Statutory Approvals Committee – minutes

Centre 0035 (Oxford Fertility)

Pre-implantation Genetic Diagnosis (PGD) application for Oculodentodigital Dysplasia (ODDD), OMIM #164200

Thursday, 26 October 2017

Church House Westminster, Dean's Yard, Westminster SW1P 3NZ

Committee members	Margaret Gilmore (Chair) Anne Lampe Anthony Rutherford Bobbie Farsides	
Members of the Executive	Dee Knoyle Bernice Ash Susanna Nyarko-Parkin	Committee Secretary Committee Secretary (Observing) Governance Officer (Observing)
External adviser	Dr Mary Porteous	
Legal Adviser	Jane Williams	Mills & Reeve LLP
Observers	Gerard Hanratty	Browne Jacobson LLP

Declarations of interest

- Members of the committee declared that they had no conflicts of interest in relation to this item.

The committee had before it:

- 8th edition of the HFEA Code of Practice
- Standard licensing and approvals pack for committee members.

The following papers were considered by the committee:

- Executive Summary
- PGD Application Form
- Redacted Peer Review
- Genetic Alliance opinion
- Patient's Comment

1. Consideration of application

1.1. The committee welcomed the advice of its Specialist Adviser, Dr Mary Porteous, who confirmed that the condition was as described in the papers.

1.2. The committee noted that the description in the application for Oculodentodigital Dysplasia (ODDD), OMIM #164200 is consistent with the peer review.

1.3. The committee noted that the Genetic Alliance opinion provided a patient perspective and supported the application. The committee also considered and discussed a letter, submitted with the application, from a patient with the condition.

1.4. The committee had regard to its decision tree. The committee noted that the centre is licensed to carry out PGD. The committee was also satisfied that the centre has experience of carrying out PGD and that generic patient information about its PGD programme and associated consent forms had previously been received by the HFEA.

1.5. The committee noted that the condition being applied for is not on the list of approved PGD conditions.

1.6. The committee noted that the proposed purpose of testing the embryos was as set out in paragraph 1ZA(1)(b) of Schedule 2 of the Act, i.e. 'where there is a particular risk that the embryo may have any gene, chromosome or mitochondrion abnormality, establishing whether it has that abnormality or any other gene, chromosome or mitochondrion abnormality'.

1.7. The committee noted that the condition is usually inherited in an autosomal dominant pattern which means there is a 50% chance of having an affected child in each pregnancy, if either parent has a relevant mutation. For the more common dominant type, penetrance appears to be virtually complete, with gene carriers being affected.

1.8. The peer reviewer reports that there is a more severe recessive form of ODDD caused by homozygous mutations in the same gene, GJA1, which is implicated in ODDD OMIM #164200. Autosomal recessive ODDD has the OMIM number #257850. The parents of a child affected by autosomal recessive ODDD are usually unaffected by the single GJA1 mutation they carry. The committee noted that the peer reviewer states that autosomal recessive ODDD has only been seen in a few families.

1.9. Oculodentodigital dysplasia (ODDD) is a disorder characterised by eye and digital anomalies, usually present at birth, together with characteristic patterns of dental anomalies and facial features.

1.10. Anomalies of the eyes range from cataracts and glaucoma to severe underdevelopment of the eye (microphthalmia). Visual loss and blindness may occur if there is severe microphthalmia or glaucoma. Cataracts may be removed surgically and glaucoma treated with eye drops or surgery.

1.11. Dental anomalies are a consist feature and the teeth may be absent or conical in shape. Affected individuals may require reconstructive and cosmetic dental procedures.

1.12. Approximately a third of affected individuals will develop neurological features such as spastic paraplegia. Neurological impairment can affect bowel and bladder function, causing incontinence and an unusual gait. The neurological problems are generally untreatable.

1.13. Digital anomalies usually involve webbing between the digits (syndactyly) which is often complete along the length of the digit. The digits may be curved. Digital anomalies usually require surgery to separate the digits to enhance function and this often leaves scarring between the digits.

1.14. Rarer complications of the condition are hearing loss, cardiac defects and oro-facial clefting. Hearing loss is usually conductive, requiring hearing aids. Occasionally there are structural malformations of the heart or cleft lip and palate which may require surgery.

1.15. There may be structural abnormalities of the brain and white matter abnormalities. In a small minority of cases, intellectual disability may be present in affected individuals and individuals may have special educational needs.

1.16. There is no cure for this condition or treatment which specifically modifies the disease process. There are possibilities for symptomatic treatment and psychological support and genetic counselling can be offered.

1.17. The committee noted the inspectorate's request to consider whether Oculodentodigital Dysplasia (ODDD), OMIM #164200 should be approved for inclusion on the PGD List and to consider adding autosomal recessive ODDD, OMIM #257850 to the PGD List since this is a more severe form of the condition. The committee agreed to consider the application on this basis.

2. Decision

2.1. The committee considered that Oculodentodigital Dysplasia (ODDD) is serious, given the significant risk that babies could be born with visual impairment causing blindness, develop complications causing hearing loss and later require dental surgery as well as surgery to separate digits with repeated skin grafts. Affected individuals could also develop neurological problems. The committee considered the psychological impact on the individual of not knowing what the future holds and to what extent the condition will debilitate them. The condition can be associated with various complications which can be distressing and difficult to manage.

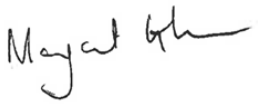
2.2. The committee had regard to its explanatory note and confirmed that, on the basis of the information presented, it was satisfied that there is a particular risk that an embryo may have the abnormality in question and that there is a significant risk, given the condition's worst symptoms, that a person with the abnormality will have or develop a serious physical or mental disability, a serious illness or any other serious medical condition. The committee was therefore satisfied that the condition Oculodentodigital Dysplasia (ODDD), OMIM #164200 meets the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act.

2.3. The committee agreed to authorise testing for Oculodentodigital Dysplasia (ODDD), OMIM #164200 and autosomal recessive ODDD, OMIM #257850, a more severe form of the condition.

3. Chair's signature

3.1. I confirm this is a true and accurate record of the meeting,

Signature



Name

Margaret Gilmore

Date

16 November 2017