Individuals with Pathogenic Variants in ANKRD26: Management Guidelines for Healthcare Professionals

General information

- Germline pathogenic variants (GPV- including class 4 likely pathogenic and class 5 pathogenic variants) in the ANKRD26 gene are associated with thrombocytopenia 2 (OMIM #188000) (also referred to as ANKRD26-related thrombocytopenia) and follow an autosomal dominant inheritance pattern.
- ANKRD26 heterozygotes are at increased risk of acute myeloid leukaemia (AML), myelodysplastic syndrome (MDS) and chronic myeloid leukaemia (CML).
- They usually have a family history of thrombocytopenia.
- ANKRD26 heterozygotes have lifelong mild to moderate thrombocytopenia with normal platelet size and absent or mild bleeding tendency.

Associated cancer risks

AML/MDS/CML

- Lifetime risk data are not currently available. Penetrance is incomplete.
- In a series of 222 ANKRD26 heterozygotes 4.9% had AML, 2.2% had MDS and 1.3% had CML6.

Management recommendations

Surveillance

All patients with ANKRD26-related thrombocytopenia should be referred to a haematologist with specialist interest in Haemostasis and offered registration with a UK Haemophilia Centre.

- Planned and unplanned invasive procedures including dental procedures, pregnancy and delivery should be discussed with the patient’s Haemophilia Centre.

No clinical practice guidelines exist relating to surveillance for myeloid malignancies. There is lack of evidence regarding the utility of surveillance (type and frequency)3.

- All patients should be offered advice about symptom awareness.
- Patients need to seek medical advice promptly, if they develop easy bleeding/bruising or any constitutional signs and symptoms of MDS/AML (e.g., fatigue, infections, bleeding, and skin changes).
- You can find more information regarding additional surveillance options in the FAQs here: https://www.ukcgg.org/information-education/ukcgg-leaflets-and-guidelines/

- Referral to haematology of all ANKRD26 heterozygotes who develop a blood phenotype (pre-malignant/malignant) for monitoring and follow up (if not already under the care of haematology).

Transplant considerations

- Where possible allogeneic haematopoietic stem cell transplant using related donors with pathogenic germline ANKRD26 variants should be avoided due to risk of donor cell-derived leukaemia2.
- Urgent referral to Clinical Genetics of potential donor at-risk relatives for genetic counselling and consideration of germline testing.

Lifestyle advice

- Use of medications that may increase risk of bleeding or affect platelet function (e.g., anticoagulants, NSAIDS and anti-platelet agents) should be discussed with the patient’s Haemophilia Centre.
- Encourage patients to discuss work or leisure activities that place them at risk of trauma or bleeding with their Haemophilia Centre.
- Provide information on the benefits of smoking cessation, maintaining a healthy weight and minimising exposure to chemicals and radiation to lower the chance of developing haematological cancer.

Family matters

- Refer to clinical genetics for further genetic counselling and for discussion of predictive genetic testing in at-risk family members (if not seen in genetics previously). Genetic counselling may be provided in some Haemophilia Centres.
- The age at which predictive testing is offered to asymptomatic at-risk children should be individualised taking into account the genotype and family history, in shared decision making with the family.
- Refer to clinical genetics for discussions on reproductive options, where applicable.

Key references


Patient resources

- Under development by UKCGG in collaboration with Leukaemia Care and MDS UK Patient Support Group
- https://www.pdsa.org

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