GP Fact Sheet: Genetic Testing

Autism

We are currently experiencing unprecedented demand for outpatient clinical genetics appointments. Due to our very long waiting list, we would like to suggest an alternative way of managing the referral process for children with autism.

Prior to referral to a geneticist, there is now a panel of investigations that we would suggest you arrange to assist in diagnosis of a potential underlying genetic disorder and discussion of recurrence risk.

Investigations for autism

Blood tests:
- Chromosome microarray
- Fragile X molecular gene testing
- 7 Dehydrocholesterol level (to assess for Smith-Lemli-Opitz syndrome)
- Transferrin isoforms (to assess for congenital disorders of glycosylation)
- Urate
- Other standard tests for developmental delay if not previously done (e.g., CBP/TFTs/CK etc)

Urine tests:
- Amino acid/organic acid/MPS screen
- Creatinine/creatinine ratio
- Purine/pyrimidine screen

If a child has any focal neurological signs, signs of developmental regression, micro or macrocephaly then an MRI head should also be considered.

Once these investigations have been performed, referral to a geneticist may be of value if:
- A genetic diagnosis is reached on the basis of the results of the investigations.
- The child has complex autism (refer to Table 1), as syndromal assessment or more specialised gene testing (eg PTEN, MECP2 gene testing), should be considered.
- There are multiple affected family members.

In isolated cases of essential autism (refer to Table 1), with normal results from the recommended panel of investigations, referral to a clinical geneticist is unlikely to be of further diagnostic benefit.

If the primary reason for considering referral to a geneticist is to discuss recurrence risks, then the information in Table 2 may be of assistance.

If you have any further questions regarding this issue or wish to discuss an individual case, then please feel free to contact us at the Paediatric and Reproductive Genetics Unit (PRGU) on 8161 7375.
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Table 1: Definition of complex vs essential autism

**Essential** autism is defined by the absence of generalized dysmorphology and microcephaly. Approximately 70%-80% of children with autism have essential autism. Children with essential autism are more likely to be male. The currently available testing is less likely to reveal an exact etiologic diagnosis in essential autism than in complex autism.

**Complex** autism is defined by the presence of dysmorphic features or microcephaly or macrocephaly (>98th centile). Approximately 20%-30% of children ascertained because of a diagnosis of autism have complex autism. Approximately 30% of children with complex autism can be diagnosed with an autism associated syndrome or chromosome disorder using currently available diagnostic tests.

Table 2: Recurrence risk information for families

The empiric risk to siblings of individuals with autism spectrum disorders of unknown cause varies across studies but is generally considered to range from 10-15%. The risk to male sibs (brothers) of a proband (male or female) is 3-fold higher than for female sibs. Recurrence risk if 2 sibs are affected approaches 35%. (Ozonoff et al Paediatrics 2011)

The recurrence risk to siblings of a proband with complex autism is 1% for autism and an additional 2% for milder autism spectrum symptoms if no specific syndromal or single gene condition is diagnosed. No recurrence risk data are available for families who have one autistic child plus another child or relative with mild autistic symptoms. Therefore, the amount of weight to put on mild autistic symptoms in siblings, parents, and other relatives when estimating recurrence risk for families is currently unknown. There is no specific prenatal diagnosis that can be offered if all the above investigations detect no abnormality.

Due to the increased risk for male siblings, consideration of sex selection via IVF with preferential transfer of female embryos is an option that some couples may consider. Referral to a geneticist at an IVF unit may be considered to discuss this issue. In the situation where a specific diagnosis is reached through the panel of investigations, then recurrence risk is dependent on the diagnosis made and referral to genetics may be considered.

For more information
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