GeNeDit

Marching towards Prenatal Treatments: Training in Ethics and Communications the Need of the Hour

Editorial

Diagnosis of genetic disorders has taken a big leap in the 21st century. The ease with which the whole exome and whole genome can be sequenced suggests that this can be the first step of medical evaluation for any individual, may be immediately after birth or prenatally. Clinicians are awestruck by the diagnostic power of next generation sequencing (NGS)-based diagnostics. Whole exome sequencing can now detect sequence variations causing monogenic disorders as well as chromosomal disorders and copy number variations. Limitations of the utility of NGS in the diagnosis of triplet repeat disorders, structural rearrangements of the genome and pathogenic variations in non-coding regions are getting resolved. NGS-based testing is getting applied in prenatal settings also. A large study from UK covered in GenExpress in this issue has shown an overall diagnostic yield of 8.5% in fetuses with a wide spectrum of antenatally detected structural anomalies. Additionally, variants of uncertain significance with potential clinical usefulness were detected in 3.9% fetuses. Counseling for variations of uncertain significance and secondary findings unrelated to the disease are nightmares for geneticists. These issues become much more complex in prenatal settings as the decision of termination or continuation of the pregnancy may depend entirely on the molecular diagnosis. Further evaluation of such variations of uncertain significance for their pathogenic nature quickly is a challenge in front of researchers and communicating the uncertainty associated with such molecular reports to the family and being involved in the process of decision making of the family is a great challenge for the clinical geneticist. Also, irreversible decisions like termination of pregnancy based on variations of uncertain significance pose an enormous ethical dilemma.

Though prenatal diagnosis and termination of fetuses with serious disorders is acceptable to most families and societies, it can never really be considered the ethically right approach to prevention of diseases. Treatment after diagnosis is always sought by the patients. Even after considerable experience in counseling many families about prenatally detected untreatable disorders or disorders with poor outcomes, I cannot prevent myself from feeling sad after each such counselling session and I try to convey to my students the need to understand the gravity and seriousness of each such situation involving decision of termination of a pregnancy by the family. Fetal therapies are exciting and sometimes dramatic in nature. Intrauterine blood transfusions, drug therapies, minimally invasive interventions and open fetal surgeries are being successfully done. Total cure by prenatal gene therapy or fetal stem cell transplantation is the way forward especially for disorders which are developmental in origin and start affecting the individual from fetal life. For some disorders like fetal hydrops due to alpha thalassemia, survival may not be possible without fetal therapy. Extensive research in fetal gene therapy and fetal bone marrow transplantation is being done. The GenExpress in this issue also highlights some recent successes in fetal therapies. The success story of fetal therapy for ectodermal dysplasia through intra-amniotic recombinant ectodysplasin is a major milestone in the treatment of genetic disorders. The success of this strategy in animal models was shown in 2014 and within 4 years the drug has been successfully tried in affected human fetuses. With this I feel medical genetics has taken a leap forward in the direction of curative medicine. The wish list of genetic disorders for which fetal therapies are needed is very long. But the promise shown by easy, effective and probably harmless therapy for ectodermal dysplasia has brought positivity to the strategy of prenatal diagnosis. This new era of prenatal and pre-symptomatic diagnosis and may be population-based screening at the prenatal and neonatal level by whole genome sequencing will pose complex ethical and psychosocial dilemmas. Involvement of families in decision making will

need better skills and means of communication. Evaluation of societal views, capabilities of medical geneticists and clinicians to provide pre-test and post-test counseling for NGS-based testing and training them for communicating the issues involved need to be taken up on a priority basis, so that the technology is ethically and usefully applied by the clinicians. I wish to stress upon the need for some training modules in ethics and communication in medical genetics education and for clinicians at any stage of their careers.

Dr. Shubha Phadke
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