Editorial Comments

How well do we manage and support patients and families with dominantly inherited renal disease?

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Introduction

Diagnosis of an inherited disease in an individual affects every member of the family. Consequently, the disease should be viewed as a family issue, not an individual one. However, the care of a person with chronic renal disease places a heavy demand on an overburdened health care system ill equipped to address secondary issues involving unaffected family members. Personal experience with support issues was explored during interviews with patients presenting with Alport syndrome (AS) [1], von Hippel–Lindau (VHL) disease [2], and autosomal dominant polycystic kidney disease (ADPKD) (Levy, unpublished data), and within a patient organization for genetic renal diseases.

The interviews revealed that most patients carry a substantial burden of stress, related not only to the chronic renal disease itself, but also to the fear of discrimination based on genetic risk (health care, insurance, employment), difficulties in their intimate relationships (marital conflict, separation, or familial breakup), and concerns for children and grandchildren. Although reactions and answers to interview questions ranged widely, a few themes emerged that may indicate avenues for improvement of care.

The shock of the announcement

Little work has been devoted to the announcement of a heritable, late-onset disease [3]. Most patients interviewed recalled the announcement of their renal disease, even after many years. Its psychological impact, obviously related to patient age and the stage of the disease, also involved family history and the patients’ knowledge of the disease. Some patients were unaware of the family history because of a climate of family secrecy (a frequent situation). Others knew the family history, but had not been told that they were at risk (another frequent situation). Within a brief time-span, these individuals heard the name of the disease, received information about prognosis, and learned that there were no curative therapies nor ways to predict disease severity. They also learned that the disease was an inherited condition and were informed about their risks (the term ‘chances’ being ill-tolerated) of transmitting, or having transmitted, the disease to their children. The idea that they may have passed the disease to their children was, for some, devastating. Several still reproached their parents, or their siblings, for not having transmitted accurate information. Some received the diagnosis as a ‘bomb’. Those patients in whom the disease (e.g. renal cysts) had been casually diagnosed by ultrasonography (US) performed for another disorder or during pregnancy were especially shocked. For patients who knew the risk of disease, the knowledge had often severely disturbed their adolescence, or even their childhood. Some thought they would inevitably get the disease because of resemblance to a parent with the disease (‘I am marked by the familial sign’), or felt vulnerable because of age similarity to an affected relative, or had a fatalistic attitude (‘Things always happen to me, so I’ll be the one to get the disease.’) Others, however, felt ‘relieved’ when the first clinical manifestations occurred. Several patients, frightened by the prospect of developing the disease, especially when they had seen the chronic illness, dialysis, or death of a close relative, avoided any medical contact until the occurrence of complications, and denied themselves the possibility of having children.

Distressing presymptomatic genetic testing

In a symptom-free individual at risk for a dominantly inherited disease, an abnormal DNA result generally indicates the development of the disease at some point in later life [4], but neither age of onset, nor overall severity can be predicted. Experience with the psychological implications of presymptomatic genetic testing in renal patients is still limited, but testing is likely to
be considered by an increasing number of individuals as, for example, those belonging to VHL families.

Genetic testing is different from other medical examinations. Ethical practice for its conduct has been established by different professional organizations, mostly based on experience gathered by studies on Huntington disease [5]. Individuals cope well when testing is offered in the context of a structured protocol with careful screening, counselling with a trained professional, and follow-up. Genetic testing for renal diseases should obey a definite set of rules. The initial offer of testing should be separated in time from the laboratory appointment. Before at-risk individuals decide to undergo a test, they should receive clear, oral and written information from a physician having adequate clinical knowledge (i.e. nephrology) and genetic knowledge. Such information should include the advantages and disadvantages of testing as well as the meaning of any possible test result. Test results should be disclosed in a face-to-face encounter with a competent physician (perhaps a geneticist). Support should be offered to all those tested and to their relatives. In addition, the individual should understand that he (she) may refuse the test and that, even after being tested, he (she) may refuse knowledge of the results. The individual’s right not to know about his/her own genetic status is fundamental [6].

The particular case of presymptomatic ultrasonography in ADPKD

In addition to genetic screening, there are tests that measure the manifestations of a hereditary disease in asymptomatic individuals (e.g. iron overload in haemochromatosis). Renal US, detecting cysts, is the method of choice for presymptomatic diagnosis of ADPKD because it is non-invasive, readily available, and has good sensitivity at low cost [7]. Nevertheless, because it is a test with far reaching consequences for patients and their families, it should not be regarded as a simple radiological examination, but as part of a larger process including a pre-US phase of information and preparation, and a post-US phase of interpretation and support, irrespective of the test results. For example, the likelihood that the person may develop the disease when cysts are not found must be discussed previously.

Presymptomatic US differs from presymptomatic genetic tests in several ways. Firstly, a third party, the ‘ultrasonographer’, who has no established relationship with the patient, is involved in the diagnosis. Some interviewees described having suffered a lack of precautions when, for example, they received the US prescription from an affected parent without any information provided by the nephrologist, or when US results were given to them directly by the radiologist. Secondly, unlike genetic testing, young people who have a negative result, i.e. no cysts, cannot be told that they are definitely not carriers. While the age at which a normal US reliably excludes the diagnosis has been established in ADPKD-1 [8], it should be remembered that it has not yet been determined in ADPKD-2 [9]. Thirdly, it is well known that long-term recall of the meaning of a negative test result is often incorrect. Several patients, who had negative or indeterminate US results when young, expressed regrets at not having been appropriately followed or recontacted by their physician. It may be appropriate for professional organizations to develop a comprehensive policy on presymptomatic renal US, as geneticists did for genetic testing.

The anxious uncertainty of children’s health status

As with other inherited conditions, parents request testing of their healthy children as soon as possible, even in utero or at birth. Several patients who wanted to use prenatal diagnosis ‘just to know’ disapproved of termination of pregnancy of an affected fetus. Paradoxically, most said that they would not have appreciated knowing earlier that they were affected by the disease.

Geneticists and psychologists around the world have voiced opinions on the important issue of genetic testing for late-onset disorders in young people [10]. In the absence of any specific clinical indication, justifications have been advanced for both testing and not testing. Advantages include creating opportunities for children to adjust their situations, fostering openness within families, and relief of parental uncertainty. Disadvantages include possible harm to a child’s self-esteem, distortion of family perceptions of a child, and deprivation of an adult choice for testing. When such tests are performed in young children, their privacy and freedom to choose for themselves are inevitably violated. There is still very little knowledge of how those tested for genetic disorders in childhood have reacted and no knowledge on the best age for discussion of a positive result with the child.

As indicated by the American Society for Clinical Oncology, for diseases such as VHL disease, increased surveillance (i.e. of the retina, central nervous system, adrenal glands, kidneys) and early treatment can reduce the morbidity and mortality in carriers of the mutation [11]. Furthermore, genetic testing eliminates the need for periodic surveillance in non-carrier children. However, even if all researchers agree on the need for testing, the age at which testing should be done is still debated.

Conversely, since for most genetic disorders there are no preventive or therapeutic measures that must be initiated in childhood, most medical organizations judge as ethically unacceptable the genetic testing of symptom-free individuals before the age of majority (but the legal concept of majority varies between countries) [10]. Another argument against renal US in young children at risk of ADPKD is the discordance between US and DNA linkage data (performed in research studies) at that age, and the absence of clear-cut US diagnostic criteria in ADPKD-2 [9]. Consequently, most nephrologists judge that
Symptom-free children should not have US for ADPKD on their parents’ request, but that they should be informed of their at-risk status upon reaching the age of discretion. Under pressure from a paediatrician or primary-care physician, some healthy young children have had renal US. Positive US results have increased parental anxiety and led to their considering children as if they were already sick. Although screening for occult cerebral aneurysm is debated, children with a family history of cerebral aneurysms probably represent an exception to these rules. Nevertheless, in ADPKD families, all children should have their blood pressure checked regularly to allow early treatment of hypertension [12].

Whatever the circumstances for testing children, parents have subsequently raised several worrisome questions: when should they transmit accurate information to their carrier children? Will they be able to help their children understand the meaning of positive results? How will they help their children cope with their unaffected sibs? How will they help unaffected children cope with their sibling who is ‘ill without symptoms’?

**Particular difficulties with at-risk adolescents**

At-risk adolescents experience significant distress (feelings of shame, stigma, and even ideas of suicide). At an age when life-shaping decisions are taken, the possibility of renal disease appeared to weigh heavily on their minds and impact life choices, e.g. hesitation regarding job orientation and hesitation about marriage.

Presymptomatic testing the vulnerable adolescent age group, is a complicated issue. Various authors have indicated that adolescents should be differentiated from children and that a very flexible approach should be maintained. For example, testing should not be carried out in an adolescent against his (her) will, or if parental pressure is suspected. Conversely, there do not seem to be sufficient arguments to deny testing to a mature adolescent [13]. Adolescents’ wishes should foster open and sensitive discussion among parents, geneticists, nephrologists, and psychologists.

**Distress about future children**

Advances in molecular genetic analysis and chorionic villus sampling in the first trimester of pregnancy will allow prenatal diagnosis for more and more diseases. Although this may offer hope, the psychological trauma associated with a choice of abortion is always present and must be acknowledged. Many couples have had little genetic knowledge on which to base their decisions. A large number made erroneous assumptions concerning genetic facts (especially X-dominant transmission) and some were unable to identify their personal risk of having an affected child.

Very few ADPKD patients would consider termination of pregnancy of an affected fetus [14,15], and demand is, in fact, very low. By contrast, some AS [1,16] and VHL [2] patients viewed their disease as an unacceptable burden and would choose (or have chosen) termination of pregnancy of an affected fetus. Several others, changing their reproductive plans, have chosen to remain childless or to undergo permanent sterilization. Some parents had the feeling that physicians may not have offered them the full range of reproductive options. Health-care professionals’ ignorance of the advances in prenatal diagnosis and of possible genetic services available in a country (or region), and lack of communication at a level understandable to the patients, are well-known obstacles that may prevent couples from making informed choices. Furthermore, attitudes of health-care professionals towards termination of pregnancy remain controversial both nationally (and indeed there are very large differences in use of genetic services within and between regions), and cross-culturally, resulting in unequal access of patients to the procedure.

Couples with moral and/or religious objections to pregnancy termination have expressed hopes in pre-implantation diagnosis, a procedure performed before the establishment of pregnancy. Used at present to detect extremely severe single-gene diseases, its indications might be enlarged in the future.

**Conclusion**

Apart from ADPKD, the number of cases of each disorder encountered by a nephrologist is small and scattered. Yet every nephrologist involved in the long-term follow-up will inevitably support the integration of genetic information to patients’ lives, help them to understand the present state of medical and genetic knowledge so as to be able to make informed decisions in the future, and finally help them cope with the consequences of their decisions. The rapidly changing knowledge of genetics places an increasing responsibility on clinicians [17]. Some may choose to become ‘geneticists’ to some extent, whereas others may choose to rely on genetic services.

Renal patients and their family members deal with a genetic diagnosis in various ways. Some confront it openly, some will not talk about it, and some dwell only on the negative aspects. No one can predict individual coping. Ideally, patients and their families should be offered psychological support tailored to the stage of their coping process (i.e. shock or denial, anxiety, anger or guilt, depression, and acceptance) [18].

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References