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Presymptomatic Testing in Twins with Unknown Zygosity: A Reflective Report on Ethical Challenges

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ABSTRACT

Portugal is one of the European countries where genetic counseling is emerging although the profession of non-medical genetic counsellors has not yet been recognized. Presymptomatic testing for late-onset neurodegenerative disorders in Portugal was implemented in the mid-nineties following a national protocol base on the international pioneer experience of Huntington Disease. Twins do pose a unique issue in the context of predictive genetic testing. Although ethical guidelines consider in advance possible dilemmas that may arise during presymptomatic testing, the genetic counselling practice at this context is far much more complex. We present here a short report of counselling practice at presymptomatic testing of twins with unknown zygosity. Authors reflect on ethical challenges and multidisciplinary case approach. The publication of this kind of complex situations can be an opportunity for the discussion of issues that are less common for other genetic counsellors, medical geneticist and psychologist at clinical genetic services.

A BRIEF INTRODUCTION TO THE CLINICAL SETTING

The first national programme for Presymptomatic Testing (PST) in Portugal was implemented in the mid-nineties at four genetic services in the country [1], primarily targeting two Late-Onset Neurological Disorders (LONDs): Machado–Joseph Disease (MJD), also known as spinocerebellar ataxia type 3 (SCA3), and familial amyloid polyneuropathy type I (FAP ATTR V30M), a peripheral neuropathy [2]. The national protocol follows the International Huntington Association and the World Federation of Neurology Research Group on Huntington's chorea guidelines (IHA/ WFN, 1994) and aims to ensure that all the conditions for presymptomatic testing are dealt with maximum confidentiality and appropriate care. This includes at least two pre-test genetic counselling appointments, psychosocial evaluation, two blood sample collection and follow-up sessions that are offered either for non-carriers or for asymptomatic carriers 3 weeks, 6 months and 1 year after the result disclosure [1].

Portugal is one of the European countries where genetic counselling is emerging as an independent clinical and scientific field. Nevertheless, the profession of non-medical genetic counsellors has not yet been recognized and those existing are not all incorporated into genetic services [2]. Portugal has some legislation on ethical issues of genetic testing provision and personal genetic information approved at the National Health Ministry [3], the Parliament [4] and the National Council of Ethics for Life

Sciences [5]. Recently the CNECV officially supported the Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Genetic Testing for Health Purposes [6] and it is currently under discussion a new national Code of Ethics for Healthcare provision http://www.cnecv.pt/admin/files/data/docs/1413213430_Parecer%2078%20CNECV%202014%20Aprovado.pdf.

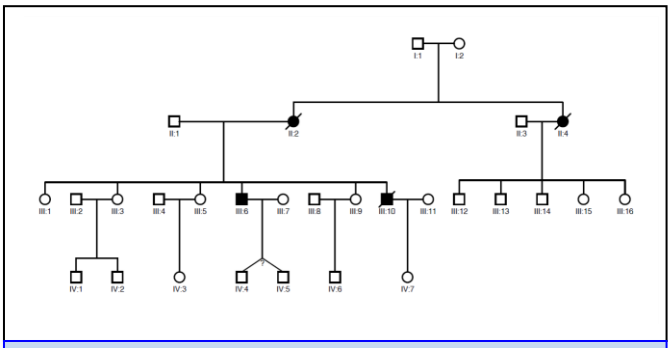

Figure 1: Pedigree of consultands family history.

The 21 years old twins, Paulo and Salvador (pseudonyms for individuals IV: 4 and IV: 5), arrived at the centre accompanied by their mother. Their father is affected by FAP (ATTRV30M). The father has 5 siblings, 1 who had already passed way from the disease and 4 others who are non-carriers. The family originates from Póvoa de Varzim, the geographical region where the highest prevalence of this disease has been reported [7]. The age of onset of both affected brothers (father and uncle of the consultands) was 28 and 25, respectively, as is observed in families with a classic pattern of FAP. Nevertheless, it was only 2 years before coming to the centre that the consultands became aware of the existence of the disease and the possibility of it being transmitted in their family.

Paulo and Salvador are twins with unknown zygosity, although the mother had been previously informed by a physician that they are non-identical. Salvador completed the 9th grade, and was now working as a mechanic. Paulo dropped out of school after completing the 8th grade, which was justified by the mother as due to his learning disabilities. Both are single and living with their parent's. During our first appointment Paulo and Salvador were accompanied by their mother. As the history of the disease in the family had only recently been disclosed, the session was mainly focused on collecting the family history and providing information about the disease, its inheritance pattern, risks, and the possible therapeutical options Salvador expressed he was ready and thought to be beneficial to go forward with PST. When questioned about anticipated changes following the results, he only associated relief with a possible non-carrier result, and acceptance if he knew he would be affected by the disease. On the contrary, it was difficult to perceive Paulo's thoughts about the PST, and repeatedly his mother answered for him. The only thing Paulo made clear was his willingness to know if he had his father's disease. Data from the clinical psychological interview reinforced our concern about Paulo´s autonomy; he seems to have a mild mental retardation, although without a formal evaluation. The mother highlighted their age's proximity to the age of onset of the disease on their father.

DISCUSSION OF THE ETHICAL ISSUES OF THIS CASE

Predictive testing, as other genetic tests, is guided by core ethical principles. Justice, for example, is guaranteed through the equal access and quality of care that should exist for all at-risk individuals requesting PST. Non-maleficence, sustained by the availability of psychological support and counselling along the whole protocol aiming at the identification of vulnerabilities and concerns about the impact of test results, avoiding potential harms, is another ethical principle. Also, beneficence should be balanced through the opportunity of enough counselling support, promoting education and helping consultands to make decisions that are really appropriate for their personal values and preferences [1,8-10].

Especially, in the context of PST there are two core ethical tenets: confidentiality and respect for autonomy of all consultands. The right of privacy of all consultands includes all information shared within the multidisciplinary team as well as the PST perse. Some forms of genetic discrimination are being reported [11] resulting in efforts to prevent undesirable societal consequences. Confidentiality also involve issues of intrafamilial communication of genetic information, which can sometimes be nuanced by the secrecy and long silences [12] involving PST and the disease itself, as it was the case of this family. The respect for autonomy is crucial as voluntariness is essential from the beginning, at requesting PST. It also might be guaranteed along the PST protocol allowing all consultands to proceed or abandon the protocol at any time, without any consequences. Respecting consultands autonomy during counselling also involves assuring that consultand's decisions are

sufficiently informed and that the given informative guidance is accurate and provided in a nondirective way. However, non-directiveness does not mean just presenting full and unbiased information and letting people make their own decisions without support.

This case brought into consideration some of the latter ethical issues and other questions not as much discussed in literature. First, we need to acknowledge the issue of the consultands' unknown zygosity and the simultaneous performance of PST. It has been recommended that predictive testing can proced when twins voluntarily and simultaneously request counselling and evaluation in a PST program [13]. Literature has shown how in some cases where one of the co-twins refuses to participate in a predictive program, monozygosity could be considered as an exclusion criteria. This was based on the need of fully protecting all individuals and their right to not know their genetic status [13,14]. It is even more complex when reproductive decisions and prenatal diagnosis are involved. A Cuban study reported monozygotic twins with different ages at onset where the first symptomatic twin implicates the carrier status for the co-twin [14]. Additionally, it was an ethical challenge to enable each consultand to discuss doubts and emotional needs independently, raising the issue of confidentiality and autonomy. As we described above, the first appointment was a joint session, in accord with as both mother and consultands will. It has been discussed how the presence of more than one consultand may either facilitate or inhibit the expression of emotions as well as the willingness for an open communication of difficult issues [15].

This case was even more complex, as one consultand has a mild mental retardation. Offering PST to both consultands simultaneously would have been consistent with beneficence. But, were they both equally prepared, capable of taking informed decisions and able to follow the same protocol? We should consider that these cases may have singular needs in terms of psychological support, including the need of additional support for the family facing a "double event" where in both twins are concomitantly identified as gene positive [14].

Respect for Paulo´s autonomy involved the examination of his competency in understanding and deciding as well as his voluntariness in making a decision and consenting for the PST. Respect for his integrity, in our opinion, also included acknowledges him as a vulnerable person. The Universal Declaration on Bioethics and Human Rights of UNESCO placed special attention to the issue of human vulnerability and personal integrity, recommending special measures for persons who are not capable of exercising autonomy to be taken to protect their rights and interests [16]. A decision of not performing Paulo´s PST could be explained by the goal of securing Paulo´s integrity, therefore, aiming for his beneficence. Paulo could be at risk for psychological harm if predictive information about FAP was revealed without his very competent consent. Thus the principle of respect for his autonomy required thorough consideration, and was further discussed with them.

Was he able of an informed consent? Implicit in an informed consent is a discussion of the purpose, potential benefits, risks and limitations of a specific genetic test and that the patient understands the information, and the possible consequences of the test. Respect for Paulo's autonomy should also rely on the certainty that he has understood the medical facts, possible test results and their clinical and psychosocial implications, options available as well as limitations and consequences of each option in terms of their own life goals. That is also the reason most of international protocols for PST require a written informed consent during the pre-test counselling consultations [1,7,17].

Another ethical issue raised by Paulo's lack of autonomy, was the respect for Salvador´s right to information and his right to make his own decisions about PST. Similar scenarios to this dilemma can arise when there are discordant interests among individuals at 50% of risk versus a 25% of risk, or when a couple is making decisions regarding pre-natal diagnosis; these are commonly challenging scenarios for genetic counselling practice [18-21].

OUR ROLE AS A MULTIDISCIPLINARY TEAM

As part of the counselling process at PST consultands were discussing the protocol information with the genetic counsellor, the purpose of each consultation as an integrative process, as well as the consultands' right to withdrawal from the PST protocol at any time. As always, ethical principles underlining this type of predictive diagnosis were emphasized. As the zygosity for these twins was unknown the genetic counsellor opted for a careful approach assessing genetic risk and

discussing the two possibilities: if monozygotic they share 100% of genetic information and PST results should be concordant; but if they were dizygotic, then test results would be independent and could be different.

As the initial contact allowed the identification of ethical concerns the genetic counsellor tried to involve them into a reflective process about PST implications as well as the reasons for an additional care due to the potential ethical dilemmas we may face answering their request. At that point, debate was focused in exploring previous experiences of Paulo making decisions for other healthcare issues, though genetic counsellor realized the need of a psychological assessment in order to ascertain the extent in which he was being able to be engaged in such discussions.

In parallel, it was noticed that the presence of the mother and Paulo was inhibiting Salvador from fully expressing his feelings and thoughts. For that reason, an additional meeting with the genetic counsellor was proposed just after the psychology consultation for a more personal contact with them separately. Between the two pre-test counselling sessions, as part of our clinical routine, I presented this case for discussion. The team acknowledged the complexity of the ethical issues surrounding this case and the principles that were in conflict. We discussed how to achieve the greater good possible while assessing the possible course of actions of this case. Some counselling aspects were delineated to be approached in further sessions. The multidisciplinary team was concerned on Paulo's eligibility but as there were advantages on undertaking PST we agreed to enhance the possibilities of beneficence by involving the mother as much as possible in Paulo's decision-making. As they have a previous belief of being dizygotic twins, the team suggested more emphasis at counselling on the potential impacts of the test results, either if dizygotic or monozygotic. The team recommended as well to assume they were dizygotic, in order to individualize as much as possible each consultand process. This would potentially contribute for a more autonomous decision making. As our PST protocol does not include specific guidelines for this type of cases, it was also a good opportunity to consider the need for local policy consensus.

During the second visit to the centre, the consultands were seen by the genetic counsellor individually, as well as their mother. This session included discussions with the mother about the cost-benefit and implications of Paulo´s PST, as well as how autonomous Paulo was along his life. The genetic counsellor spent more time with Paulo in a more in depth discussion about the PST implications trying to make him as far as possible part of the consent process. He recalled reasonably what we discussed in the first session and elaborated more on his wish of knowing his genetic status. At that time, both twins seemed to continue interested in PST and we obtained their informed consent. Regardless, they took blood samples and never returned to our centre for the communication of results.

How the counselling process and the multidisciplinary approach may have influenced this decision? Was the team overzealous? Has Salvador put his own interest at a lower priority level? Does he felt coerced by his results could reveal something about his brother's genetic status? Our goal and hope was to clearly promote a greater good with the least possible harm [13].

CONCLUSION

The ethical imperative of offering nondirective genetic counselling to the twins was fulfilled as well as it was consistent with the best interest of both consultands. Although ethical guidelines consider in advance possible dilemmas that may arise during PST, the genetic counselling practice at this context is far much more complex. The publication of this kind of challenging situations can be an opportunity for the discussion of issues that are less common for other genetic counsellors as well as for our own reflection on the way we manage ethical challenges. Also, genetic counsellors should be trained as reflective practitioners, engaging in continual self-scrutiny of their personal values and ethical principles and how they might influence our professional practice [22-24].

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COMPLIANCE WITH ETHICAL STANDARDS

This manuscript has not been submitted to another journal for simultaneous consideration. No data have been fabricated or manipulated to support our conclusions. Consent to submit has

been received explicitly from all co-authors and the four authors whose names appear on the submission have contributed sufficiently to the scientific work and therefore share collective responsibility and accountability for this short report.

CONFLICTS OF INTEREST

The authors declare they have no conflicts of interest.

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