Petition briefing – PE2080: Implement the recommended screening guidelines for people with Li-Fraumeni Syndrome

Background

The petitioner is calling on the Scottish Parliament to urge the Scottish Government to implement screening for people with, or at risk of, Li-Fraumeni Syndrome (LFS) (TP53 gene mutation), in line with the guidelines recommended by the UK Cancer Genetics Group.

It is not fully clear from the wording of the petition, but it is assumed that the petitioner wishes to see LFS genetic screening for people diagnosed with LFS related cancers, and then for encouragement for initial screening of any close relatives of those individuals to see if they too have LFS. The guidelines cited by the petitioner do not recommend routine cancer screening for those identified as having a 50% risk of a faulty TP53 gene.

LFS is caused by a gene mutation on a gene that controls cell growth in the body. It is a condition that makes it more likely that someone will develop cancer, often at a young age.

Cancer Research UK say that it is extremely rare and that data is limited, but researchers estimate that there are a few thousand people in the UK with LFS.

Genes

Genes are in the nucleus of all cells, carried on chromosomes, and give instructions for how cells in the body grow and function. Genes come in pairs and a person inherits one copy from each parent.

The function of the TP53 gene, that the petitioner highlights, is a gene that protects a person from cancer by controlling the growth of cells.

If someone inherits a mutation (fault) in one copy of the TP53 gene, they will be more likely to develop cancer. People with a change in the TP53 gene have Li-Fraumeni syndrome.

Someone with a TP53 gene mutation also has one normal copy. Only one copy of each gene pair is passed on to a child. If someone has a mutation in one copy of the gene, they have a 1 in 2 (50%) chance of passing on this mutation to each child they have, regardless of their biological sex or the child's sex.

Because it is an inherited condition based on a gene mutation, it is not something that can be treated.

Li-Fraumeni syndrome

According to the Manchester Cancer Research Centre:

> "Li Fraumeni Syndrome or LFS is caused by a TP53 germline mutation (a gene change in an egg or sperm cell of a parent that then appears in the DNA of every cell of the body of the child), which was one of the first hereditary cancer predisposition genes identified in the 1990s. Around 1 in 5,000 people in the UK have this inherited condition, which results in a high cancer lifetime risk. This means around 80% of people with this syndrome will develop cancer by age 70 (greater than a 70% chance for men and 80% chance in women). In addition, 40-49% of individuals with LFS have a risk of developing a second cancer.
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> Five cancer types account for the majority of tumours caused by LFS, including tumours located in the adrenal glands, breast, central nervous system, bones and soft tissues. Young women with LFS commonly develop breast cancer, while children and young adults with the syndrome can be seen to develop sarcomas, and brain tumours.
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> The average onset of cancers in individuals with LFS is in early adulthood with one study showing the average age at onset of the first cancer being around 25 years, with around 20% of carriers having developed a cancer by age just 5 years and 40% by age 18 years. Furthermore, 40-50% of individuals will go on to further primary cancers. As such, there is a need to identify adolescents, children and young adults with TP53 mutations."

Testing and screening for Li-Fraumeni Syndrome

According to the NHS Scotland Genomic Test Directory, testing for LFS is available in Aberdeen and Glasgow, two of four regional genetics centres in Scotland commissioned by NHS National Services Scotland (NHS NSS). These centres carry out genetic testing for Scotland and can test for over 200 conditions listed in the directory. LFS is one of 17 inherited cancers that can be tested for.

The referral criteria associated with testing for LFS appear to only apply to a person diagnosed with specific cancers and in certain age ranges. That is, it is not used

specifically for screening relatives and children of people found to have LFS. However, in the Directory's introduction, there is reference to the testing of one person having implications for other family members, and this association appears to be recognised in the referral criteria for testing.

Guy's and St Thomas's NHS Foundation Trust explain more about the way that testing is carried out for LFS.

The Manchester Cancer Research Centre explain that there are two ways that someone is identified as having LFS: if they present with cancer and are tested for the inherited mutation or where there is known to be LFS in the family other family members are offered predictive genetic testing for the TP53 gene alteration and surveillance is offered to those testing positive.

The petitioner refers to guidelines, published in June 2020 – written as a position statement – which emerged from a consensus meeting organised by the UKCGG using a preworkshop survey, followed by structured discussion on the day. A consensus was achieved for a UK surveillance protocol for carriers of the mutation which could be adopted by UK Clinical Genetics services. The key recommendations for screening those who have the TP53 gene mutation are:

- for annual WB-MRI (whole body magnetic resonance imaging) and dedicated brain MRI from birth,
- annual breast MRI from 20 years in women and
- three-four monthly abdominal ultrasound in children along with
- review in a dedicated clinic

The background to the guideline states that most carriers of the TP53 carriers have been identified through referral to clinical genetics services due to a personal or family history of cancer. Testing can be offered to at-risk relatives. However, it should be remembered that not everyone offered testing for the condition will wish to take it up. These guidelines set out more comprehensive surveillance proposals for carriers than have existed previously. The authors do not recommend screening of patients with a 50% risk of the gene mutation (from one parent), but should be provided with 'appropriate counselling and support, but should be encouraged to consider testing in order to access cancer screening." The reason that it is not recommended is because of the "intensity of the surveillance protocol".

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