Date: March 13, 2023

DISCIPLINE: GENOMICS

Fabry Protocol

Date effective: March 13, 2023

Background Information:

Fabry disease is an X-linked genetic disorder caused by defects in the GLA gene encoding the alpha galactosidase enzyme. Testing for this disorder can include biochemical and/or molecular genetic analysis.

The Molecular Diagnostics and Biochemical Genetics laboratories in collaboration members of the clinical genetics, neurology, nephrology, and cardiology teams reviewed and updated our testing practices to improve testing workflow and test accessibility.

Change in Test Procedure:

Biochemical screening will no longer be offered for female patients (see below).

For **female individuals with a clinical suspicion of Fabry disease AND** who meet one of the following criteria (see below), molecular testing for Fabry disease may be ordered by neurologists, nephrologists, cardiologists and geneticists.

As with all genetic testing, the patient must be aware that:

1. Genetic testing is voluntary.
2. A negative result reduces the chances of Fabry but does not conclusively rule out Fabry disease.
3. A positive result may have implications for their family members.
4. A variant of uncertain significance result does not confirm a diagnosis of Fabry disease and should not be used to inform clinical management.

Patient's ethnicity information guides testing and ethnicity should be noted on the requisition.

Fabry disease criteria:

- ☐ Diffuse Angiokeratoma on skin biopsy or as assessed by dermatology
- ☐ Periodic crises of severe pain in the extremities / acroparasthesias
- ☐ Corneal opacity and lenticular opacities
- ☐ **Unexplained** left ventricular hypertrophy or cardiac arrhythmia
- ☐ **Unexplained** stroke or small vessel disease before age 55 years
- ☐ Chronic kidney disease **of unknown etiology** (stage 3 or worse with proteinuria greater than 300mg/day/1.73m^2)

Fabry Biochemical and Molecular Genetic Testing Protocol

Female patients:

1. **No** biochemical testing will be offered for female patients unless special permission from Dr. Marie-Claude Dery, Clinical Biochemistry
2. If ordered by a specialist in Medical Genetics, Neurology, Nephrology, or Cardiology, molecular genetic testing is available as long as patient has at least one symptom from checklist.
3. All other requests for genetic testing of Fabry disease must submit F190-20-0106 Out of Province Molecular Genetic Testing Form .

Male patients:

1. Biochemical testing restricted to patients with findings consistent with Fabry disease
2. Genetic testing to be offered ONLY IF (all of the below):
    a. Test is ordered by Genetics
    b. Biochemical testing is suggestive of Fabry disease or indeterminate
    c. Patient's partner or a first-degree female relative of the patient is currently planning a pregnancy and intends to pursue prenatal diagnosis
3. All other requests for genetic testing of Fabry disease must submit must submit F190-20-0106 Out of Province Molecular Genetic Testing Form

References/Resources:

- Gene Reviews: https://www.ncbi.nlm.nih.gov/books/NBK1292/

Patient Impact:

- Improved patient care.

System Improvements:

- Better utilization of laboratory testing.

More Information:

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