Conveying the status of a female DMD carrier foetus - A dilemma

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Abstract

This case study discusses the question of whether or not the information that a female foetus is a carrier of Duchene Muscular Dystrophy (DMD) should be conveyed to expecting parents. As only a female foetus can be a carrier of DMD, conveying the information of its carrier status would effectively disclose the sex of the foetus, which is against the provisions of the Pre-conception and Pre-natal Diagnostic Techniques Act (PC-PNDT Act), 1994. The Act states that the gender of the foetus may not be conveyed except in those cases where the foetus (itself) has genetic or metabolic disorders, chromosomal abnormalities or congenital malformations including sex-linked disorders. Further, while the Medical Termination of Pregnancy Act (MTP Act) permits termination of foetuses with certain abnormalities or diseases, it does not permit termination of a foetus with carrier status of a disease. We suggest that suitable modifications may be made to the PC-PNDT Act as also to the MTP Act.

Introduction

Duchene Muscular Dystrophy (DMD) is a neuromuscular disorder caused by a mutation in the dystrophin gene, which results in muscle degeneration, inability to walk and eventually death. DMD is passed on from one generation to another through the X-chromosome. Females have two X chromosomes, one from the father and one from the mother. Males have one X chromosome which comes from the mother, and one Y chromosome which comes from the father. In the case of DMD, if the mother has the mutated gene and passes it on to a male, the boy will have DMD. If either the father (with DMD) or the mother (with carrier status) passes the mutated gene to a girl, the girl will be a carrier of the disease. (The father cannot pass on the mutated gene to a boy to whom he contributes his Y chromosome.) However, DMD may also occur in patients who do not have any family history of DMD. (1)

A person suffering from DMD can be diagnosed with genetic testing and sequencing; or with biochemical testing for levels of serum creatine kinase, an enzyme present in muscles, which are abnormally elevated in DMD-affected patients; or with immunohistochemical tests such as muscle biopsy (2). There is no known cure for DMD, and a better quality of life can only be provided through management of the disease (3).

One of the major dilemmas faced by doctors in India today is whether or not the information that a foetus is a carrier of DMD should be conveyed to the expecting parents. Since only females can be carriers of DMD, conveying the foetus' disease carrier status at the time of prenatal testing would effectively convey the sex of the foetus. This would result in a violation of the provisions of the Pre-conception and Pre-natal Diagnostic Techniques (PC-PNDT) Act, 1994 and amendments, 2003. Section 4 (2) of the Act specifies only that the diseased status of a foetus may be revealed, and the law is silent on revealing its carrier status (4).

Pre-conception and pre-natal diagnostic procedures can be of great benefit to families with a risk of genetic or metabolic disorders, chromosomal abnormalities or congenital malformations; these procedures can be used to detect foetal abnormalities, allowing the woman to medically terminate the pregnancy. However, in a society with high son preference, such technologies have been used by some in the medical fraternity for purposes of sex selection. The Pre-conception and Pre-natal Diagnostic Techniques Act (PC-PNDT Act) was enacted to put a stop to sex selection and halt the decline in the sex ratio.[1] However, the law, as it is currently worded, can also come in the way of parents who are not biased towards a male child but only want a healthy baby. For such parents, the restrictions under the PC-PNDT Act can have terrible consequences if the foetus is a carrier of a disease like DMD.

It is a misconception that DMD carriers always remain unaffected by the disease. In fact, carrier females may have muscular weakness in a manner similar to affected males and for this reason, they are called "*manifesting carriers*". In fact, studies suggest that more than 8% of female DMD carriers are manifesting carriers and have muscle weakness to varying extents (5). Manifesting carriers may also have other symptoms such as muscle pain, fatigue, tachycardia, and impaired intellectual development (6). The literature contains reports of female carriers of DMD with muscular as well as neurological symptoms, sometimes going through immense suffering (5).

In this context, three examples have been taken from the literature related to DMD which calls for a rethinking of the clauses of the PC-PNDT Act and the MTP Act.

Case 1

A couple with a family history of DMD requested a prenatal diagnosis in their third pregnancy. The couple already had

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a son affected by DMD and a non-carrier daughter, and the pregnant woman's brother had also been affected by DMD; this family history confirmed that the woman was a carrier of the mutant gene. On prenatal testing, the foetus was identified as a female carrier of DMD. The laboratory told the couple that the foetus was normal and did not suffer from DMD. The couple was not satisfied because the information could be interpreted to mean that the foetus was an unaffected male, or an unaffected female, or a carrier female. The couple would have been happy to continue the pregnancy in the first two cases, but they wished to terminate the pregnancy if the foetus was a carrier female. They argued that a carrier female would face difficulty later in life, in finding a husband or in pregnancy. However, the laboratory refused to disclose the foetal sex or carrier status because the PC-PNDT Act did not permit such disclosure (7).

Case 2

A 32-year-old woman was admitted with progressive weakness of the limbs over a nine-year period. She already had two sons with DMD, confirming that she was a carrier of the disease. A neurological examination revealed intellectual disability with an IQ of 70, whereas an average IQ is between 90 and 110. Serum creatine kinase levels, which are abnormally elevated in DMD-affected patients, were mildly elevated. Further molecular testing confirmed that she was a carrier of the disease (5).

Case 3

A 20-year-old female with no family history of DMD was brought to the doctor. She had developed calf hypertrophy at the age of 18 months; she had difficulty changing positions from the age of five, with confirmed weakness in the lower limbs and foot deformities. She lost the ability to walk at the age of nine and by the age of 20, she had to be confined to bed (8).

Discussion

In India, under Section 4(2) of the amended PC-PNDT Act, if a foetus is found to be suffering from any genetic or metabolic disorders, chromosomal abnormalities or congenital malformations or sex-linked disorders, the law allows the information to be conveyed to the parents because of the pain, suffering and burden of the disease; if the parents wish, they may abort the foetus. Since DMD is a sex-linked genetic disease, if prenatal testing detects that the foetus is suffering from the disease, the information is passed on to the expecting parents. However, as per the PC-PNDT Act if a female foetus is found to be a carrier of DMD, the female foetus is not considered to suffer from the disease, and information on the carrier status must not be conveyed to the expecting parents. The parents of a female foetus found to be a carrier of DMD may wish to terminate the pregnancy. If such a pregnancy is carried to term, there is a small but significant probability that the female child will develop symptoms of the disease, and undergo suffering due to the disease. Further, the future children of the carrier female may suffer from the disease (if male) or be carriers (if female). The stigma of being a DMD carrier, as well as the related healthcare costs, may lead parents to wish to terminate such pregnancies. This option does not exist under the current laws.

Muscular dystrophy is defined as a physical disability under clause 1 (A) (d) of the Schedule under clause (z)(c) of Section 2 of the Rights of Persons with Disabilities Act, 2016 (9); it is covered by Section 3 (2) (ii) of the Medical Termination of Pregnancy Act, 1971, which allows abortion if there is a substantial risk of the child being born suffering from physical or mental abnormalities (10). DMD manifesting carriers can suffer from all the symptoms of the disease, thus making them eligible to be called physically disabled. If a woman is pregnant with a DMD carrier foetus, she should have the right to medically terminate the pregnancy.

Moreover, Section 3 (2) (i) of the Medical Termination of Pregnancy Act, 1971 permits medical termination if the pregnancy would cause mental or physical harm to the woman (10). Raising a differently-abled child could put the mother through emotional strain, affecting her mental health. For this reason, a woman expecting a child with a disability has the right to choose whether or not to continue the pregnancy to term. As described in the cases above, DMD carriers may show the same symptoms as a DMD sufferer.

Conclusion

Looking at the cases cited above related to carriers of DMD, we suggest that in the case of a female foetus found to be a carrier of DMD, the information should be passed on to the expecting parents and a medical termination of pregnancy should be permitted on the grounds described above. Accordingly, section 4(2) of the PC-PNDT Act should be modified to include a provision for conveying the information about the carrier status of the female foetus to the parents.

As per Section 4 (3) of the PC-PNDT Act, prenatal and preconceptual diagnostic tests are recommended only if the mother's age, family history, medical history, or previous pregnancies suggest increased risk of the foetus having certain diseases (4). However, it is evident from case 3 that it is not true that a carrier always has a family history of the disease and one can be a carrier or sufferer because of any mutation as well. So, we also argue that Section 4(3) of the PC-PNDT Act should be modified to make prenatal diagnosis available (but not compulsory) for all pregnancies so as to reduce the burden of disease, or the possibility of suffering. The testing pattern may be followed from less invasive tests to more invasive ones (depending upon the requirements and uncertainties) to eliminate the fear of false positive results. It may be noted that such tests may not always be economically or socially acceptable to families; in such cases an open option should be given to the willing parents.

We also suggest that Section 3 (2) of the existing MTP Act be amended to include DMD carrier status as one of the abnormalities which can serve as a basis for termination of

pregnancy. It would defeat the purpose of conveying a foetus' DMD carrier status to the expecting parents if they are legally prohibited from terminating the pregnancy by the provisions of the MTP Act.

We would like to assert that we do not support discrimination against any person due to disability. We are only pointing out that the MTP Act permits medical termination if the foetus is found to be suffering from various disabilities, including DMD. This permission should be extended to the foetus with carrier status of such conditions.

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There are no submissions of similar work or references to a previous submission.

[1]Note

Even otherwise, the PC-PNDT Act has not been able to check the declining child sex ratio. According to the last three census reports, the child sex ratio (females/1000 males) was 945 in 1991, 927 in 2001, and 919 in 2011 (11, 12). Therefore, the suggested change will not affect the effectiveness of the PC-PNDT Act.

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Can doctors advise beyond the purely professional?

HIMMATRAO SALUBA BAWASKAR

Abstract

A 25-year-old woman, six-months pregnant, came to me in great distress. She said she had been happily married for five years. Unexpectedly, a minor accidental injury to her husband had revealed that he had been suffering from a brain tumour since 2012. He had been operated on at the time but the tumour had subsequently metastasised and had required further surgery. His condition had not been revealed to the wife either at the time of the marriage or later. The husband and his family were unapologetic about the non-disclosure. When the wife confronted her husband's regular attending neurosurgeon, asking why he had not counselled the patient against marriage, he had argued that it was not his responsibility to do so. The issue this case raises is: Is it not the duty of a responsible treating doctor towards a patient with a life-threatening condition and his parents, to counsel them regarding marriage? A doctor occupies the position of a respected adviser and his counsel would surely be considered seriously.

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A 25-year-old woman, six-months pregnant, came to me in great distress. She told me she had married a mechanical engineer in 2014 and been very happy with her husband and his family, until four days earlier. Her husband had an accidental fall from his scooter and became semiconscious. He was admitted to a tertiary care hospital and had undergone perfusion MRI, suspecting a big haematoma. His regular doctor being on leave, he was seen by another available neurologist. During history taking by a resident doctor, her husband asked her to stay outside the room, but she could hear the history. The patient informed the resident doctor that he had been detected with grade IV Glioblastoma multiformy in the year