Genetic Tales

Abstract:

Sir

Genetic diagnoses do not always happen in a clinic or as a result of a blood test. We describe how two relatively rare genetic diagnoses were made in unusual circumstances, one by self-diagnosis, the second by pattern recognition in a public space. At a recent meeting of the Irish American Pediatric Society in Charleston NC, eminent cardiologist and discoverer of Noonan Syndrome, Jacqueline Noonan, spoke of a man who wrote to her having made a self-diagnosis of Noonan syndrome: a characteristic configuration of facial features including a webbed neck and a flat nose bridge, short stature and heart defects[1]. Dr Noonan arranged to meet this 65 year-old man and personally validated him as perhaps the oldest confirmed, and first ever self-diagnosed, case of Noonan syndrome.

Another story was recalled by a Professor of Medical Genetics. A young woman, on a ferry boat trip, was approached by a harried young man who told her to â hurry up, we are all ready to leaveâ . When the young girlâ s sister intervened, it turned out the man was supervising a Prader-Willi Syndrome (PWS) Association day-outing and inadvertantly mistook the young lady for one of his clients. Upon returning home, a genetic consultation and testing confirmed that the young lady did indeed have PWS, explaining her plump short stature and mild learning difficulties during her schooldays.

These anecdotes serve to remind us of the underdiagnosis of many genetic conditions in the general population and the importance of pattern recognition in recognizing such rare conditions. It is not known how many people in the general population have unrecognised rare syndromes. Some experts say that between 30 to 40 percent of children with special needs do not have an exact diagnosis. There are also many children with multiple malformations and developmental delay, but without a specific diagnosis - SWAN: Syndromes without a name[2]. Experts make diagnoses through a combination of intuition (pattern recognition)[3] and metacognition (thinking about how one and others think, that includes clinical reasoning and analytical thinking)[3]. Sometimes a diagnosis by pattern recognition is instantaneous and exact, as seen in the second case here, although pattern recognition can often be unreliable if not supported with metacognition[3].

Geneticists are deriving enormous benefits from newer diagnostic aids especially high resolution microarray comparative genome hybridization which compares the amount of DNA present for each chromosome in a single cell, to that of a normal standard. Whole exome sequencing, with analysis of the coding regions of 24,700 genes simultaneously, is now coming into clinical practice[4]. Nevertheless, there is always a place for a discriminating pair of eyes which initiates the search for a diagnosis in the first instance, often not medically-trained eyes, as seen in the cases here.

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