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ORIGINAL PAPER

Report of the clinical donor case workshop of the European Association of Tissue Banks annual meeting 2012

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Abstract The European Association of Tissue Banks (EATB) donor case workshop is a forum held within the program of the EATB annual congress. The workshop offers an opportunity to discuss and evaluate approaches taken to challenging situations regarding donor selection, it promotes consensus development in deciding tissue donor acceptability when donor health issues are not addressed in standards and regulations, and serves to strengthen the professional tissue banking networks across Europe and beyond. This report reflects some of the discussion at the workshop during the annual congress in Vienna in 2012. The cases presented dealt with problems encountered by tissue bank facilities concerning idiopathic thrombocytopenia and autoimmune disorders, hemodilution and blood sample identification, premalignant and malignant lesions, and Huntington's disease. The discussions during the workshop demonstrate that the implications on the safety of tissue transplantation of various tissue donor illnesses, physical findings and behaviours, and the preventive measures taken by tissue facilities, may not always be agreed by tissue facility medical directors and other professionals. Moreover, they reveal that operating procedures, regulations and standards cannot comprehensively cover all tissue donor findings, medical histories and circumstances surrounding the

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cause of death. For many of the issues raised, there is a need for scientific research to provide a better evidence base for future deliberations about the suitability and eligibility of tissue allograft donors.

Keywords Tissue donor selection · Tissue donor suitability · Disease transmission · Tissue transplantation · Idiopathic thrombocytopenia · Hemodilution · Huntington's disease · Malignancies

Introduction

The European Association of Tissue Banks (EATB), serves its members in many ways including supporting European and other international endeavors to improve all aspects of tissue banking. This includes working with professionals in the field and with their regulators to constantly strive for greater safety and quality of tissue allografts. The EATB holds annual congresses to provide a forum for scientific, ethical and clinical aspects related to tissue banking and for presentation of research and collaborative projects. At the 21st International Congress of the EATB held on 21–23 November 2012 in Vienna, Austria, the ninth donor case workshop was held. As in previous workshops held at congresses in Bruges, Prague, Florence, Varna, Budapest (Saegeman et al. 2009), Edinburgh, Krakow (Van Wijk et al. 2012) and Berlin, an opportunity was provided to discuss and evaluate approaches to challenging situations and to strengthen the professional tissue banking and regulatory networks across Europe. This kind of workshop actively engages participants in an informal, secure and enjoyable setting, facilitating learning from peers and providing potential solutions to those submitting cases.

This paper is a report of the cases and findings from the 2012 clinical donor case workshop. The methodology used for these workshops has previously been published (Saegeman et al. 2009). The current event was attended by approximately 50 participants ranging from novices to experts and included scientists, clinicians and regulators. There were four discussion groups, each with a facilitator and a rapporteur. Dr. Ted Eastlund acted as a final adjudicator, providing comments and feedback at the end of each case, after the reportage from the discussion groups.

This report not only reflects discussion at the congress workshop but also subsequent correspondence between individuals who submitted cases and other persons involved in the organisation of the workshop. Although some of the cases could still benefit from additional discussion and further research, it was considered useful to address in this paper some of the questions requiring resolution. The descriptions of these cases reflect individual points of view and discussion during the workshop and afterwards. This report does not constitute the opinion of tissue bank institutions or governmental regulators, nor does it result from a mere scientific literature review as such. Instead, it includes individual judgments and opinions, especially in some cases, where there is lack of information in published literature for many of the issues raised. This is one of the main reasons why we consider it useful to publish a summary of the discussions. Furthermore, this written report will reach a wider audience and may stimulate individuals to undertake further literature reviews or research to help develop pertinent evidence that can be used for making decisions.

Case 1: Autoimmune disease in a prospective tissue donor

Donor: Female, 57-year old, deceased donor of cardiovascular and musculoskeletal tissues and corneas.

Cause of death: Intracerebral bleeding.

Relevant history: The donor had insulin dependent diabetes mellitus, hypertension, obesity and depression. One year and a half before death, she already had an intracerebral bleeding caused by thrombocytopenia of unknown cause. Autoimmune thrombocytopenia was a diagnosis of exclusion but corticosteroid therapy did not lead to clinical recovery. Subsequently, a splenectomy was carried out 3 months after the cerebral bleeding. The patient received a short course of rituximab therapy, an anti-CD20 monoclonal antibody that targets B cells, and this resulted in complete recovery of her platelet count. She remained under strict hematological follow-up until the time of death, and maintained a normal blood count. At the time of death, she was receiving Omeprazol, Diclofenac, Amlodipin, Mirtazepin and Hydrochlorothiazid.

Relevant issues:

Is the immunological disease or its (unknown) underlying cause an exclusion criterion for donation of tissues?

Is the therapy administered a reason for exclusion?

Discussion

Regarding the immunologically induced thrombocytopenia, most participants requested additional information to confirm the diagnosis. Not enough information was provided to exclude thrombocytopenia due to lupus, tumours, lymphoma, toxic reaction to medications or HIV infection. However, the treatment that was used is typical for autoimmune idiopathic thrombocytopenic purpura (ITP). The fact that a splenectomy had been carried out, suggests that no other underlying causes were found that would have required other treatment. Therefore, an immunologically mediated process seems likely. Some would therefore consider it an autoimmune disease and reject the donor for this reason. Others would consider it a temporary event that has been resolved with therapy and would not consider it as a problem at the time of death. Some pointed out that antibody-mediated autoimmune disorders in prospective tissue donors are not transmitted by bone, skin, ocular and cardiovascular tissue transplantation and do not pose a risk.

The surgery report and the report on the histological examination of the resected spleen might provide further information on this subject. A postmortem autopsy might be helpful in revealing an underlying cause of death. Some would consider acceptance of the donor if the autopsy had not revealed any contraindications for transplantation.

The second issue that was discussed was the steroid medication taken by the donor. In this regard, the most important features to consider are the dose and the duration of use. Long-term use of steroids (months to years) can affect the quality of skin and musculoskeletal tissues. Fragility of the aorta has also been observed by cardiovascular tissue banks; these banks sometimes reject donors on long term steroid therapy. However, during the processing of bone allografts, the physical quality of the tissue is examined and deleterious effects of steroid therapy such as severe osteoporosis can be detected. For example, the thumbnail indentation test (pressing the thumbnail into the tissue that should resist indentation) can detect severely affected bone with poor strength. It was also discussed whether long-term steroid therapy could cause bone marrow and immune depression and thus suboptimal antibody production and falsely negative infectious disease testing. However, long-term steroid therapy does not primarily affect the function of the B cells, which are the cells which produce antibodies and, thus, no significant effect on microbiological serological testing should be expected (Sabbele et al. 1987). The other medications that were taken by the potential donor were not considered a problem for tissue donor eligibility, including the rituximab that was used more than a year before death.

Outcome of the case

Although the majority of the workshop participants would not accept this donor, the presenting center had not rejected the donor based on the information provided above. An autopsy performed on the donor had revealed no abnormalities that might contraindicate donor suitability, however, the blood results revealed a positive syphilis test, and therefore the donor was rejected. This case demonstrates that although some standards and regulations may promote or require the rejection of a donor with any autoimmune disease, there may be certain autoimmune diseases in donors that do not pose significant risks to tissue allograft recipients.

Case 2: Hemodilution due to transfusion and infectious disease testing

Donor: Female, 25-year old, deceased donor of corneas, sclera and heart valves.

Cause of death: Hypovolemia due to accidental gunshot wound and massive bleeding.

Relevant history: The donor suffered an accidental gunshot wound to her thigh and fell off her horse, while participating in a fox hunt early one morning. She was admitted in the evening to the intensive care unit (ICU), but whilst in the emergency ward in the afternoon she had been transfused as the patient had lost blood during the long transport from the hunting field to hospital. Emergency personnel administered 2,000 mL of red cells, 500 mL of plasma, and 1,500 mL of crystalloid. In the ICU, the patient suffered a pulmonary embolus, had a respiratory arrest followed by cardiac arrest, and was pronounced dead. During resuscitation efforts, a further 1,000 mL of crystalloids were given and a further unit of red cells had just been started at the moment she died, but the volume infused of this unit was not documented. One pre-mortem blood sample collected at admission was found in the hospital laboratory but it had been mislabeled, so it could not be used for donor testing. An evaluation of the blood sample collected post mortem is required to determine its acceptability for serological testing of the donor. The donor's weight was estimated to be 110 kg and her height at 194 cm.

continued

Relevant issues:

Is the postmortem blood sample acceptable for donor testing, considering the large amount of blood and crystalloid infused prior to blood sampling?

Discussion

EU Directive 2006/17 states that when potential donors have lost blood and received donated blood or blood components, colloids or crystalloids shortly before death, or if blood, blood components or colloids were infused in the 48 h preceding death, an evaluation and algorithm must be applied to assess the degree of donor hemodilution (Commission Directive 2006/17/EC 2006). Tissue establishments may accept tissues and cells from donors with plasma dilution of more than 50 % only if the testing procedures used are validated for such diluted plasma or if a pre-transfusion sample is available for testing. Therefore, in this case, it is important to assess the degree of hemodilution.

To start this calculation the blood and plasma volume of the donor should be calculated first. If the formula of the United States food and drug administration are followed (U.S. Department of Health and Human Services Food and Drug Administration Center for Biologics Evaluation and Research 2007), the estimated blood volume (BV) can be deduced from the formula:

$$\mathrm{BV} = 110\,\mathrm{kg}/0.015 = 7,333\,\mathrm{mL}.$$

and plasma volume (PV) by the formula

$$\mathrm{PV} = 110\,\mathrm{kg}/0.025 = 4,400\,\mathrm{mL}.$$

Using these formulas, the plasma and blood volume dilution is calculated: a result $\leq$50 % dilution would mean that the sample is acceptable for serological testing.

The donor received:

$$\begin{aligned}&\text{blood} + \text{colloid} + \text{crystalloid (crystalloid last hour only)}\\&\quad = 3,500\,\mathrm{mL},\ \text{or } 3{,}750\,\mathrm{mL} \text{ if we consider the}\\&\quad \text{last blood unit as been transfused completely}\\&\quad \text{colloid} + \text{crystalloid (crystalloid last hour only)}\\&\quad = 1,500\,\mathrm{mL}\end{aligned}$$

From these data and using the US FDA formulas, it had been calculated that there was a blood volume dilution of 3,500 mL up to 3,750 mL/7,333 mL and a plasma dilution of 1,500 mL/4,400 mL resulting in a sample acceptable for serological testing.

The discussion among participants revealed that different formulas are used in different tissue establishments resulting in acceptance or rejection of the blood sample for analysis. Furthermore, there are different formulas used for men and for women and separate algorithms for obese persons. Some groups discussed whether it was important to take into account the amount of blood lost, since this has an influence on total blood volume and total plasma volume. Another discussion focused on how quickly antibodies can be delivered into the bloodstream from the extravascular space following blood loss. It was discussed that antibodies in the extravascular space can move into the vascular space when blood loss occurs; however, antigens, such as surface antigen for hepatitis B, might not be replenished from outside the vascular system. The importance of hemodilution was discussed in relation to the use of polymerase chain reaction (PCR) testing. In some banks, and for some types of tissues, pooling of donor samples for PCR is allowed which also results in an example of acceptable levels of sample dilution.

An alternative approach to acceptance of pre-mortem sampling where the sample was inadequately labeled, was discussed. Whilst the labeling is an important issue, there may be procedures to demonstrate that the unlabelled sample obtained ante-mortem, was actually from the donor. This can be undertaken by using DNA profiling using short tandem repeat sequences to show that the donor blood sample and the retrieved tissues carry the same pattern, as described by Warwick et al. (2008). This provides evidence that the donor sample came from the donor making the donation.

Thirdly it was suggested that, if a tissue donor was also a donor of organs, an investigation of the organ recipients might be carried out. If organ recipients can be tested and are negative for all relevant transmittable diseases at least 3 or 6 months after receiving an organ from this donor, then the donor might be considered suitable and tissues could be released. Due to immune suppression therapy and the possibility of delayed production of antibodies, the recipient of an organ would need to be tested for relevant viruses using PCR or nucleic acid technology (NAT) assays.

It was also discussed whether the height (194 cm) and weight (110 kg) of this female donor could be

considered normal or whether there was a specific reason for her large size (i.e. acromegaly connective tissue disease). However, information from the participants that had submitted this case, revealed that this height had been altered in order to provoke extra discussion.

Outcome of the case

The presenter reported that the standard formula used for estimating hemodilution is recommended for use within a stated weight range (45–100 kg) and this donor was outside this range (110 kg). It was described that, since fat tissue is much less vascularized than muscle, the calculation of the TBV and TPV in an obese person may be overestimated if the standard algorithm is used. This should be taken into account when determining the acceptability of the blood sample.

Furthermore, it was difficult to get an exact idea of the amount transfused. The management of an additional transfusion amount at the moment of death poses a dilemma for qualifying this donor's blood specimen. Should it be included in the calculation and what volume should be used to estimate what was actually transfused?

The documented evaluation by the tissue establishment's responsible person should describe why the algorithm that was used is acceptable for this donor and why the blood sample collected post mortem qualifies to be used for infectious disease testing.

Even if an entire unit of blood (volume = 250 mL) that was started just prior to death is considered to have been transfused, the calculation for TBV dilution is still not >50 % (3,750/7,333).

Although this donor's weight is high and outside the range suggested for this algorithm, this donor is not considered "obese." Her height and weight do not indicate obesity for an adult as per the following definitions (Mosby 2009) and a well-recognized table (U.K. National Health Services 2013):

- Obese: pertaining to a corpulent or excessively heavy individual. A body mass index of ≥30.0 indicates obesity. Because the "average" human body is approximately 25 % fat, the proportion may be doubled for a medically defined obese person.
- Body mass index (BMI)—the weight in kilograms divided by the square of the height in meters, is generally used in the assessment of underweight and obesity.
- This donor's BMI calculation (29.2) fits an "overweight" adult, but it is not considered "obese."

The presenter explained that what had been learnt from this case is that the blood sample evaluation, as it has been carried out, is probably the best way to estimate the dilution, but it may require justification as described above. Documented evidence to support decision making by the responsible person is expected. The tissue establishment's standard operating procedure (SOP) concerning hemodilution should be reviewed and revised as needed to include a clarification that, in exceptional circumstances, the responsible person can use all available information to justify decision-making regarding acceptance of the blood sample to be used for biological tests.

At the workshop, it was decided that the algorithms in current use are quite conservative, inconsistent and outdated. It might be useful to review these formulas, taking into account current knowledge and current practices.

Case 3: Premalignant skin lesion

Donor: Male, 74-year old, deceased skin donor.

Cause of death: Cerebrovascular disease.

Relevant history: The donor had hypertension and hypercholesterolemia. A recent visit to the dermatologist (2 months before death) revealed the presence of actinic keratosis, a pre-cancerous skin disease that can develop into squamous cell carcinoma. As required, a physical examination of the donor was carried out. The report described that several "skin disorders" were observed on the chest and upper part of back and these were indicated on the physical assessment form. No pictures were taken and a biopsy was not obtained. Skin was procured from the donor's back and from the legs.

Relevant issues:

Is the presence of a premalignant skin lesion a contraindication for donation?

Discussion

It was discussed whether there was sufficient information about the skin lesion, how it had been diagnosed and whether it had been removed. Without biopsy or resection, and histological examination of the resected specimen, the possibility of a squamous

cell carcinoma remains. Visual assessment cannot fully distinguish between malignant and premalignant lesions (Beele et al. 2009). Training of personnel and their ability to recognize these lesions and the regulatory framework that requires evaluation for safety and quality are relevant. Some tissue bank personnel would reject this donor unless the lesion had been resected with a 6-month, recurrence free interval.

This kind of lesion has a high and increasing prevalence in the population and rejection of all donors with premalignant skin lesions would probably have severe implications for the availability of certain types of tissues.

In some tissue facilities age criteria for skin donation exclude donation over the age of 70 years, because of the increased risk for (skin) malignancies.

During the EATB conference in Vienna a risk assessment had been presented by Richters et al. (2012) that was initiated by a similar case. It considered the risk of transmission of pre-cancerous and cancerous skin lesions taking into account the high prevalence, the limited chance of evolution towards squamous cell carcinoma, the possibility of presence of viral oncogenic factors in the lesions and surrounding skin, and the very low transmissibility of non-melanoma skin cancer (no reported donor-related transmission, even in highly immunosuppressed organ recipients). This risk analysis showed that it is cautious, but sensible, not to release the skin that contains a lesion, but that there is no reason not to use the skin that does not contain a lesion. There is also very little to no risk in the use of other tissues and cells of donors with pre-malignant or malignant non-melanoma skin cancer. The risk assessment did indicate that there are several reports of transmission of malignant melanoma, although only attributable to immunosuppressed organ recipients (not in tissue recipients), and that melanoma is highly aggressive with high mortality rate in these patients. Thus, it seems unwise to consider a donor with malignant melanoma for tissue donation (Richters et al. 2012).

Outcome of the case

The current donor was rejected for skin donation by the tissue establishment, because there was no 6-month recurrence free interval after resection of the lesion. In addition, it could not be excluded that skin recovered from the back contained lesions. The physical examination form indicated that skin disorders were present on the upper part of the back.

Case 4: Huntington's disease

Donor: Female, 64-year old, heart-beating donor of organs, and donor of musculoskeletal tissues and corneas.

Cause of death: Intracerebral bleeding after trauma.

Relevant history: The donor stayed in a home for elderly for 3 years and experienced a fall from her bed. At arrival in the hospital, there was bilateral mydriasis, she was unresponsive and there was no cornea reflex. She was declared dead 24 h after admission. The donor medical history included a hysteroscopy in 1998; arterial hypertension, and she was known to have Huntington's disease with postural instability, dyskinetic movements and increasing cognitive deficit. In 2007, 5 years before her death, molecular genetic findings had confirmed the diagnosis of Huntington's disease by showing the presence of a completely penetrant expanded allele of 42 CAG repetitions, next to the wild type allele of 17 CAG repetitions in the Huntington's disease gene.

Relevant issues:

Is (confirmed) Huntington's disease a contraindication for tissue donation?

Discussion

Most participants would accept a donor with a confirmed diagnosis of Huntington's disease. The donor selection guidelines of the UK blood transfusion and tissue transplant services (UK Blood Transfusion and Transplant Services 2005) state that potential donors with Huntington's disease can be accepted if the diagnosis is confirmed. Cognitive impairment could be an issue if it was uncertain whether all the symptoms were related to Huntington's disease. However, if the treating neurologist could confirm Huntington's disease as the cause, most participants would accept the donor. Some facilities would require additional confirmation from an autopsy of the brain. There has been some discussion in the literature about the connection between Huntington's disease and prion disease, but no substantial evidence to support this theory. The confirmed genetic profile in this donor provides additional evidence for a genetic pathogenesis. Some of the participants would not accept any genetic disease, and thus, would also reject this donor.

Another issue that was discussed is whether the cognitive impairment may pose a problem in obtaining consent, particularly for living donors, however, for most countries the late onset of cognitive impairment and the previous years of ability to consent would not constitute a problem for donor consent.

This donor's age, for procurement of musculoskeletal tissues, would not be acceptable for some tissue banks.

Finally, it was discussed whether the impaired mobility or even immobility of the patient associated with late stage Huntington's chorea, might have a deleterious effect on the quality of the bone.

Outcome of the case

The tissue establishment involved looked for further information. The father of the patient had suffered from similar symptoms (dyskinetic movements and cognitive deficit) at the end of his life. The combination of the clinical picture, the genetic findings and the positive familial anamnesis was sufficient for the consulted neurologist to confirm the diagnosis of Huntington's disease to be certain in this patient. The organs and the corneas of the donor have meanwhile been transplanted. The musculoskeletal tissues are still in quarantine.

Case 5: Medication revealing malignancy

Donor: Female, 76-year old, living femoral head donor.

Relevant history: The donor received a femoral hip prosthesis. Before donation, she signed an informed consent form and completed a medical and social history questionnaire. This included classical questions about previous major illnesses and surgical interventions, underlying neurological disease, malignancy, risk behavior, travel history, infectious diseases, etc. The patient mentioned no major surgical interventions but reported hepatitis at age 10 years. She has hypertension and diabetes type II that is under control with dietary measures only. Her current medication consists of amlodipine, tamoxifen and oxazepam.

The serological tests for HBV, HCV, HIV and syphilis are negative. NAT testing for HIV, HBV and HCV is also negative.

Relevant issues:

Tamoxifen use and hepatitis in the medical history.

Discussion

The hepatitis when she was a child was discussed. The most likely cause for it was viral hepatitis. Serological tests will exclude infection with hepatitis B and C virus. Hepatitis A infection or infection with other viruses, such as cytomegalovirus or Epstein Barr virus, in the remote past are not contra-indications for donation. Other hepatitis viruses, such as hepatitis D and E were highly unlikely at the time of her childhood. Thus, most participants would accept a donor with a remote history of childhood hepatitis if the serological test results do not indicate chronic or occult infection with hepatitis B or C virus.

The use of tamoxifen is highly likely to indicate breast cancer in the medical history. Tamoxifen is an estrogen antagonist that is used as an adjuvant therapy in patients with estrogen-sensitive breast cancer. It is sometimes also used for those with a strong family history of breast cancer. Therefore in this case it is important to establish why tamoxifen was indicated for the patient and if there had been an undeclared malignant disease. The duration of the tamoxifen treatment may give some additional information about the timing of the malignancy.

It is debatable whether a treated malignancy in the medical history, longer that 3 or 5 years ago, without metastasis or recurrence should be considered a contraindication for donation. The presence or history of malignant disease is listed in EU Directive 2006/17/EC as a criterion for the exclusion of a potential donor (Commission Directive 2006/17/EC 2006). However, the Directive also states that donors not meeting the general acceptance criteria may be accepted on the basis of a documented risk assessment authorised by the responsible person of the tissue establishment (Cox and Brubaker 2012). The Directives provide a common framework of minimum requirements, and stricter requirements in the national or local laws can be applied. Belgian legislation e.g. excludes donors with any malignancies (except basal cell skin carcinoma, carcinoma in situ of the cervix and certain types of brain tumors). However exceptions can be allowed based on a documented risk assessment, but only in the exceptional case of a documented absolute necessity for a well established individual patient.

This concept was discussed during the EATB conference in a presentation by Warwick and Eastlund.

They had been asked to present whether it is time to consider a change to the requirements for exclusion for history of malignancy. Currently for deceased donors the Commission Directive 2006/17/EC states that it is a contra-indication to donation when the donor has the presence, or previous history, of malignant disease, except for primary basal cell carcinoma, carcinoma in situ of the uterine cervix, and some primary tumours of the central nervous system that have to be evaluated according to scientific evidence. Donors with malignant diseases can be evaluated and considered for cornea donation, except for those with retinoblastoma, haematological neoplasm, and malignant tumours of the anterior segment of the eye.

However, in femoral heads and other tissues stored frozen and used without processing, cells can survive long-term storage at −80 °C. Bone may contain unsuspected malignant cells (Palmer et al. 1999; Sugihara et al. 1999; Zwitser et al. 2009). Unsuspected malignancies including lymphoma and chondrosarcoma, have been observed in femoral heads.

Yet, there are no reported cases of neoplasm transmission by skin, heart valve, bone or tendon transplantation. However, there have been two cases of accidental transplantation of patient-derived malignancies into the hands of surgeons through fresh needle stick injury where the nodules were excised and thus viable fresh malignant cells were transplanted across immunological barriers into an immune competent person (Gartner et al. 1996; Gugel and Sanders 1986). Despite this, there is a very low possibility of transmitting malignancies from tissue allografts for immunocompetent recipients because processed or frozen tissue allografts are likely to have a very low number of viable cells and the histocompatibility barrier is effective and immunosuppression is not used or necessary for successful tissue transplantation.

Current practice for traditional tissues varies by country and continent. Prospective donors with (certain) active malignancies, lymphomas, or leukemias are excluded from donating blood, tissues and organs. Potential organ donors with primary malignancies of the brain without spread are considered eligible and often also as tissue donors. Many tissue banks will accept deceased tissue donors with a remote history of malignancy, but donor eligibility policies vary widely but generally require at least curative treatment and several years of disease free status.

It is reasonable that facilities exclude tissue donors with disseminated malignancy (tissues, especially bone, may be damaged by metastases) and that an evidence-based risk assessment for individual cases should be undertaken by the tissue establishment's medical officer. In many cases this will be acceptable for processed tissues where the donor has a remote history of malignancy without metastasis. The only tissues which are reported to transmit malignancy are corneas where the donor was known to have disseminated malignancy in the eye. Eye donation is also different as corneas contain viable cells, are not highly treated during processing and they are not frozen.

It is important to check the history, examine the eyes, balance supply against the risk, but beware of potential risk in immunosuppressed recipients. It may indeed be time to enlarge the criteria of Commission Directives 2006/17/EC concerning malignancy, based on a risk assessment based approach to malignancy. References and evidence base for this discussion can be found in a chapter titled "Diseases transmitted by transplantation of organs, tissues, and cells" by Eastlund and Warwick (2012) and in the WHO project Notify Library (2013).

Caution should be exercised about donor malignancies which may have secondary spread especially those with a known with a propensity for dissemination and associated damage to bone, making it unsuitable for transplant (poor quality) as a separate issue to the risks of dissemination by the graft.

It was also discussed whether diabetes type II could be a contraindication for donation. Diabetes type I is considered a contraindication by some facilities because of its autoimmune origin. Type II diabetes is usually not a reason to reject a donor, although some tissue banks would consider prolonged insulin therapy an issue to consider. These are tissue quality issues; they are not related to transmission of disease.

Outcome of the case

The tissue establishment involved contacted the patient. Concerning the hepatitis, the patient mentioned that her brother and both her sisters also had hepatitis when she had jaundice as a child. This makes it more likely that the donor had hepatitis A. Hepatitis B and hepatitis C NAT results were negative.

Concerning the potential for breast cancer, the patient confirmed that she had a small surgical intervention in the right breast, one and a half years earlier, because of a "beginning cancer lesion". Further consultation with the treating physician found that the patient had been treated 2 years before for a breast cancer with lumpectomy. As the tumor proved to be local, but hormone dependent, a treatment with tamoxifen was started.

However, because of the malignancy and a more strict national interpretation of the Directive concerning malignancy as a contra-indication, the donor was rejected. In other countries, e.g. in the USA, tissue facilities accept donors with a history of malignancy such as breast cancer as long as there was no metastasis and the patient was disease-free for several years and considered cured by his or her physicians (American Association of Tissue Banking 2012). Even in these countries, this donor would probably have been rejected, because she has not yet had a long disease-free interval.

Overall workshop discussion and general workshop conclusion

Criteria for accepting and rejecting donors were divergent between discussion groups within the workshop and adjudicators. Overall, prior to a discussion by all the participants, groups decided within their group to accept most of the donors (80 % of the five cases) whereas other groups rejected most of the cases (80 % of the five cases). Thus, there was a good basis for discussing differences of opinions and opportunity to move towards consensus in some cases. It was clear that added scientific investigation is needed to provide sounder evidence-based decision making in the future, particularly in the risk of disease transmission and donor risk factors.

The issues discussed demonstrated that a balance is needed in using donor risk assessments that reject donors to ensure that recipient safety is not compromised and on the other hand that useful, irreplaceable tissues and cells that are safe, are not wasted.

The workshop provided an opportunity to present difficult cases in an informal atmosphere with access to a wide array of international expertise. Access to such varied expertise in a single setting is rare, but is very useful since it provides active peer support and cooperation in a specialist discipline. It is also an opportunity for all attendees to be reassured that most tissue banks have to deal with difficult cases and occasionally struggle with defining policy.

The donor case workshop, now in its ninth edition, was a success and establishes a useful tool for personal professional development and promotes networking between tissue facilities. The workshop format offers a channel for EATB to help its members comply with its mission.

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