ECMGG Examination: Sample Structured Oral Assessment (SOA)

Structured Oral Assessment

Materials provided to candidate

You have 3 minutes to read and understand the materials provided, followed by an 8 minute discussion of the clinical case with your examinersex, who will ask you specific questions.

Referral Letter and Laboratory Information:

Dr J Brown
Consultant in Clinical Genetics
Genetics Service

1st April 2017

Dear Jon,

I would be very grateful if you could see Joanna Scarlet, age 23 years. Her mother unfortunately died suddenly at the age of 50 earlier this year. I am not aware of any other family history, although their grandfather died following a heart attack at 52.

I have received a copy of a DNA report that I enclose with this letter, and look forward to hearing your advice.

Yours sincerely,

General Practitioner

Genetics Service

National Accredited Laboratory

Patient: Elizabeth Scarlet (deceased) **Hosp No:** ABC123

Date received: 12/09/2017

Date reported: 22/09/2017

Disorder: Sudden Death ? cause

Reason for Referral: Previously well. Sudden death age 42 from a possible cardiac cause.

Results Summary:

Heterozygous pathogenic mutation p.ARG79X mutation identified in *PKP2*.

Comments:

This variant in the *PKP2* gene changes an Arginine codon to a stop codon at position 79 in the *PKP2* gene. This variant is known to be pathogenic, and has been reported frequently in Dutch families with either a history of sudden death or arrhythmogenic right ventricular dysplasia. An abstract referring to this mutation is attached.

Presymptomatic testing can be offered to family members and they should be offered referral to Clinical Genetics.

Neth Heart J. 2010 Nov;18(12):583-91. doi: 10.1007/s12471-010-0839-5.

Recurrent and founder mutations in the Netherlands: Plakophilin-2 p.Arg79X mutation causing arrhythmogenic right ventricular cardiomyopathy/dysplasia.

van der Zwaag PA[1], Cox MG, van der Werf C, Wiesfeld AC, Jongbloed JD, Dooijes D, Bikker H, Jongbloed R, Suurmeijer AJ, van den Berg MP, Hofstra RM, Hauer RN, Wilde AA, van Tintelen JP.

Author information

Abstract

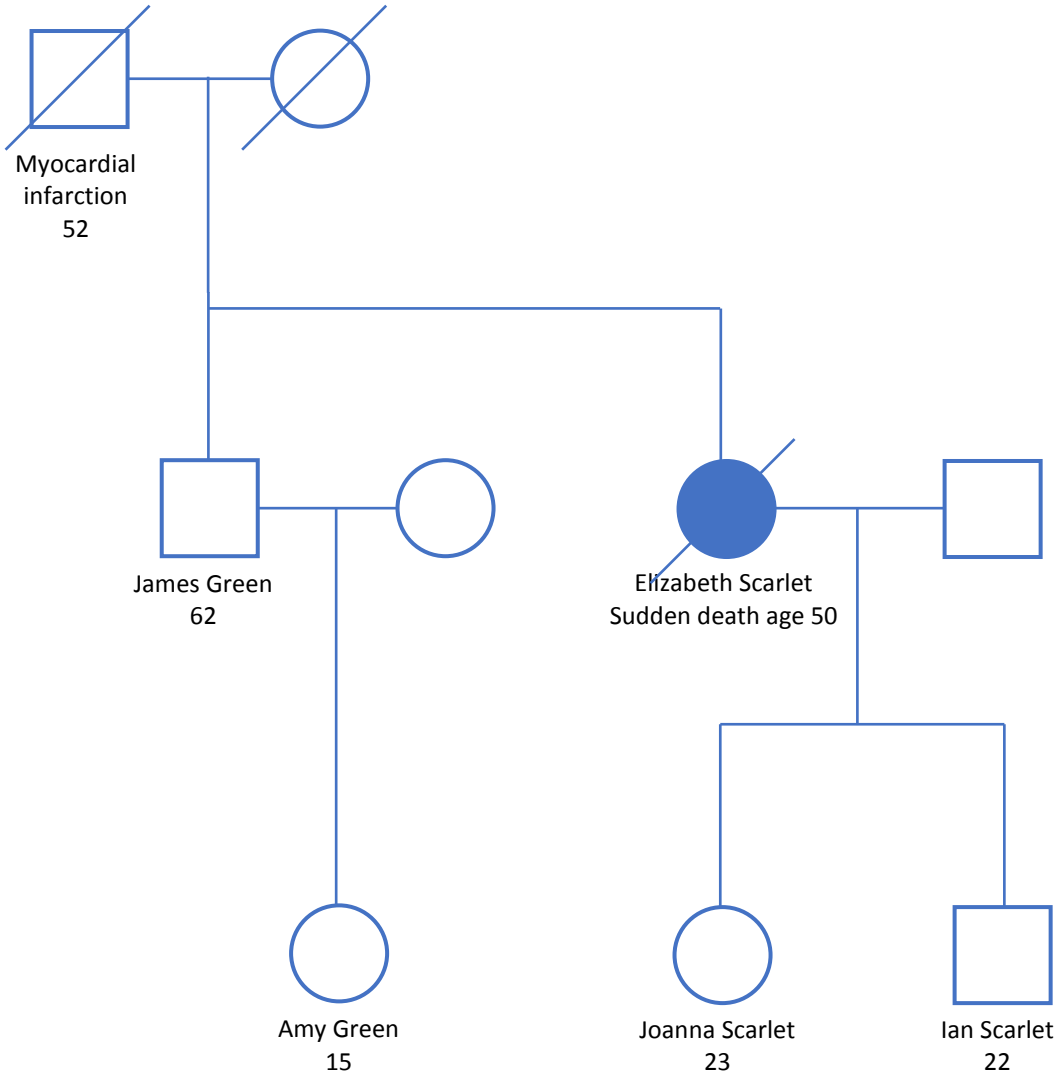
Background. Arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D) is an inherited cardiac disease with reduced penetrance and a highly variable expression. Mutations in the gene encoding the plakophilin-2 gene (PKP2) are detected in about 50% of ARVC/D patients. The p.Arg79X mutation in PKP2 has been identified in Europe and North America and has been functionally characterised. We evaluated the prevalence of the p.Arg79X mutation in PKP2 in the Dutch population.

Methods. Twelve index patients and 41 family members were evaluated in three university hospitals in the Netherlands. The diagnosis of ARVC/D was established according to the recently revised Task Force Criteria. Segregation of the p.Arg79X mutation was studied and haplotypes were reconstructed to determine whether the p.Arg79X mutation was a recurrent or a founder mutation.

Results. The p.Arg79X mutation in PKP2 was identified in 12 index patients. Haplotype analysis revealed a shared haplotype among Dutch p.Arg79X mutation carriers, indicating a common founder. Six index patients (50%) had a first- or second-degree relative who had died of sudden cardiac death below 40 years of age. At age 60, only 60% of the mutation carriers had experienced any symptoms. There was no significant difference in symptom-free survival and event-free survival between men and women.

Conclusion. We have identified the largest series of patients with the same desmosome gene mutation in ARVC/D reported to date. This p.Arg79X mutation in PKP2 is a founder mutation in the Dutch population. The phenotypes of PKP2 p.Arg79X mutation carriers illustrate the clinical variability and reduced penetrance often seen in ARVC/D. (Neth Heart J 2010;18:583-91.).

Pedigree


Myocardial
infarction
52
James Green
62
Elizabeth Scarlet
Sudden death age 50
Amy Green
15
Joanna Scarlet
23
Ian Scarlet
22

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Materials provided to examiners

QUESTIONS

Please ask each question in bold italics, exactly as phrased. Suggested follow on questions are given to assist in developing the theme if a candidate does not develop the theme spontaneously. Approximately 2.5 minutes should be used for each of the 3 questions.

Question 1
(Testing domains a, b)

What is meant by the term 'penetrance' ?
Why is penetrance important in this case ?
What is a 'founder mutation' – and why is this important to a clinical geneticist ?

ANSWERS EXPECTED TO INCLUDE:

***Penetrance* – percentage likelihood of phenotype given genotype – all or nothing phenomenon**

Mutation / variant has element of *age-dependant* penetrance – and also *incomplete* penetrance, which makes it difficult to counsel patient – may remain asymptomatic through life even if affected – with adverse financial consequences if mutation / variant is identified.

***Founder* mutation is one that has become amplified in population owing to a small starting population. Such mutations may be well known in a specific population and are more likely to have clinical outcome data associated with them.**

Follow on if details not elicited:

(a) So, classically, penetrance refers to an all or nothing phenomenon – either the patient has symptoms or they do not. Why is this complicated for a mutation / variant such as this one in the *PKP2* gene ?

(b) Why is the issue of penetrance important in the *clinical* management of this patient ?

Question 2
(Testing domains b, c)

(a) What is the risk, for Joanna Scarlet, of inheriting the mutation ?

50%

(b) What issues would you likely discuss with Joanna when she has an appointment to see you in the genetics clinic ?

Level of risk
Variable penetrance – may not have features
Risk of cardiac events / sudden death
Financial Issues
Reproductive issues and options
Presymptomatic testing protocol
Option to not have test

Question 3
(Testing domains c, d)

You contact James Green by letter, but he writes back to tell you that he is an airline pilot, and is too busy to be seen in the clinic. What are your concerns, and what action should you take ?

Have concerns about profession of Mr Green – consider whether more forceful approach. Also consider public health risks against right of autonomy/confidentiality.
Criteria for breach of confidentiality will vary between countries – so a more general understanding that different countries have different rules – and that it may be relevant in some jurisdictions should suffice for full marks.

(Note, if they say no action possible, ask if you should be permitted to breach confidentiality in any situation, and what criteria they would apply)

Follow on:

James Green still refuses to be tested, but his daughter Amy becomes aware of the family situation and attends your clinic. What are the Genetic counselling issues that you should consider ?

Here the issue is that testing Amy will test her father; also, do you have permission to use the test result to offer Amy test? If you do – various approaches and considerations, including whether you can re-approach the father and at least make him aware that his daughter is being tested.

CANDIDATE No.	

Name: …….

Station …

Scoring Grid

Please score each domain independently, using the criteria provided – place a tick in the appropriate score for each of the 4 domains.

	(a) Understanding Basic Scientific Principles	**(b) Demonstrating Clinical Management**	**(c) Demonstrating Clinical Communication**	**(d) Understanding ethical and legal considerations**
Clear Fail				
Borderline Fail				
Borderline pass				
Clear Pass				