Aktiv Druck & Verlag GmbH | ISSN 0170 - 5334 I 02330

www.ai-online.info

64. Jahrgang | Mai 2023

A&I

ANÄSTHESIOLOGIE & INTENSIVMEDIZIN

Offizielles Organ: Deutsche Gesellschaft für Anästhesiologie und Intensivmedizin e. V. (DGAI)
Berufsverband Deutscher Anästhesistinnen und Anästhesisten e. V. (BDA)
Organ: Deutsche Interdisziplinäre Vereinigung für Intensiv- und Notfallmedizin e. V. (DIVI)

MYH9-related disease (MYH9-RD)

Neuromyotonia

orphanaesthesia

a project of the German Society
of Anaesthesiology and Intensive Care Medicine

SUPPLEMENT NR. 8 | 2023

OrphanAnesthesia –
ein krankheitsübergreifendes Projekt des Wissenschaftlichen Arbeitskreises Kinderanästhesie der Deutschen Gesellschaft für Anästhesiologie und Intensivmedizin e.V.

Ziel des Projektes ist die Veröffentlichung von Handlungsempfehlungen zur anästhesiologischen Betreuung von Patientinnen und Patienten mit seltenen Erkrankungen. Damit will OrphanAnesthesia einen wichtigen Beitrag zur Erhöhung der Patientensicherheit leisten.

Patientinnen und Patienten mit seltenen Erkrankungen benötigen für verschiedene diagnostische oder therapeutische Prozeduren eine anästhesiologische Betreuung, die mit einem erhöhten Risiko für anästhesieassoziierte Komplikationen einhergehen. Weil diese Erkrankungen selten auftreten, können Anästhesistinnen und Anästhesisten damit keine Erfahrungen gesammelt haben, sodass für die Planung der Narkose die Einholung weiterer Information unerlässlich ist. Durch vorhandene spezifische Informationen kann die Inzidenz von mit der Narkose assoziierten Komplikationen gesenkt werden. Zur Verfügung stehendes Wissen schafft Sicherheit im Prozess der Patientenversorgung.

Die Handlungsempfehlungen von OrphanAnesthesia sind standardisiert und durchlaufen nach ihrer Erstellung einen Peer-Review-Prozess, an dem eine Anästhesistin bzw. ein Anästhesist sowie eine weitere Krankheitsexpertin bzw. ein weiterer Krankheitsexperte (z. B. Pädiaterin bzw. Pädiater oder Neurologin bzw. Neurologe) beteiligt sind. Das Projekt ist international ausgerichtet, sodass die Handlungsempfehlungen grundsätzlich in englischer Sprache veröffentlicht werden.

Ab Heft 5/2014 werden im monatlichen Rhythmus je zwei Handlungsempfehlungen als Supplement der A&I unter www.ai-online.info veröffentlicht. Als Bestandteil der A&I sind die Handlungsempfehlungen damit auch zitierfähig. Sonderdrucke können gegen Entgelt bestellt werden.

Bisher in A&I publizierte Handlungsempfehlungen finden Sie unter:

www.ai-online.info/Orphsuppl
www.orphananesthesia.eu

OrphanAnesthesia –
a project of the Scientific Working Group of Paediatric Anaesthesia of the German Society of Anaesthesiology and Intensive Care Medicine

The target of OrphanAnesthesia is the publication of anaesthesia recommendations for patients suffering from rare diseases in order to improve patients' safety. When it comes to the management of patients with rare diseases, there are only sparse evidence-based facts and even far less knowledge in the anaesthetic outcome. OrphanAnesthesia would like to merge this knowledge based on scientific publications and proven experience of specialists making it available for physicians worldwide free of charge.

All OrphanAnesthesia recommendations are standardized and need to pass a peer review process. They are being reviewed by at least one anaesthesiologist and another disease expert (e.g. paediatrician or neurologist) involved in the treatment of this group of patients.

The project OrphanAnesthesia is internationally oriented. Thus all recommendations will be published in English.

Starting with issue 5/2014, we'll publish the OrphanAnesthesia recommenations as a monthly supplement of A&I (Anästhesiologie & Intensivmedizin). Thus they can be accessed and downloaded via www.ai-online.info. As being part of the journal, the recommendations will be quotable. Reprints can be ordered for payment.

Find a survey of the recommendations published until now on:

www.ai-online.info/Orphsuppl
www.orphananesthesia.eu

Projektleitung
Prof. Dr. Tino Münster, MHBA
Chefarzt
Klinik für Anästhesie und operative Intensivmedizin
Krankenhaus Barmherzige Brüder Regensburg
Prüfeninger Straße 86
93049 Regensburg,
Deutschland
Tel.: 0941 369-2350
E-Mail: Tino.Muenster@barmherzige-regensburg.de

DGAI
Deutsche Gesellschaft für Anästhesiologie & Intensivmedizin
www.dgai.de

A&I
ANÄSTHESIOLOGIE & INTENSIVMEDIZIN
www.ai-online.info

orphananesthesia

Anaesthesia recommendations for

MYH9-related disease (MYH9-RD)

Disease name: MYH9 related disease (OMIM 600208)

ICD 10: D69.4

Synonyms: May-Hegglin anomaly, Epstein syndrome, Fechtner syndrome, Sebastian syndrome, MYH9-related thrombocytopenia, MYH9-related syndrome, MYH9-related syndromic thrombocytopenia, MYH9-related disorder, MYH9-related disease (MYH9-RD).

Disease summary: With more than 300 families reported in the literature, MYH9-RD is the most frequent form of inherited thrombocytopenia [1,2]. It encompasses four dominant disorders previously considered as distinct disorders (see synonyms). MYH9-RD is phenotypically variable and characterised by congenital macrothrombocytopenia as well as characteristic leucocyte inclusions (Döhle bodies) in all patients. Some patients may develop additional clinical features such as cataracts, hearing loss and/or progressive kidney disease. This is a rare autosomal dominant inherited disorder caused by mutations of the MYH9 gene encoding for the heavy chain of non-muscle myosin-IIA (myosin9). The bleeding tendency is broadly related to the level of platelet count. The main anaesthetic concerns in the management of patients with MYH9-RD are the development of a strategy to reduce haemorrhagic complications and the screening of associated disorders, particularly renal and hepatic impairment. The possibility of performing neuraxial anaesthesia will depend on platelet levels and normal platelet function.

In 1909, May observed that the blood smear of a woman referred to him showed many leukocytes which contained one or several pale blue inclusion bodies [3]. Thirty-six years later, Hegglin described in three members of the same family the combination of a thrombocytopenia with giant platelets and the presence of Döhle-like bodies in their neutrophils [4]. The name “May-Hegglin anomaly” was used in a case report published by Scholer et al. which Hegglin commented as being identical to his own report. Thereafter, the conjoined eponym “May-Hegglin anomaly” was used.

The disease locus was mapped to chromosome 22q12.3-q132 by linkage analysis [5,6,9]. The gene responsible for this disorder was identified as MYH9, which encodes a large cytoplasmic protein (NMMHC-IIA), expressed in many different tissues including blood cells, kidney, cochlea, hepatocytes. This protein regulates the cytoskeleton and acts as a key component of the activities that drive cell migration, cell-cell interaction and cell matrix adhesion. The pathogenesis of thrombocytopenia is mainly secondary to defective proplatelet formation by increased contractibility.

Several other inherited disorders that were previously considered to be separate entities (see synonyms) were in fact caused by mutations in the MYH9 gene. Therefore, the name MYH9-related disease or MYH9 disorder has been proposed [7]. To date, over 80 different mutations have been identified [8,9]. The majority of patients are heterozygous for missense mutations and some patients for nonsense or frameshift mutations or deletions or

▶ **Citation:** Favier R, Rigouzzo A, Piana F, Louvet N: MYH9-related disease (MYH9-RD). Anästh Intensivmed 2023;64:S253–S262. DOI: 10.19224/ai2023.S253

duplications. Importantly, 35 % of MYH9-RD cases are sporadic and in half of them a de novo mutation is confirmed by molecular testing in parents.

The thrombocytopenia is characterised by large platelets (i.e. 40 % of platelets > 3.9 µm in diameter) and a platelet count <150x10^9/l, both detected from birth. Sometimes the platelet count decreased may be more severe < 30x10^9/l. Platelet aggregation, serotonin release, clot retraction are more often normal or slightly altered. Döhle bodies stained with May-Grunwald-Giemsa are present in 42–84 % of individuals with MYH9-RD, but detectable in all affected patients by immunofluorescence labelling of the non-muscle myosin heavy chain IIA protein in granulocytes [1].

The severity of bleeding is broadly related to the platelet count but most patients have a low haemorrhagic score as defined by the bleeding assessment tool of the International Society of Thrombosis and Haemostasis (ISTH/BAT) [10,11]. The prevalence of mucocutaneous bleeding was significantly higher in patients with head domain mutations of Myosin-9 [12]. As a result, the diagnosis may wait until adulthood as they are at risk to develop renal failure, deafness or cataract in early or middle life. Easy bruising, spontaneous mucocutaneous bleedings, excessive bleedings after haemostatic challenges, or treatment with drugs interfering with platelet function, are manifestations of thrombocytopenia. In some rare patients with severe bleeding due to menorrhagia or intracranial bleeding, platelet transfusions should be used. Nevertheless, recent progress in the preoperative management by using thrombopoietin (TPO) mimetics must be noticed and are an interesting alternative in adults and children [13,14,15,16].

Differential diagnosis includes other macrothrombocytopenias (MTP) such as Bernard-Soulier syndrome (OMIM 213200/153670) or ACTN1 (OMIM 615193) or ITGA2B ITGB3 (OMIM187800) or TUBB1 (OMIM613112) or DIAPH1 (OMIM124900) related thrombocytopenias [17].

Medicine is in progress

Perhaps new knowledge

Every patient is unique

Perhaps the diagnosis is wrong

Find more information on the disease, its centres of reference and patient organisations on Orphanet: www.orpha.net

© Anästh Intensivmed 2023;64:S253–S262 Aktiv Druck & Verlag GmbH

Typical surgery

Surgical procedures that are specific to MYH9-RD can be related to the associated syndromes. These are cochlear implantation, ophthalmic surgery, renal transplantation [18,19,20]. All other types of surgical procedures may be performed in these patients [21,22,23,24]. Ideally, all patients should be managed, in particular during pregnancy, by a multidisciplinary team combining several experts in anaesthesia, haemostasis and obstetrics during pregnancy.

Several important points should be kept in mind by the anaesthesiologist for the management of a patient: Is the decision for the surgical procedure elective or is there a state of emergency? Is it necessary to obtain an urgent increase in platelet count for patients at high risk of bleeding? Ensure that the most appropriate expert advice has been obtained.

Type of anaesthesia

No explicit recommendations or guidelines have been published for patients with haemostatic disorders, in particular inherited platelet disorders.

Potential renal or hepatic damage should be integrated into the pharmacokinetics of the anaesthesia agents used.

Before performing neuroaxial or peripheral nerve blocks, and in order to prevent the risk of haematoma secondary to regional anaesthesia, the severity of the thrombocytopenia, the coagulation status (platelet functions), the presence of clinical bleeding, and the benefit-risk balance of the procedure for a given patient should be taken into account. It is important to underline that an exact optical and manual platelet count must be requested when the haematological analysers used are incapable of register the presence of giant platelets [24].

Neuroaxial anaesthesia was successfully performed in several studies with platelet counts of at least $80x10^9$/l [25,26]. Spinal or epidural anaesthesia is generally safe when the platelet count is at least equal to $80x10^9$/l, but in some reports it has been performed in women with platelet counts under $50x10^9$/l [27]. Nevertheless, there is insufficient published evidence to make recommendations for lower platelet counts presently. For this reason, in accordance with published recommendations [28,29], loco-regional anaesthesia procedures remain possible if platelet functions are normal and their count is ≥ $80x10^9$/l. For patients with platelet counts less than $75x10^9$/l, an individual decision must be made based on the benefits and risks [30].

No contraindication for sedation or certain pain management methods are known at the present time, but it has been recommended that any repeated applications of NSAIDs should be administered carefully in patients with MYH9-RD.

Necessary additional preoperative testing (beside standard care)

Besides the necessity to obtain a correct platelet count in the preoperative or prepartum period, it is necessary also to obtain data on platelet functions, i.e. platelet aggregation and platelet secretion, when the level of thrombocytopenia allows these investigations. It should be noted that these functions are normal for the majority of patients, but it is important to verify this point and to exclude, for example, acquired additive abnormalities. These functions may be tested by applying different methods depending on the level of the platelet count. If

© Anästh Intensivmed 2023;64:S253–S262 Aktiv Druck & Verlag GmbH

this count is above 80x10^9/l, the aggregometry method can be used; if under this level, we recommend to test platelet function by flow cytometry, a very interesting method that requires a low quantity of blood and can be used not only for adults but also for children. Another alternative which might be beneficial in the future for making decisions in cases of surgical or obstetrical emergencies is to perform preoperative thromboelastography (TEG) [30] but, so far, no consensus has been obtained and no official recommendation can be made.

Assessment of renal function and hepatic function is indicated regardless of the patient's age. Patients may be asked whether they present a hearing loss and whether or not they have a cataract.

Particular preparation for airway management

Bleeding after airway trauma and intubation is a theoretical risk in these patients, but it has not been reported up to now. No consensus has been published concerning the selection of the therapeutic method and no specific guideline about platelet counts being necessary to prevent airway trauma is available at the moment. In case of difficult intubation and particularly if the platelet count is at least 50x10^9/l, the use of a fibrescope or video laryngoscope may reduce the risk of bleeding.

Particular preparation for transfusion or administration of blood products

Transfusion of platelet concentrates may be helpful in the immediate preoperative period or at the very beginning of the surgical procedure. In some reports, HLA-matched platelet transfusions were used as a better option, so it is necessary to treat these patients in surgical or obstetrical centres connected with blood banks that allow for a rapid access to these blood products.

Similar to previous guidance provided for ITP [31], the following platelet counts could be necessary for the various procedures; simple dental extraction or regional dental block: >30x10^9/l; complex extractions: > 50x10^9/l; - minor surgery > 50X10^9/l; major surgery such as neurosurgery, renal transplantation >100x10^9/l [32,33].
If the surgery is not urgent, we recommend to administrate TPO mimetics either each day per os or by one subcutaneous injection per week. The increase of platelet count is detected from 2 to 4 weeks after the beginning of this treatment which may avoid platelet transfusion [12,13,14,15]. If indicated during the perioperative period, treatment is generally started 4 weeks before surgery and the minimal platelet count to be reached is 50 x 109/l, but it also depends on the type of surgery (see above). The platelet level and liver enzymes must be monitored every week. Duration of treatment by TPO mimetics will be adjusted to the haemorrhagic risk in the postoperative period: the platelet count will return to its baseline rate one to three weeks after the end of treatment.

Particular preparation for anticoagulation

MYH9-RD thrombocytopenia does not protect against thromboembolic complications [34,35,36] that can also be present after surgery in the absence of adequate antithrombotic prophylaxis. So prophylactic anticoagulation must be administrated when needed in the postoperative period of surgeries associated with a high risk of thrombosis. Mechanical prophylaxis (compression stocking) should be also considered.

© Anästh Intensivmed 2023;64:S253–S262 Aktiv Druck & Verlag GmbH

Particular precautions for positioning, transportation and mobilisation

No special precaution for positioning, transport or mobilisation is recommended. Any trauma must be avoided.

Interactions of chronic disease and anaesthesia medications

All medication interfering with platelet function: aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs) or antiplatelet agents must be avoided.

Conversely, antifibrinolytic agents such oral or IV tranexamic acid and epsilon aminocaproic acid may be useful in preventing recurrent bleeding in these patients and in cases of certain dental or surgical procedures [37].

Anaesthetic procedure

All kind of general anaesthesia methods may be used for emergency and elective surgeries in patients with MYH9-related disease.

Particular or additional monitoring

Additional monitoring is dependent on the type of surgery and the risk of bleeding. To consider central venous catheter in patients at great risk of bleeding during surgery, the platelet count must be > 50-60x10^9/l and platelet function normal. If bleeding is expected, haemodynamic monitoring and cell salvage have to be anticipated as well as a constant connection with the blood bank and delocalised haemoglobin and coagulation follow-up. In cases of renal or hepatic dysfunction, strict noninvasive or semi-invasive haemodynamic monitoring should be anticipated preoperatively for surgery and the postoperative period.

Possible complications

The risk of fatal bleeding is very low but this risk is, as in the general population, increased in elderly patients, in patients with a previous history of bleeding, or in patients with other associated comorbidities: hypertension, liver cirrhosis, cardiovascular events inducing the use of antiplatelet agents or anticoagulants.

Fatal bleeding complications in children and adults have never been reported to date, even if the bleeding tendency is associated with a lower platelet count in bleeders than in non-bleeders [9].

Complications due to the use of TPO mimetics must be known also: A risk of thrombosis has been described in some rare reports, and a platelet count must be performed one month after termination of the treatment [16].

© Anästh Intensivmed 2023;64:S253–S262 Aktiv Druck & Verlag GmbH

Postoperative care

Postoperative care is necessary and depends on the known risk of bleeding of the surgery and whether the patients are known to have a high bleeding score. In some types of surgery, e.g. renal transplantation or neurosurgery, a preoperative and postoperative platelet count equal to or higher than $100x10^9$/l has been recommended [32,33]. Consequently, all these clinical data demonstrate the necessity of paying close attention to platelet counts and bleeding in the postoperative period for 6–7 days after minor surgery, and for 14 days after major surgery. We think that all these patients also require a close follow-up after their release from the hospital.

As previously mentioned, MYH9-RD macrothrombocytopenia does not protect against postoperative venous thromboembolism, and patients should be considered for routine postoperative thromboprophylaxis in situations with a high risk of thrombosis.

Disease-related acute problems and effect on anaesthesia and recovery

As with other patients, emergency situations may occur before or after surgery itself. In the event of uncontrolled bleeding, platelet transfusion should be considered. Possible therapeutic approaches might include recombinant factor VIIa (rFVIIa), but no reports on this alternative have been published.

Desmopressin has been tested in MYH9-RD with success [38]. However, due to the observed interindividual variability of the biological effects it will always be necessary to test the therapeutic response of the drug before using it. Hence desmopressin is only indicated in surgery with a moderate or low risk of bleeding and whenever a correction of primary haemostasis is necessary for a short time. Desmopressin cannot be used in cases of emergency.

The particular case of peripartum haemorrhages is discussed below.

Ambulatory anaesthesia

There are no reports concerning ambulatory anaesthesia in patients with MYH9-RD, but we think that in cases of some patients with a low bleeding risk, surgery can benefit from ambulatory procedures.

Obstetrical anaesthesia

Due to the absence of any established recommendations, the management of patients with inherited platelet disorders (IPD) raises questions not only as regards both the pregnant woman and the neonate. Nevertheless, recent retrospective studies provide some insights into pregnancy monitoring, childbirth and the peripartum period.

It is well established that the platelet count decreases during pregnancy. Interestingly, the comprehensive analysis of 339 pregnancies of 181 women with 13 different forms of IPD [39], indicates that the bleeding complications were significantly increased for women with a platelet count of less than $40X10^9$/l before delivery or $<50X10^9$/l platelets at delivery, and also for women with haemorrhagic complications observed during previous surgical procedures.

© Anästh Intensivmed 2023;64:S253–S262 Aktiv Druck & Verlag GmbH

Women with no bleeding and a platelet count of at least 80x10^9/l are at low risk for bleeding and do not require platelet transfusion for labour or delivery. It is noteworthy that this report included 185 pregnancies of patients with MYH9-RD also appearing in combination with MTP and hearing loss; normal vaginal delivery was observed in 94 cases with a median platelet count of 60X10^9/l (34–80X10^9/l) and spinal or epidural analgesia was performed in 34 cases of delivery. For the patients with the lowest platelet count, prophylactic platelet transfusion was performed.

A frequent improvement of haemorrhagic symptomatology is observed during pregnancy and can be investigated by questioning and repeating platelet function studies (flow cytometry). Platelet concentrates must be available on site for delivery: preferentially HLA compatible platelets may be prepared before delivery to avoid immunisation and a long-term platelet transfusion inefficiency. There is no indication for systematic prophylactic platelet transfusion due to the phenotypic variability. A multidisciplinary discussion should be conducted on a case-by-case basis, depending on platelet count, platelet function at the end of pregnancy and mode of delivery.

Management of delivery is similar to other acquired or inherited platelet disorders. In case of postpartum haemorrhage (PPH) the algorithm for the management of PPH will be adapted with early platelet transfusion.

Neuraxial anaesthesia remains contraindicated when the platelet count is <75-80x10^9/l [28,29,31] but it has been performed in some patients with a lower platelet count [27,40].

Caesarean sections are possible with platelet transfusion often required, especially if abnormal platelet functions and/or a high bleeding score and/or if the platelet count is less than 50X109/l. They are often required, especially if there are abnormal platelet functions and/or a high bleeding score and/or if the platelet count is less than 50X10^9/L. Recently, several reports highlighted the use of TPO mimetics during pregnancy in women with inherited or acquired thrombocytopenia [41,42]. In these reports, eltrombopag has been used if its benefits outweighed the risks. Side effects are rare, but maternal thrombocytosis and hepatotoxicity might occur. This possibility opens new prospects in the treatment of pregnant women with MYH9-RD, particularly those who have very low platelet counts, and the drug reduces the potential risks associated with repeated platelet transfusions. In IPD, we suggest to start this specific treatment at the beginning of the last month of pregnancy, because this time is far from the embryonic period. Nevertheless, it is assigned to pregnancy category C by the Food and Drug Administration (FDA) and controlled studies in pregnancy are lacking.

The perinatal period is an important time in the management of bleeding risks in women and newborns. A platelet count evaluation is essential in both the woman and the newborn. The systematic research of intracranial haemorrhages by echography should be programmed also in the neonate. In the study published by Noris et al. [39], two neonates of pregnant women with MYH9-RD died of cerebral haemorrhage and the authors suggested that the infants delivered vaginally by severely thrombocytopenic women with MYH9-RD must have been at risk of intracranial bleeding [39]. We also suggest the preventive and systematical administration of platelet concentrates to neonates with a severe thrombocytopenia.

A follow-up of the mother after delivery is also essential due to the possibility of postpartum bleeding appearing as early as one week after the delivery or later [43].

© Anästh Intensivmed 2023;64:S253–S262 Aktiv Druck & Verlag GmbH

References

1. Savoia A, Pecci A. MYH9-related disorders: in Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJH, Stephens K, Armemiya A, editors. Gene Reviews [internet]. Seatte (WA): University of Washington, Seattle; 1993–2018. 2008 Nov 20 [updated 2015 Jul16]
2. Balduini CL, Melazzini F, Pecci A. Inherited thrombocytopenia-recent advances in clinical and molecular aspects. Platelets 2017;28:3–13
3. May R. Leukocytoteneinschlüsse. Dtsch Arch Klin Med 1909;96:1–6
4. Hegglin R. Gleichzeitige konstitutionelle Veränderungen an Neutrophilen und Thrombocyten. Helv Med Acta 1945;12:439–440
5. Kunishima S, Kojima T, Tanaka T, Kamiya T, Ozawa K, Nakamura Y, et al. Mapping of a gene for May-Hegglin anomaly to chromosome 22q. Hum Genet 1999;105:379–383
6. Martignetti JA, Heath KE, Harris J, Bizzaro N, Savoia A, Balduini CL, et al. The gene for May-Hegglin anomaly localizes to a <1-Mb region on chromosome 22q12.3-13.1 Am J Hum Genet 2000;66:1449–1454
7. Seri M, Cusano R, Gangarossa S, Caridi G, Bordo D, Lo Nigro C, et al. Mutations in MYH9 result in the May-Hegglin anomaly, and Fechtner and Sebastian syndromes. The May-Hegglin/Fechtner Syndrome Consortium. Nat Genet 2000;26:103–105
8. Pecci A, Ma X, Savoia A, Adelstein RS. MYH9: structure, functions and role of non-muscle myosin IIA in human disease. Gene 2018;664:152–162
9. Saposnik B, Binard S, Fenneteau O, Nurden A, Nurden P, Hurtaud-Roux MF, et al. French networks; Mutation spectrum and genotype-phenotype correlations in a large French cohort of MYH9-related disorders. Mol Genet Genomic Med 2014;2:297–312
10. Rodeghiero F, Tosetto A, Abshire T, et al. ISTH/SSC bleeding assessment tool: a standardized questionnaire and a proposal for a new bleeding score for inherited bleeding disorders. J Thromb Haemost 2010;8:2063–2065
11. Elbatarny M, Mollah S, Grabell J, Bae S, Deforest M, Tuttle A, et al. Normal range of bleeding scores for the ISTH-BAT: adult and pediatric data from the merging project. Haemophilia 2014;20:831–835
12. Savoia A, De Rocco D, Pecci A. MYH9 gene mutation associated with bleeding. Platelets 2017;28:313–315
13. Pecci A, Barozzi S, d'Amico S, Balduini CL. Short term eltrombopag for surgical preparation of a patient with inherited thrombocytopenia deriving from MYH9 mutation. Thromb Haemost 2012b;107:1188–1189
14. Gröpper S, Althaus K, Najm J, Haase S, Aul C, Greinacher A,et al. A patient with Fechtner syndrome successfully treated with romiplostim. Thromb Haemost 2012,107:590–591
15. Favier R, Feriel J, Favier M, Denoyelle F, Martignetti JA. First successful use of eltrombopag before surgery in a child with MYH9-related thrombocytopenia. Pediatrics 2013;132:e793–795
16. Rodeghiero F, Pecci A, Balduini CL. Thrombopoietin receptor agonists in hereditary thrombocytopenias. J Thromb Haemost 2018;16:1700–1710
17. Favier R, Raslova H. Progress in understanding the diagnosis and molecular genetics of macrothrombocytopenias. Br J Haematol 2015;170:629–639
18. Pecci A, Verver EJ, Schlegel N, Canzi P, Boccio CM, Platokouki H, et al. Cochlear implantation is safe and effective in patients with MYH9-related disease. Orphanet J Rare Dis 2014b;9,100:1–9
19. Min SY, Ahn Hj, Park XW and Kim JW. Successful renal transplantation in MYH9-related disorder with severe macrothrombocytopenia: first report in Korea. Transplant Proc 2014;46: 664–666
20. Hashimoto J, Hamasaki Y, Yanagisawa T, Sekine T, Aikawa A, Shishido S. Successful kidney transplantation in Epstein syndrome with antiplatelet antibodies and donor specific antibodies: a case report. Transplant Proc 2015;47:2541–2543
21. Sehbai AS, Abraham J, Brown V. Perioperative of a patient with May-Hegglin anomaly requiring craniotomy. Am J Hem 2005;79:303–308
22. Eichel Y, Tornos LM, Squites JE. Preoperative use of platelets in a 6-year-old with acute appendicitis and a myosin heavy chain 9-related disorder: a case report and review of literature. Transfusion 2016;56:349–353
23. Orsini S, Noris P, Bury L, Heller PG, Santoro C, Kadir RA, et al. Bleeding risk of surgery and its prevention in patients with inherited platelet disorders. Haematologica 2017;102:1192–1203

© Anästh Intensivmed 2023;64:S253–S262 Aktiv Druck & Verlag GmbH

24. Kumemura M, Omae T, Kou K, Sakuraba S, Niimi N, Kunishima S. Anesthetic management without perioperative platelet transfusion for cervical laminectomy and laminoplasty in a case of May-Hegglin anomaly. J Anesth 2018;32:641–644
25. Choi S, Brull R. Neuroaxial techniques in obstetric and non obstetric patients with common bleeding diatheses. Anest Ana 2009;109:628–660
26. Gernsheimer T, James AH, Stasi R. How I treat thrombocytopenia in pregnancy. Blood 2013;121:38–47
27. Fishman ER, Connors JM, Camann WR. Anesthetic management of seven deliveries in three sisters with the May-Hegglin anomaly. Anesth Ana 2009;108:1603–1605
28. American College of Obstetricians and Gynecologists' Committee on Practice Bulletin Thrombocytopenia in pregnancy. Obstet Gynecol 2016;128:e43–e53
29. French Society of Anesthesiology. Guidelines. Neuroaxial anaesthesia in adults. Ann Fr Anaest Rea 2007;26:720–752
30. Huang J, McKennay N, Babins N. Utility of thromboelastography during neuraxial blockade in the parturient with thrombocytopenia. AANA Journal 2014; 82:127–130
31. British Committee for standards in Haematology. Guidelines for the investigation and management of idiopathic thrombocytopenic purpura in adults, children and in pregnancy. Br J Haematol 2003;120:574–596
32. Palandri F, Zoli M, Polverelli N, Noris P, Sollazzo D, Catani L, et al. MYH9-related thrombocytopenia and intracranial bleeding: a complex clinical/surgical management and review of the literature. Br J Haematol 2015;170:729–731
33. Hashimoto J, Hamasaki Y, Takahashi Y, Kubota M, Yanagisawa T, Itabashi Y, Muramatsu M, et al. Management of patients with severe Epstein syndrome: a review of four patients who received living donor renal transplantation. Nephrology 2019;24:450–455
34. Selleng K, Lubenow LE, Greinacher A, Wartenkin TE. Perioperative management of MYH9 hereditary macrothrombocytopenia. Eur J Haem 2007;79:213–218
35. Kerros H, Roule V, Ivascau C, Labombarda F. Management of May-Hegglin anomaly referred for coronary artery bypass. Platelets 2011;22:471–472
36. Girolami A, Sambado L, Bonamigo E, Vettore S, Lombardi AM. Occurrence of thrombosis congenital thrombocytopenic disorders: a critical review of the literature. Blood Coagul Fibrinolysis 2013;24:18–22
37. Althaus K, Greinacher A. MYH9-related platelet disorders: strategies for management and diagnosis. Transf Med Hemother 2010;37:260–267
38. Coppola A, DiMinno G. Desmopressin in inherited platelet function. Haemophilia 2008;14:31–39
39. Noris P, Schlegel N, Klersky C, Heller PG, Civashi E, Pujol-Moix N, et al. Analysis of 339 pregnancies in 181 women with 13 different forms of inherited thrombocytopenia. Haematologica 2014b;99:1387–1394
40. Garcia Vallejo G, Cabellos M, Kabiri M, Fraile JR, Cuesta J. Anaesthetic implications in a pregnant patient with an extreme thrombocytopenia due to a May-Hegglin anomaly: general or regional anaesthesia? Rev Esp Anesthesiol Reanim 2014;61:460–465
41. Favier R, De Carne C, Elefant E, Lapusneanu R, Gkalea V, Rigouzzo A. Eltrombopag to treat thrombocytopenia during last month of pregnancy in a woman with MYH9 related disease: a case report. AA Pract 2018;10:10–12
42. Kong Z, Qin P, Xiao S, Zhou H, Li H, Yang R et al. A novel recombinant human thrombopoietin therapy for the management of immune thrombocytopenia in pregnancy. Blood 2017;130:1097–1103
43. Hussein BA, Gomez K, Kadir R. May-Hegglin anomaly and pregnancy: a systematic review. Blood Coagul Fibrinolysis 2013,24:554–561.

© Anästh Intensivmed 2023;64:S253–S262 Aktiv Druck & Verlag GmbH

Date last modified: June 2019

Authors

Remi Favier, Haematologist, French reference centre for platelet disorders, Armand Trousseau Hospital, 75012 Paris, France
remi.favier@aphp.fr

Agnes Rigouzzo, Anaesthesiologist, Anaesthesiology and Intensive Care Department, Armand Trousseau Hospital, 75012 Paris, France
Agnes.rigouzzo@aphp.fr

Co-authors:

Federica Piana, Anaesthesiologist, Anaesthesiology and Intensive Care Department, CHU Lyon, France

Nicolas Louvet, Anaesthesiologist, Anaesthesiology and Intensive Care Department Armand Trousseau Hospital, 75012 Paris, France

Disclosure The authors have no financial or other competing interest to disclose. This recommendation was unfunded.

Reviewers

Anne-Sophie Ducloys-Bouthors, Anaesthesiologist, Department of Anesthesiology and Critical Care Medicine, Lille University Hospital, Lille, France
anne-sophie.bouthors@chru-lille.fr

Paquita Nurden, Haematologist, founder of the French Reference Center for Inherited platelet diseases, Scientific advisor, Liryc Institute, Pessac, 33600, France
Paquita.nurden@gmail.com

Disclosure The reviewers have no financial or other competing interest to disclose.

© Anästh Intensivmed 2023;64:S253–S262 Aktiv Druck & Verlag GmbH

Herausgeber

DGAI
Deutsche Gesellschaft für Anästhesiologie und Intensivmedizin e.V.
Präsident: Prof. Dr. B. Pannen, Düsseldorf

BDA
Berufsverband Deutscher Anästhesistinnen und Anästhesisten e.V.
Präsident: Prof. Dr. G. Geldner, Ludwigsburg †

Schriftleitung
Präsident/in der Herausgeberverbände

Gesamtschriftleiter/Editor-in-Chief:
Prof. Dr. Dr. Kai Zacharowski, ML FRCA FESAIC, Frankfurt

Stellvertretender Gesamtschriftleiter/Deputy Editor:
Prof. Dr. T. Volk, Homburg/Saar

CME-Schriftleiter/CME-Editor:
Prof. Dr. W. Zink, Ludwigshafen

Redaktion/Editorial Staff
Carolin Sofia Kopp B.A.
Korrespondenzadresse:
Neuwieder Straße 9 | 90411 Nürnberg | Deutschland | Tel.: 0911 9337812
E-Mail: anaesth.intensivmed@dgai-ev.de

Die Beiträge aus der A&I finden Sie online unter:
www.ai-online.info

Verlag & Druckerei

Aktiv Druck & Verlag GmbH
An der Lohwiese 36 |
97500 Ebelsbach | Deutschland
www.aktiv-druck.de

Geschäftsführung
Wolfgang Schröder | Jan Schröder | Nadja Schwarz
Tel.: 09522 943560 | Fax: 09522 943567
E-Mail: info@aktiv-druck.de

Anzeigen | Vertrieb
Pia Müller | Robert Kux
Tel.: 09522 943570 | Fax: 09522 943577
E-Mail: anzeigen@aktiv-druck.de

Verlagsrepräsentanz
Jürgen Distler
Neuwieder Straße 9 | 90411 Nürnberg
Tel.: 0171 9432534
E-Mail: jdistler@bda-ev.de

Herstellung | Gestaltung
Pia Müller | Robert Kux | Stefanie Triebert
Tel.: 09522 943570 | Fax: 09522 943577
E-Mail: ai@aktiv-druck.de

Titelbild
Dipl.-Designerin Monique Minde, Nürnberg

Erscheinungsweise 2023
Der 64. Jahrgang erscheint jeweils zum Monatsanfang, Heft 7/8 als Doppelausgabe.

Bezugspreise (inkl. Versandkosten):

- **Einzelhefte** 30,- €
- **Jahresabonnement:**
  Europa (ohne Schweiz) (inkl. 7 % MwSt.) 258,- €
  Schweiz 266,- €
  Rest der Welt 241,- €

  Mitarbeiter aus Pflege, Labor, Studenten und Auszubildende (bei Vorlage eines entsprechenden Nachweises)
  Europa (ohne Schweiz) (inkl. 7 % MwSt.) 94,- €
  Schweiz 90,- €
  Rest der Welt 94,- €

Für Mitglieder der DGAI und/oder des BDA ist der Bezug der Zeitschrift im Mitgliedsbeitrag enthalten.

Allgemeine Geschäfts- und Lieferbedingungen
Die allgemeinen Geschäfts- und Lieferbedingungen entnehmen Sie bitte dem Impressum auf www.ai-online.info

Indexed in **Current Contents®/Clinical Medicine, EMBASE/Excerpta Medica; Medical Documentation Service; Research Alert; Sci Search; SUBIS Current Awareness in Biomedicine; VINITI: Russian Academy of Science.**

Wichtiger Hinweis
Für Angaben über Dosierungsanweisungen und Applikationsformen kann vom Verlag und den Herausgebern keine Gewähr übernommen werden. Derartige Angaben müssen vom jeweiligen Anwender im Einzelfall anhand anderer Literaturstellen auf ihre Richtigkeit überprüft werden. Gleiches gilt für berufs- und verbandspolitische Stellungnahmen und Empfehlungen.

Allein aus Gründen der besseren Lesbarkeit wird auf die gleichzeitige Verwendung männlicher, weiblicher und weiterer Sprachformen verzichtet. Sämtliche Personenbezeichnungen gelten für alle Geschlechterformen. Dies impliziert keinesfalls eine Benachteiligung der jeweils anderen Geschlechter, sondern ist als geschlechtsneutral zu verstehen.

CONTACT US

Please do not hesitate to contact us. We will be glad to answer and provide further information to you at any time.

.....
Name

.....
First Name

.....
Department / Hospital

.....
Place

.....
Telephone

.....
E-Mail

.....
Date / Signature

Please contact me for further information ○

I would like to participate in the project ○

ADDRESS

German Society of Anaesthesiology and
Intensive Care Medicine
Neuwieder Straße 9 I 90411 Nuremberg I Germany
Tel.: +49-911-933780
Email: info@orphananesthesia.eu