[1]

- Progressively increasing hydrocephalus or hydrothorax
- Gastroschisis or ruptured omphalocele with damaged bowel
- Intestinal ischemia and necrosis secondary to volvulus or meconium ileus
- Progressive hydrops fetalis
- Intrauterine growth retardation
- Fetal arrhythmias, e.g. supraventricular tachycardia with failure

Defects that may require Extrauterine Intrapartum Technique (EXIT) Procedure[1]

A technique wherein the child is delivered, and the surgery is performed by maintaining the placental circulation:

- Congenital high airway obstruction syndrome (CHAOS)
- Large cervical tumors, e.g. teratoma
- Mass obstructing trachea or mouth, e.g. cystic hygromas
- Conditions requiring immediate ECMO cannulation
- Large chest mass preventing lung expansion

Defects that may require Intervention before Birth

It could be medical treatment (Table 1), surgical treatment (Table 2), nonlife-threatening defects that may benefit from antenatal intervention (Table 3).

Table 1: Fetal deficiencies that may require medical treatment[2]

Defects	*Treatment*
Erythroblastosis fetalis (erythrocyte deficiency)	Erythrocytes—intraperitoneal or intravenous
Pulmonary immaturity (surfactant deficiency)	Glucocorticoids—transplacental
Metabolic block, e.g. methylmalonic acidemia, multiple carboxylase deficiency	Vitamin B12—transplacental Biotin—transplacental
Cardiac arrhythmia (supraventricular tachycardia)	Digitalis—transplacental Propranolol—transplacental Procainamide—transplacental
Endocrine deficiency, e.g. hypothyroidism, adrenal hyperplasia	Thyroid—transamniotic Corticosteroids—transplacental
Nutritional deficiency, e.g. intrauterine growth retardation	Protein calories—transamniotic or intravenous

Table 2: Life-threatening malformations that may benefit from surgical correction[3]

Pathology	*Rationale*	*Treatment*
Posterior urethral valves	Renal failure, pulmonary hypoplasia	Vesicoamniotic shunting/fetoscopic ablation of valves/open vesicostomy
Large congenital cystic adenomatoid lung malformations	Hydrops, death	Open lobectomy/laser ablation
Congenital diaphragmatic hernia	Lung hypoplasia, pulmonary failure	Temporary tracheal occlusion in the form of PLUG therapy (plug the lung until growth)
Large sacrococcygeal teratoma	High output failure leading to hydrops, death	Open resection/radiofrequency ablation (RFA)
Twin-twin transfusion syndrome	Donar recepient steal through placenta leading to hydrops, death and neurologic damage of the survivor	Fetoscopic laser ablation of selected placental vessels/amnioreduction
Acardiac/anomalous twin (TRAP)	Vascular steal leading to damage/death of the donor twin	Selective ablation of placental vessels using laser/RFA
Congenital aqueductal stenosis	Hydrocephalus	Ventriculoperitoneal shunt
Congenital valvular obstruction	Hypoplastic heart leading to cardiac failure	Balloon valvuloplasty
Congenital high airway obstruction syndrome	Over distension by lung fluid leading to hydrops, death	Fetal tracheostomy
Large cervical teratoma	Airway obstruction, high output cardiac failure	Vascular occlusion using RFA/intralesional alcohol injection/open resection/resection using EXIT procedure

Table 3: Nonlife-threatening defects that may benefit from antenatal intervention[3]

Pathology	*Rationale*	*Intervention*
Gastroschisis	Bowel damage	Serial amnio-exchange
Meningomyelocele	Spinal cord damage	Open repair/ fetoscopic coverage
Cleft lip/palate	Persistent deformity	Open/fetoscopic repair

Prenatal Diagnostic Techniques

The commonest imaging modality used in the detection of antenatal anomalies is ultrasound scan (USG). It is cheaper, easily available, and gives a real-time picture to screen for anomalies. However, it is operator dependent and may miss subtle anomalies. It is important that the USG is done by an experienced radiologist, at the right time in gestation for picking up these anomalies.

Occasionally, magnetic resonance imaging (MRI) scan is being used when screening for CNS anomalies and for screening conjoint twins.

Timing of Antenatal Ultrasound

Since the legal age cut-off for medical termination of pregnancy in India is 20 weeks, it is important that the anomaly scan is done atleast 1 to 2 weeks prior to this as adequate time needs to be given to the parents for taking a proper decision.

MANAGEMENT OF THE MOTHER AND FETUS DURING SURGERY[4]

Any insult to the uterus, either by incision or by puncture incites uterine contractions. Despite technical advances, disruption of membranes and preterm labor are the Achilles heel of fetal therapy. Halogenated anesthetics, though produce satisfactory anesthesia, can produce fetal and myocardial depression and affect placental perfusion. Presently, inhaled nitric oxide and intravenous nitroglycerin are being used as adjutants for optimal anesthesia.

The advances in fetal surgery closely relate to the advances in anesthetic practice.

Maternal Complications associated with Fetal Surgery[4]

- Premature rupture of membranes
- Preterm delivery
- Pulmonary edema
- Abruptio placenta
- Postoperative vaginal bleeding
- Later deliveries by C-section only

Putting It in a Nutshell

Having said all this, 'fetal surgery' as a branch is still in its infancy in our country. A quick search on the internet where some antenatal interventions are being done in our country hardly yields one or two centers. But, at this point of time, it is our responsibility to properly counsel the parents regarding the anomaly, its natural course, complications and the treatment options and let them have the final say whether to terminate the pregnancy or not. A dedicated team comprising an obstetrician, pediatric surgeon, neonatologist, radiologist needs to be established at each center to provide proper, timely care for these 'patients'.

Today, many of the nonlethal anomalies (e.g. cleft palate/lip, unilateral hydronephrosis) are being unnecessarily terminated. This needs to be condemned.

Finally, it is not just the pathology that matters to the parents. Many social and emotional factors play a role. Enthusiasm for fetal intervention must be tempered by reverence for the interest of the mother and her family.

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