Appendix I
(Oral Free Paper Session)

ORAL PRESENTATION 5:

Clinical application of whole exome sequencing for paediatric undiagnosed dieases in Hong Kong – experience from first sixty cases

Mak CCY, Chu YWY, Wong WL, Leung GKC, Chung BHY
Department of Paediatrics & Adolescent Medicine, LKS Faculty of Medicine, The University of Hong Kong, Hong Kong

Background and aims

By using next generation technology to sequence all the coding regions of the genome, whole-exome sequencing (WES) is now a more affordable and an increasingly important tool in diagnosing unsolved diseases. Worldwide, there has been growing collaborative efforts to solve rare and undiagnosed diseases using WES technology, with a diagnostic yield of up to 30%. We introduced the use of whole exome sequencing to paediatric patients with rare diseases in Hong Kong, and share our findings of the first 60 cases.

Methods

Sixty children with undiagnosed diseases referred to the genetics service in Queen Mary Hospital were recruited. These patients had all been assessed by a geneticist and genetic counsellor with conventional cytogenetic and molecular testing performed where appropriate. For those where a genetic diagnosis could not be obtained, the patients were offered singleton whole-exome sequencing. The results were validated and the relevant literature reviewed to determine the pathogenic nature of the mutation.

Results

A diagnostic rate of pathogenic causal variants was found in over 25% of patients, comparable to internationally reported figures. In addition to mutations in known rare diseases, we also discovered extended phenotypes of known syndromes and mutations contributing to newly described syndromes.

Conclusion

We share our experience in establishing WES as a useful tool for obtaining difficult diagnoses, as well as a valuable research tool to discover new genetic causes of rare diseases. The overall aim is not only to help more families to raise awareness and reach a diagnosis in the local population, but also to establish a pipeline to deal with the challenges of future application of next generation sequencing in the diagnosis of rare paediatric diseases.

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