U.S. National Library of Medicine
National Center for Biotechnology Information

NLM Citation: Petit F, Boussion S. Thrombocytopenia Absent Radius Syndrome. 2009 Dec 8 [Updated 2023 Nov 2]. In: Adam MP, Feldman J, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024.
Bookshelf URL: https://www.ncbi.nlm.nih.gov/books/

Thrombocytopenia Absent Radius Syndrome

Synonym: TAR Syndrome

Florence Petit, MD, PhD[1] and Simon Boussion, MD[1]

Created: December 8, 2009; Revised: November 2, 2023.

Summary

Clinical characteristics

Thrombocytopenia absent radius (TAR) syndrome is characterized by bilateral absence of the radii with the presence of both thumbs, and thrombocytopenia that is generally transient. Thrombocytopenia may be congenital or may develop within the first few weeks to months of life; in general, thrombocytopenic episodes decrease with age. Cow's milk allergy is common and can be associated with exacerbation of thrombocytopenia. Other anomalies of the skeleton (upper and lower limbs, ribs, and vertebrae), heart, and genitourinary system (renal anomalies and agenesis of uterus, cervix, and upper part of the vagina) can occur.

Diagnosis/testing

The diagnosis of TAR syndrome is established in a proband with bilateral absent radii, present thumbs, and thrombocytopenia. Identification of a heterozygous null allele (most often a minimally deleted 200-kb region at chromosome band 1q21.1) in *trans* with a heterozygous *RBM8A* hypomorphic allele on molecular genetic testing confirms the diagnosis.

Management

Treatment of manifestations: Orthopedic intervention as needed to maximize limb function. Platelet transfusion for thrombocytopenia as needed; to reduce the risks of alloimmunization and infection, avoid platelet transfusion in older individuals whose platelet counts exceed a particular threshold (10 platelets/nL). Standard treatments for cardiac and genitourinary anomalies. Avoidance of cow's milk to reduce the severity of gastroenteritis and to avoid exacerbations of thrombocytopenia. Central venous catheter as an alternative to repeated venipuncture.

Surveillance: Platelet count when evidence of increased bleeding tendency (bruising, petechiae) occurs. Assess for gastrointestinal manifestations in children, which may indicate cow's milk allergy, at each visit. Serum electrolytes, blood urea nitrogen, and creatinine to assess kidney function per nephrologist.

Author Affiliation: 1 Clinique de génétique, Hôpital Jeanne de Flandre, CHU de Lille, Lille, France; Email: florence.petit@chu-lille.fr; Email: simon.boussion@chu-lille.fr.

Agents/circumstances to avoid: Avoid cow's milk to reduce the severity of gastroenteritis and associated thrombocytopenia (in older children). Platelet function is somewhat impaired, suggesting that drugs such as nonsteroidal anti-inflammatory drugs or aspirin should be avoided or used with caution.

Genetic counseling

TAR syndrome is caused by compound heterozygosity for a null allele and an *RBM8A* hypomorphic allele and is inherited in an autosomal recessive manner. However, because null alleles are rare (and often occur *de novo* in the proband) and *RBM8A* hypomorphic alleles are common, inheritance of TAR syndrome is associated with several features unusual in autosomal recessive disorders: a paucity of affected sibs, apparent parent-to-child transmission, and affected second- and third-degree relatives. The risk to sibs of a proband varies depending on the genetic status of the parents; for example:

- If one parent is known to be heterozygous for a null allele and the other parent is heterozygous for an *RBM8A* hypomorphic allele, each sib of an affected individual has at conception a 25% chance of being affected.
- If one parent is known to be heterozygous for a null allele and the other parent has biallelic *RBM8A* hypomorphic alleles, each sib of an affected individual has at conception a 50% chance of being affected.
- If one parent is known to be heterozygous for an *RBM8A* hypomorphic allele and the other parent has two normal *RBM8A* alleles, each sib of an affected individual has at conception a 50% chance of being an asymptomatic carrier of an *RBM8A* hypomorphic allele and a 50% chance of being unaffected and not a carrier.

Individuals who are heterozygotes (carriers) for one TAR syndrome-related pathogenic variant (either an *RBM8A* hypomorphic allele or a null allele) are asymptomatic; individuals with biallelic *RBM8A* hypomorphic alleles are asymptomatic. Once the causative null allele and *RBM8A* hypomorphic allele have been identified in an affected family member, carrier testing for at-risk relatives as well as prenatal and preimplantation genetic testing are possible.

Diagnosis

Suggestive Findings

Thrombocytopenia absent radius (TAR) syndrome **should be suspected** in individuals with:

- Bilateral absence of the radii with the presence of both thumbs
- Thrombocytopenia, usually <50 platelets/nL (normal range: 150-400 platelets/nL)

Establishing the Diagnosis

The diagnosis of TAR syndrome **is established** in a proband with Suggestive Findings and a null heterozygous variant (most often a 500-kb deletion or 200-kb deletion including *RBM8A* at chromosome band 1q21.1) in *trans* with a heterozygous *RBM8A* hypomorphic allele identified by molecular genetic testing (see Table 1).

Molecular genetic testing approaches can include a combination of **gene-targeted testing** (single-gene testing, multigene panel) and **comprehensive genomic testing** (exome sequencing, genome sequencing) depending on the phenotype.

Gene-targeted testing requires that the clinician determine which gene(s) are likely involved, whereas genomic testing does not. Individuals with the distinctive findings described in Suggestive Findings are likely to be diagnosed using gene-targeted testing (see Option 1), whereas those with a phenotype indistinguishable from

many other inherited disorders with radial ray defects are more likely to be diagnosed using genomic testing (see Option 2).

Option 1

Single-gene testing. Gene-targeted deletion/duplication analysis of *RBM8A* is performed first, followed by sequence analysis of *RBM8A* if no deletion is found. Although the diagnosis of TAR syndrome can be established by identification of a heterozygous minimally deleted 200-kb region at chromosome band 1q21.1, sequence analysis of *RBM8A* can be done subsequently in individuals with the deletion to confirm the presence of a second pathogenic variant (hypomorphic allele) and allow family studies. Homozygous *RBM8A* null alleles (e.g., deletions) are thought to be lethal.

A multigene panel that includes *RBM8A* and other genes of interest (see Differential Diagnosis) may also be considered to identify the genetic cause of the condition while limiting identification of variants of uncertain significance and pathogenic variants in genes that do not explain the underlying phenotype. Note: (1) The genes included in the panel and the diagnostic sensitivity of the testing used for each gene vary by laboratory and are likely to change over time. (2) Some multigene panels may include genes not associated with the condition discussed in this *GeneReview*. (3) In some laboratories, panel options may include a custom laboratory-designed panel and/or custom phenotype-focused exome analysis that includes genes specified by the clinician. (4) Methods used in a panel may include sequence analysis, deletion/duplication analysis, and/or other non-sequencing-based tests.

For an introduction to multigene panels click here. More detailed information for clinicians ordering genetic tests can be found here.

Option 2

Comprehensive genomic testing does not require the clinician to determine which gene is likely involved. **Exome sequencing** is most commonly used; **genome sequencing** is also possible.

For an introduction to comprehensive genomic testing click here. More detailed information for clinicians ordering genomic testing can be found here.

Table 1. Molecular Genetic Testing Used in Thrombocytopenia Absent Radius Syndrome

Gene [1]	Method	Proportion of Pathogenic Variants [2] Detectable by Method
RBM8A	CMA or other CNV analysis [3]	~48% [4]
	Sequence analysis [5]	~49% [6]

CMA = chromosomal microarray; CNV = copy number variant

1. See Table A. Genes and Databases for chromosome locus and protein.

2. See Molecular Genetics for information on variants detected in this gene.

3. Copy number variation analysis detects the 1q21.1 deletion containing *RBM8A*. Methods used may include a range of techniques such as quantitative PCR, multiplex ligation-dependent probe amplification (MLPA), gene-targeted microarray, chromosomal microarrays, or next-generation sequencing.

4. Both a 200-kb and a more common 500-kb TAR syndrome-associated deletion have been described. Because the deletion often extends beyond the 200-kb minimally deleted region [Klopocki et al 2007], a test that can approximate the extent of the deletion is optimal. A 1q21.1 deletion was identified in 81/85 (95%) individuals with TAR syndrome [Albers et al 2012; Boussion et al 2020; Author, personal data].

5. Sequence analysis detects variants that are benign, likely benign, of uncertain significance, likely pathogenic, or pathogenic. Variants may include missense, nonsense, and splice site variants and small intragenic deletions/insertions; typically, exon or whole-gene deletions/duplications are not detected. For issues to consider in interpretation of sequence analysis results, click here.

6. Sequence analysis requires inclusion of the 5' UTR, 3' UTR, and intronic regions. A heterozygous *RBM8A* hypomorphic allele was identified in 24/30 affected individuals with the 200-kb deletion [Boussion et al 2020; Author, personal data]. Biallelic *RBM8A* pathogenic variants (1 null allele and 1 hypomorphic allele) were identified in 4/85 (5%) individuals [Albers et al 2012; Boussion et al 2020; Author, personal data] who did not have the 200-kb deletion. Four individuals out of 30 (13%) had a deletion identified but did not have a hypomorphic allele identified [Boussion et al 2020; Author, personal data].

Clinical Characteristics

Clinical Description

Thrombocytopenia absent radius (TAR) syndrome is characterized by bilateral absence of the radii with the presence of both thumbs and thrombocytopenia that is generally transient. Additional manifestations can include cow's milk allergy and anomalies of the lower limbs, ribs, vertebrae, heart, and genitourinary system. To date, more than 150 individuals have been reported with a TAR-related *RBM8A* variant [Klopocki et al 2007, Giordano et al 2011, Houeijeh et al 2011, Albers et al 2012, Bottillo et al 2013, Papoulidis et al 2014, Yassaee et al 2014, Kumar et al 2015, Tassano et al 2015, Nicchia et al 2016, Diep & Arcasoy 2017, Manukjan et al 2017, Brodie et al 2019, Boussion et al 2020, Miertuš et al 2020, Travessa et al 2020, Beauvais et al 2021, da Rocha et al 2021, Ding et al 2021, Morgan et al 2021, Espinoza et al 2022, Farlett et al 2022]. The following description of the phenotypic features associated with TAR syndrome is based on these reports.

Table 2. Thrombocytopenia Absent Radius Syndrome: Frequency of Select Features

Feature	% of Persons w/Feature
Limb anomalies	100%
Thrombocytopenia	96%
Cardiac anomalies	17%
Gastrointestinal manifestations	26%
Genitourinary anomalies	24%

Limb anomalies can affect both upper and lower limbs; upper limb involvement tends to be more severe than lower limb involvement. Individuals with TAR syndrome almost always have bilateral absence or hypoplasia of the radius. The thumbs are always present and are of near-normal size but somewhat wider and flatter than

usual. Thumbs are also held in flexion against the palm, and tend to have limited function, particularly in terms of grasp and pinch activities [Goldfarb et al 2007].

The upper limbs may also have hypoplasia or absence of the ulnae, humeri, and shoulder girdles. Fingers may show syndactyly, and fifth-finger clinodactyly is common.

Lower limbs are affected in almost half of indiviuals with TAR syndrome; hip dislocation, coxa valga, femoral and/or tibial torsion, genu varum, and absence of the patella are common findings. The most severe limb involvement is tetraphocomelia.

Thrombocytopenia may be congenital or may develop within the first few weeks to months of life. In most individuals, platelet counts remain low during the first two years of life; they then increase but do not reach the lower reference value [Fiedler et al 2012, Manukjan et al 2017].

Cow's milk allergy is common, and can be associated with exacerbation of thrombocytopenia, either by direct immunoglobulin E (IgE) immune-mediated mechanism or secondary to increased gastrointestinal bleeding caused by loss of coagulation proteins [Farlett et al 2022].

Cardiac anomalies usually include septal defects (e.g., atrial septal defect, ventricular septal defect, patent foramen ovale) rather than complex cardiac malformations [Hedberg & Lipton 1988, Greenhalgh et al 2002]. One individual with tetralogy of Fallot has been reported [Kumar et al 2015].

Gastrointestinal involvement includes cow's milk allergy or intolerance and an increased susceptibility to gastroenteritis [Greenhalgh et al 2002]. Both tend to improve with age. These findings may be underreported since many fetuses and adults with TAR syndrome are described in the literature. Cow's milk intolerance may present with poor weight gain, failure to thrive, vomiting, or diarrhea, requiring non-cow's milk formulas. Unrelated to cow's milk intolerance, an increased susceptibility to gastroenteritis and dehydration requiring intravenous fluids has been reported in 30% of individuals [Greenhalgh et al 2002].

Genitourinary anomalies include mostly congenital anomalies of the kidney and urinary tract (CAKUT), such as kidney agenesis or malrotation, horseshoe kidney, hydronephrosis, and pyelectasis. Rarely, Mayer-Rokitansky-Kuster-Hauser syndrome (agenesis of uterus, cervix, and upper part of the vagina) has been reported [Griesinger et al 2005, Klopocki et al 2007, Ahmad & Pope 2008].

Other hematologic features have been rarely reported. During the first year of life some children develop anemia that cannot be fully attributed to increased bleeding as a result of thrombocytopenia. Some individuals become severely anemic, requiring red blood cell transfusions (particularly those with *RBM8A* variant c.-21G>A) [Manukjan et al 2017].

Leukemoid reactions have been reported in some individuals with TAR syndrome, with white blood cell counts exceeding 35,000 cells/mm^3. Leukemoid reactions are generally transient [Klopocki et al 2007]. However, several individuals with acute myeloid leukemia [Rao et al 1997, Fadoo & Naqvi 2002, Go & Johnston 2003, Jameson-Lee et al 2018, Boussion et al 2020] or acute lymphoblastic leukemia [Camitta & Rock 1993] have been reported.

Cognitive development is usually normal in individuals with TAR syndrome.

Growth. Most have height at or below the 50th centile.

Other skeletal manifestations such as rib and vertebral anomalies (e.g., cervical rib, fused cervical vertebrae, vertebral segmentation defects) are relatively rare.

Langerhans cell histiocytosis has been rarely reported in individuals with TAR syndrome [Giordano et al 2011, Manukjan et al 2017, Hipólito et al 2019, Boussion et al 2020].

Genotype-Phenotype Correlations

Individuals with TAR syndrome have one null allele in *trans* with a hypomorphic allele. The hypomorphic allele is usually located in the 5' UTR, intron 1, or 3' UTR.

Only limited genotype-phenotype correlations have been described:

- The **c.-21G>A** hypomorphic allele has been associated with lower platelet counts and hemoglobin values below the lower reference value; the low hemoglobin levels could not be fully attributed to increased bleeding as a result of thrombocytopenia [Manukjan et al 2017].
- Individuals with intronic hypomorphic allele **c.67+32G>C** had higher platelet counts, even during the first months of life, which eventually reached the reference range. Individuals with the c.67+32G>C allele also had normal hemoglobin levels.

Penetrance

Penetrance appears to be complete in individuals who have biallelic *RBM8A* pathogenic variants (a heterozygous null allele in *trans* with a hypomorphic allele).

Prevalence

The prevalence of TAR syndrome is estimated at 1:100,000 to 1:200,000, but it is likely more frequent in populations of African descent, due to a recurrent *RBM8A* hypomorphic allele (c.Ter6C>G) with a minor allele frequency of 14.8% in the African population.

Genetically Related Disorders

No phenotypes other than those discussed in this *GeneReview* are known to be associated with the 200-kb minimally deleted region at 1q21.1. Recurrent deletion or duplication of nearby DNA segments at 1q21.1 gives rise to the variable phenotypes associated with 1q21.1 deletion (see 1q21.1 Recurrent Microdeletion) and duplication (OMIM 612475). Occasionally, these rearrangements may extend into the 200-kb minimally deleted TAR locus. See Molecular Genetics.

No phenotypes other than those discussed in this *GeneReview* are known to be associated with intragenic germline pathogenic variants in *RBM8A*.

Differential Diagnosis

Hereditary disorders of known genetic cause that include radial aplasia as a component manifestation and can show some overlap with thrombocytopenia absent radius (TAR) syndrome are summarized in Table 3. However, among the group of genetic disorders associated with radial aplasia, the presence of both thumbs is highly specific of TAR syndrome.

Table 3. Genetic Disorders Associated with Radial Aplasia in the Differential Diagnosis of Thrombocytopenia Absent Radius Syndrome

Gene(s)	Disorder	MOI	Limb Malformations	Other Key Features
23 genes [1]	Fanconi anemia	AR AD XL [2]	Unilateral or bilateral malformations of upper limbs (e.g., hypoplastic thumb & hypoplastic radius) & lower limbs	Growth deficiency, variable congenital anomalies, BMF, & ↑ risk for malignancy

Table 3. continued from previous page.

Gene(s)	Disorder	MOI	Limb Malformations	Other Key Features
ESCO2	*ESCO2* spectrum disorder (from Roberts syndrome at severe end of spectrum to SC phocomelia at milder end)	AR	Limb malformations can incl bilateral symmetric tetraphocomelia or hypomelia caused by mesomelic shortening & limb bone fusions; brachydactyly & oligodactyly w/abnormal thumb placement, hypoplasia, or aplasia	Prenatal growth restriction, craniofacial abnormalities, other congenital anomalies, & ID
RECQL4	RAPADILINO syndrome (See Rothmund-Thomson Syndrome, Genetically Related Disorders.)	AR	Radial defects incl absent or hypoplastic radii & absent or hypoplastic thumbs; absent/hypoplastic patellae	Growth deficiency, high cleft palate, diarrhea, joint dislocations, & characteristic facial features
SALL1	Townes-Brocks syndrome	AD	Thumb malformations w/normal radii	Imperforate anus, dysplastic ears, hearing impairment, & kidney disease
SALL4	*SALL4*-related disorders (Duane-radial ray syndrome [Okihiro syndrome], acro-renal-ocular syndrome, & *SALL4*-related Holt-Oram syndrome)	AD	Radial ray anomalies of varying severity, ranging from thenar hypoplasia to radial aplasia	Duane anomaly & renal abnormality
TBX5	*TBX5*-related Holt-Oram syndrome	AD	Upper limb malformations range from triphalangeal or absent thumb(s) to phocomelia; radius aplasia/hypoplasia, fusion or anomalous carpal & thenar bones, & restriction of shoulder joint movement	Congenital heart malformation & cardiac conduction disease

AD = autosomal dominant; AR = autosomal recessive; BMF = bone marrow failure; ID = intellectual disability; MOI = mode of inheritance; XL = X-linked

1. *BRCA1*, *BRCA2*, *BRIP1*, *ERCC4*, *FAAP100*, *FANCA*, *FANCB*, *FANCC*, *FANCD2*, *FANCE*, *FANCF*, *FANCG*, *FANCI*, *FANCL*, *FANCM*, *MAD2L2*, *PALB2*, *RAD51*, *RAD51C*, *RFWD3*, *SLX4*, *UBE2T*, *XRCC2* (See Fanconi Anemia.)

2. Fanconi anemia (FA) can be inherited in an autosomal recessive manner, an autosomal dominant manner (*RAD51*-related FA), or an X-linked manner (*FANCB*-related FA).

Other disorders with radial aplasia in the differential diagnosis of TAR syndrome

- **VACTERL association** (OMIM 192350) is an acronym that stands for the cardinal manifestations of *v*ertebral, *a*nal, *c*ardiac, *t*racheo*e*sophageal fistula, *r*enal anomalies, and *l*imb anomalies. The limb anomalies tend to affect the thumb and radius, although the thumb is often absent in VACTERL association. Thrombocytopenia does not occur as a manifestation of VACTERL association. The genetic cause of VACTERL association is unknown.
- **Thalidomide embryopathy** occurs secondarily to maternal ingestion of thalidomide. Affected children can have a pattern of limb, cardiac, craniofacial, and genitourinary anomalies.
- **Fetal valproate syndrome** occurs secondarily to maternal ingestion of valproate. Affected children can have radial ray malformation, craniofacial anomalies, and cognitive delays.

Management

Clinical practice guidelines for anesthesia and dental care in thrombocytopenia absent radius (TAR) syndrome have been published [Idahosa et al 2014]. Individuals with TAR syndrome have a high anesthetic risk. Considerations include potential difficulties with vascular and airway access, risk for bleeding due to altered platelet count and function, and potential congenital cardiac defects. All risks should be assessed carefully before surgery.

Evaluations Following Initial Diagnosis

To establish the extent of disease and needs in an individual diagnosed with TAR syndrome, the evaluations summarized in Table 4 (if not performed as part of the evaluation that led to the diagnosis) are recommended.

Table 4. Recommended Evaluations Following Initial Diagnosis in Individuals with Thrombocytopenia Absent Radius Syndrome

System/Concern	Evaluation	Comment
Musculoskeletal	• Clinical assessment for upper- & lower-extremity anomalies • X-rays if needed by orthopedist	Referral to orthopedist as needed
Hematologic	Blood cell count to evaluate for thrombocytopenia & anemia	• Bone marrow biopsies to confirm hypomegakaryocytic bone marrow are typically no longer performed. • Platelet function is somewhat impaired, suggesting that drugs such as NSAIDS (incl aspirin) should be avoided or monitored carefully.
Cardiac	Echocardiography	To identify septal defects or other structural cardiac anomalies
Gastrointestinal	• Assess for poor weight gain, failure to thrive, vomiting, or diarrhea. • Assess for episodes of severe gastroenteritis.	• Cow's milk allergy or intolerance is frequent; consider non-cow's milk formula. • Cow's milk allergy & gastroenteritis may precipitate thrombocytopenia.
Genitourinary	• Renal ultrasound exam • Assess renal function w/serum electrolyte concentrations, BUN, & creatinine in those w/renal malformation. • Pelvic ultrasound exam in females	To identify genitourinary malformations & renal dysfunction
Genetic counseling	By genetics professionals [1]	To inform affected persons & their families re nature, MOI, & implications of TAR syndrome to facilitate medical & personal decision making
Family support & resources	Assess need for: • Community or online resources such as Parent to Parent; • Social work involvement for parental support; • Home nursing referral.	

BUN = blood urea nitrogen; MOI = mode of inheritance; NSAIDs = nonsteroidal anti-inflammatory drugs; TAR = thrombocytopenia absent radius

1. Medical geneticist, certified genetic counselor, certified advanced genetic nurse

Treatment of Manifestations

Table 5. Treatment of Manifestations in Individuals with Thrombocytopenia Absent Radius Syndrome

Manifestation/Concern	Treatment	Considerations/Other
Limb anomalies	Orthopedic intervention incl prostheses, orthoses, adaptive devices, & surgery as indicated	To maximize limb function [1]

Table 5. continued from previous page.

Manifestation/Concern	Treatment	Considerations/Other
Thrombocytopenia	Platelet transfusion as needed: • In newborns, platelet transfusion threshold is unknown. • In older persons, platelet transfusion threshold is <10 platelets/nL.	• Frequent platelet transfusion can lead to alloimmunization & ↑ risk of infection. • Bone marrow transplantation is generally not indicated, given transient nature of thrombocytopenia in TAR syndrome.
Cardiac anomalies	Treatment per cardiologist	
Gastroenteritis	Treatment per gastroenterologist	
	Avoidance of cow's milk	To ↓ severity of gastroenteritis & ↓ exacerbations of thrombocytopenia (in older children)
Genitourinary anomalies	Treatment per nephrologist, urologist, &/or gynecologist	
Other	Use of central venous catheters as an alternative to venipuncture	Suggested to ↓ pain assoc w/repeated procedures [2]

TAR = thrombocytopenia absent radius
1. McLaurin et al [1999], Al Kaissi et al [2015]
2. Coccia et al [2012]

Surveillance

Table 6. Recommended Surveillance for Individuals with Thrombocytopenia Absent Radius Syndrome

System/Concern	Evaluation	Frequency
Thrombocytopenia	Platelet count	In those w/signs of ↑ bleeding tendency (bruising, petechiae)
Gastrointestinal manifestations	• Assess for poor weight gain, failure to thrive, vomiting, or diarrhea. • Assess for episodes of severe gastroenteritis.	During childhood, at each visit
Renal function in those w/renal malformation	Assess renal function w/serum electrolyte concentrations, BUN, & creatinine	Frequency of renal function assessment to be determined by nephrologist, depending on the malformation

BUN = blood urea nitrogen

Agents/Circumstances to Avoid

Avoid cow's milk to reduce the severity of gastroenteritis and associated thrombocytopenia (in older children).

Platelet function is somewhat impaired, suggesting that drugs such as nonsteroidal anti-inflammatory drugs including aspirin should be avoided or used with caution.

Evaluation of Relatives at Risk

See Genetic Counseling for issues related to testing of at-risk relatives for genetic counseling purposes.

Pregnancy Management

Fewer than ten pregnancies have been reported in women with TAR syndrome [Diep & Arcasoy 2017]. Almost all develop thrombocytopenia during pregnancy. Corticosteroids can be considered to treat a superimposed immune component, but platelet transfusions may be required prior to surgery or to treat bleeding. In one

pregnant woman with TAR syndrome, exacerbation of her thrombocytopenia preceded the development of preeclampsia [Wax et al 2009].

Other considerations during pregnancy include potential difficulties with administration of regional anesthetics (given potential difficulties with vascular access) and difficulties accessing the airway for general anesthesia [Wax et al 2009].

Therapies Under Investigation

Search ClinicalTrials.gov in the US and EU Clinical Trials Register in Europe for access to information on clinical studies for a wide range of diseases and conditions. Note: There may not be clinical trials for this disorder.

Genetic Counseling

Genetic counseling is the process of providing individuals and families with information on the nature, mode(s) of inheritance, and implications of genetic disorders to help them make informed medical and personal decisions. The following section deals with genetic risk assessment and the use of family history and genetic testing to clarify genetic status for family members; it is not meant to address all personal, cultural, or ethical issues that may arise or to substitute for consultation with a genetics professional. —ED.

Mode of Inheritance

Thrombocytopenia absent radius (TAR) syndrome is caused by compound heterozygosity for a null allele (most often a 500-kb deletion or 200-kb deletion including *RBM8A* at chromosome band 1q21.1) and a heterozygous *RBM8A* hypomorphic allele and is inherited in an autosomal recessive manner. However, because null alleles are rare and *RBM8A* hypomorphic alleles are common, inheritance of TAR syndrome is associated with several features unusual in autosomal recessive disorders:

- **A paucity of affected sibs.** Greenhalgh et al [2002] reported that 20% of sibs were similarly affected, while an unpublished survey found that 6% of sibs were similarly affected. The smaller-than-expected percentage of affected sibs may partially be explained by the 200-kb minimally deleted region of 1q21.1 occurring as a *de novo* event in a substantial proportion (25%-50%) of individuals [Albers et al 2012].
- **Apparent parent-to-child transmission reported.** Given that the frequency of the *RBM8A* hypomorphic alleles can be as high as 3% to 14.8%, an individual with TAR syndrome may have a reproductive partner who is a carrier of an *RBM8A* hypomorphic allele.
- **Affected second- and third-degree relatives reported** (with few or no manifestations in intervening relatives; see preceding bullet).

Risk to Family Members

Parents of a proband

- The parents of an individual with TAR syndrome are typically unaffected. One parent is presumed to be a carrier of an *RBM8A* hypomorphic allele; the other parent may or may not be a carrier of a null allele.
- Rarely, one parent of an individual with TAR syndrome is a carrier of an *RBM8A* hypomorphic allele and the other parent is affected with TAR syndrome. Apparent parent-to-child transmission [Ward et al 1986, Klopocki et al 2007, Boussion et al 2020] and the presence of affected individuals in multiple generations have been reported [Schnur et al 1987].
- Approximately 50%-75% of individuals with TAR syndrome inherited the 200-kb minimally deleted region at 1q21.1 from an unaffected parent. The deletion occurs *de novo* in about 25%-50% of probands [Klopocki et al 2007, Albers et al 2012].

- Molecular genetic testing for the TAR syndrome-related pathogenic variants identified in the proband is recommended for the parents of the proband to confirm their genetic status and to allow reliable recurrence risk assessment.
- Individuals who are heterozygotes (carriers) for one TAR-syndrome related pathogenic variant (either an *RBM8A* hypomorphic allele or a null allele) are asymptomatic. Individuals with biallelic (homozygous or compound heterozygous) *RBM8A* hypomorphic alleles are asymptomatic. (Biallelic null alleles have never been reported and are thought to be lethal.)

Sibs of a proband

- If one parent is known to be heterozygous for a null allele and the other parent is heterozygous for an *RBM8A* hypomorphic allele, each sib of an affected individual has at conception a 25% chance of being affected, a 50% chance of being an asymptomatic carrier, and a 25% chance of inheriting neither of the familial pathogenic variants.
- If one parent is known to be heterozygous for a null allele and the other parent has biallelic *RBM8A* hypomorphic alleles, each sib of an affected individual has at conception a 50% chance of being affected and a 50% chance of being an asymptomatic carrier of an *RBM8A* hypomorphic allele.
- If one parent is known to be heterozygous for an *RBM8A* hypomorphic allele and the other parent has two normal *RBM8A* alleles (i.e., the other parent is not a carrier), each sib of an affected individual has at conception a 50% chance of being an asymptomatic carrier of an *RBM8A* hypomorphic allele and a 50% chance of being unaffected and not a carrier.
- Individuals who are heterozygotes (carriers) for one TAR-syndrome related pathogenic variant (either an *RBM8A* hypomorphic allele or a null allele) are asymptomatic. Individuals with biallelic (homozygous or compound heterozygous) *RBM8A* hypomorphic alleles are asymptomatic. (Biallelic null alleles have never been reported and are thought to be lethal.)

Offspring of a proband

- An individual with TAR syndrome will transmit either a null allele or an *RBM8A* hypomorphic allele to all offspring.
- If the reproductive partner of an individual with TAR syndrome is a carrier of a heterozygous *RBM8A* hypomorphic allele, offspring have a 25% chance of inheriting a null allele and an *RBM8A* hypomorphic allele and being affected.
- If the reproductive partner of an individual with TAR syndrome has biallelic (homozygous or compound heterozygous) *RBM8A* hypomorphic alleles, offspring have a 50% chance of inheriting a null allele and an *RBM8A* hypomorphic allele and being affected.

Other family members. The risk to other family members depends on the status of the proband's parents. If the parent of a proband is a carrier of a TAR syndrome-related pathogenic variant, each sib of that parent is at increased risk of being a carrier of the pathogenic variant.

Carrier Detection

Carrier testing for at-risk relatives requires prior identification of the TAR syndrome-related pathogenic variants in the family.

Related Genetic Counseling Issues

Family planning

- The optimal time for determination of genetic risk and discussion of the availability of prenatal/preimplantation genetic testing is before pregnancy.

- It is appropriate to offer genetic counseling (including discussion of potential risks to offspring and reproductive options) to young adults who are affected, are carriers of a TAR syndrome-related pathogenic variant, or are at risk of being carriers.

Prenatal Testing and Preimplantation Genetic Testing

Once the causative null allele and *RBM8A* hypomorphic allele have been identified in an affected family member, prenatal and preimplantation genetic testing are possible.

For pregnancies known to be at increased risk for TAR syndrome – that is, either (a) both parents are known carriers of a TAR syndrome-related pathogenic variant (one parent is a carrier of a null allele and one parent is carrier of an *RBM8A* hypomorphic allele); or (b) one parent is a known carrier and the status of the other parent is unknown; or (c) one parent has TAR syndrome; or (d) one parent with unknown genetic status has a sib with TAR syndrome:

- **Molecular genetic testing.** If the pathogenic variants have been identified in an affected family member, prenatal and preimplantation genetic testing are possible.
- **Fetal ultrasound examination.** Ultrasound evaluation of fetal limbs and heart can be used either alone or in conjunction with molecular genetic testing.

For pregnancies not known to be at increased risk for TAR syndrome

- **Fetal ultrasound examination.** In a pregnancy not known to be at increased risk for TAR syndrome and in which radial anomalies are identified on routine ultrasound evaluation, the fetus with TAR syndrome may be misdiagnosed as having Holt-Oram, Roberts, or other syndromes. The detection of a heterozygous 200-kb minimally deleted region at 1q21.1 [Houeijeh et al 2011] or other heterozygous null alleles in *trans* with an *RBM8A* hypomorphic allele confirms the diagnosis of TAR syndrome in a fetus with typical radial anomalies.

Differences in perspective may exist among medical professionals and within families regarding the use of prenatal testing. While most centers would consider use of prenatal testing to be a personal decision, discussion of these issues may be helpful.

Resources

GeneReviews staff has selected the following disease-specific and/or umbrella support organizations and/or registries for the benefit of individuals with this disorder and their families. GeneReviews is not responsible for the information provided by other organizations. For information on selection criteria, click here.

- **Genetic and Rare Diseases Information Center (GARD)**

  Phone: 888-205-2311

  TAR Syndrome

- **MedlinePlus**

  Thrombocytopenia-absent radius syndrome

- **National Organization for Rare Disorders (NORD)**

  Thrombocytopenia Absent Radius Syndrome

- **MedlinePlus**

  Thrombocytopenia

- **REACH**
  Helping children with upper limb differences live life without limits.
  United Kingdom
  Phone: 0845 1306 225; 020 3478 0100
  www.reach.org.uk
- **National Cancer Institute**
  Inherited Bone Marrow Failure Syndrome Studies (IBMFS)
  IBMFS Study

Molecular Genetics

Information in the Molecular Genetics and OMIM tables may differ from that elsewhere in the GeneReview: tables may contain more recent information. —ED.

Table A. Thrombocytopenia Absent Radius Syndrome: Genes and Databases

Gene	Chromosome Locus	Protein	HGMD	ClinVar
RBM8A	1q21.1	RNA-binding protein 8A	RBM8A	RBM8A

Data are compiled from the following standard references: gene from HGNC; chromosome locus from OMIM; protein from UniProt. For a description of databases (Locus Specific, HGMD, ClinVar) to which links are provided, click here.

Table B. OMIM Entries for Thrombocytopenia Absent Radius Syndrome (View All in OMIM)

274000	THROMBOCYTOPENIA-ABSENT RADIUS SYNDROME; TAR
605313	RNA-BINDING MOTIF PROTEIN 8A; RBM8A

Molecular Pathogenesis

RBM8A encodes RNA-binding protein 8A (RBM8A; also known as Y14), a protein found predominantly in the nucleus, although it is also present in the cytoplasm. RBM8A has a conserved RNA-binding motif and is preferentially associated with mRNAs produced by splicing, including both nuclear mRNAs and newly exported cytoplasmic mRNAs. It is thought that the protein remains associated with spliced mRNAs as a tag to indicate where introns were present, thus coupling pre- and post-mRNA splicing events. RBM8A is involved with mRNA and snRNA biogenesis, based on its role as a component of the exon junction complex (EJC). RBM8A also plays a role in genomic stability; its knockdown delays the recruitment of DNA damage repair factors to damage sites and compromises the efficiency of DNA end joining [Chuang et al 2019].

Thrombocytopenia absent radius (TAR) syndrome is the result of loss of function of RBM8A, reducing the expression of RBM8A below a critical threshold [Albers et al 2012]. Experiments in model animal systems indicate that a complete deficiency of RBM8A (homozygosity for two null alleles) is lethal.

The consequences of insufficiency on the functioning of the EJC and its repercussions on cellular metabolism are not fully understood. Although the EJC appears to act ubiquitously, the reason why some tissues are consistently and severely affected by downregulation of RBM8A while other organs are spared is unknown. It has been shown, for example, that hypomorphic alleles lead to a loss of expression in osteoblastic and megakaryocytic cells in vitro, but not in human vascular cells [Albers et al 2012].

Several authors have studied the mechanism of thrombocytopenia in TAR syndrome by studying the thrombopoietin receptor (TPO) signaling pathway. In TAR syndrome, thrombocytopenia is characterized by a very low rate of megakaryocytic precursors within the bone marrow. While the TPO signaling pathway plays a

major role in the control of megakaryocyte differentiation, to date no association between it and TAR syndrome has been demonstrated [Ballmaier et al 1997, Ballmaier et al 1998, Fiedler et al 2012].

Mechanism of disease causation. Loss of function

***RBM8A*-specific laboratory technical considerations.** A closely related pseudogene, *RBM8B*, has been described [Faurholm et al 2001].

Notable *RBM8A* variants. The minimally deleted segment is a 200-kb region at 1q21.1 encompassing *RBM8A* as well as at least 12 known genes [Klopocki et al 2007]. However, the most frequently observed deleted allele (28/30 individuals with TAR syndrome) is a 500-kb deletion extending toward the telomere that spans an additional five genes [Klopocki et al 2007]. Both the 200-kb and 500-kb TAR syndrome-associated deletions are typically distinct and separate from the region of the 1q21.1 deletion/duplication syndrome (see Genetically Related Disorders). Larger rearrangements involving these regions have been reported [Brunetti-Pierri et al 2008, Mefford et al 2008]. An atypical TAR syndrome region deletion has also been described [Brunetti-Pierri et al 2008].

Table 7. Notable *RBM8A* Pathogenic Variants

Reference Sequences	DNA Nucleotide Change	Predicted Protein Change	Comment [Reference]
NM_005105.5	c.-21G>A [1]	--	Hypomorphic allele w/general population frequency of 3.05% [Albers et al 2012] [2]
	c.Ter6C>G [3]	--	Hypomorphic allele w/African population frequency of 14.8% [Boussion et al 2020] [2]
	c.67+32G>C [4]	--	Hypomorphic allele w/general population frequency of 0.41% [Albers et al 2012] [2]
	c.−19G>T	--	Hypomorphic allele w/unknown population frequency [Boussion et al 2020] [2]
NC_000001.11	g.145919695T>C [5]	--	Hypomorphic allele w/general population frequency of 0.5% [Brodie et al 2019] [2]
NM_005105.5 NP_005096.1	c.207_208insAGCG	p.Val70SerfsTer3	Null allele [Albers et al 2012]
	c.487C>T	p.Arg163Ter	
	c.206-13C>A	p.Ser69PhefsTer13	Null allele [Boussion et al 2020]
	c.205+3_205+6delGAGT	p.Glu43_Ser69delinsAla	

Variants listed in the table have been provided by the authors. *GeneReviews* staff have not independently verified the classification of variants.
GeneReviews follows the standard naming conventions of the Human Genome Variation Society
1. rs139428292
2. Note that individuals homozygous for these hypomorphic alleles do not have features of TAR syndrome.
3. rs12079762
4. rs201779890
5. rs61746197

Chapter Notes

Author Notes

Prof Florence Petit (florence.petit@chu-lille.fr) is actively involved in clinical research regarding individuals with limb malformations and especially thrombocytopenia in thrombocytopenia absent radius (TAR) syndrome. Her group would be happy to communicate with persons who have any questions regarding diagnosis of TAR syndrome or other considerations.

Prof Petit is also interested in hearing from clinicians treating families affected by TAR syndrome in whom no causative variants have been identified through molecular genetic testing.

Contact Prof Petit to inquire about review of *RBM8A* variants of uncertain significance.

Acknowledgments

We acknowledge all clinicians and researchers, patients, and families who contributed to a better description and understanding of TAR syndrome.

Author History

Simon Boussion, MD (2022-present)

Florence Petit, MD, PhD (2022-present)

Helga V Toriello, PhD; Michigan State University (2009-2022)

Revision History

- 2 November 2023 (aa) Revision: clarification of disease mechanism (loss of function) in Molecular Pathogenesis
- 25 August 2022 (sw) Comprehensive update posted live
- 8 December 2016 (sw) Comprehensive update posted live
- 29 May 2014 (me) Comprehensive update posted live
- 2 February 2012 (me) Comprehensive update posted live
- 8 December 2009 (me) Review posted live
- 26 August 2009 (hvt) Original submission

References

Literature Cited

Ahmad R, Pope S. Association of Mayer-Rokitansky-Küster-Hauser syndrome with thrombocytopenia absent radii syndrome: a rare presentation. Eur J Obstet Gynecol Reprod Biol. 2008;139:257-8 PubMed PMID: 17537565.

Albers CA, Paul DS, Schulze H, Freson K, Stephens JC, Smethurst PA, Jolley JD, Cvejic A, Kostadima M, Bertone P, Breuning MH, Debili N, Deloukas P, Favier R, Fiedler J, Hobbs CM, Huang N, Hurles ME, Kiddle G, Krapels I, Nurden P, Ruivenkamp CA, Sambrook JG, Smith K, Stemple DL, Strauss G, Thys C, van Geet C, Newbury-Ecob R, Ouwehand WH, Ghevaert C. Compound inheritance of a low-frequency regulatory SNP and a rare null mutation in exon-junction complex subunit RBM8A causes TAR syndrome. Nat Genet. 2012;44:435-9. PubMed PMID: 22366785.

Al Kaissi A, Girsch W, Kenis V, Melchenko I, Ben Ghachem M, Pospischill R, Klaushofer K, Grill F, Ganger R. Reconstruction of limb deformities in patients with thrombocytopenia-absent radius syndrome. Orthop Surg. 2015;7:50-6. PubMed PMID: 25708036.

Ballmaier M, Schulze H, Cremer M, Folman CC, Strauss G, Welte K. Defective c-Mpl signaling in the syndrome of thrombocytopenia with absent radii. Stem Cells. 1998;16:177-84.

Ballmaier M, Schulze H, Strauss G, Cherkaoui K, Wittner N, Lynen S, Wolters S, Bogenberger J, Welte K. Thrombopoietin in patients with congenital thrombocytopenia and absent radii: elevated serum levels, normal receptor expression, but defective reactivity to thrombopoietin. Blood. 1997;90:612-9. PubMed PMID: 9226161.

Beauvais D, Cabannes-Hamy A, Leblanc T, Dhédin N, Magda A, Cuccuini W, Clappier E, Vial Y, Boissel N. T-cell acute lymphoblastic leukemia in a young adult with thrombocytopenia-absent radius syndrome: a case report and review of the literature. J Pediatr Hematol Oncol. 2021;43:232-5. PubMed PMID: 32815886.

Bottillo I, Castori M, De Bernardo C, Fabbri R, Grammatico B, Preziosi N, Scassellati GS, Silvestri E, Spagnuolo A, Laino L, Grammatico P. Prenatal diagnosis and post-mortem examination in a fetus with thrombocytopenia-absent radius (TAR) syndrome due to compound heterozygosity for a 1q21.1 microdeletion and a RBM8A hypomorphic allele: a case report. BMC Res Notes. 2013;6:376. PubMed PMID: 24053387.

Boussion S, Escande F, Jourdain AS, Smol T, Brunelle P, Duhamel C, Alembik Y, Attié-Bitach T, Baujat G, Bazin A, Bonnière M, Carassou P, Carles D, Devisme L, Goizet C, Goldenberg A, Grotto S, Guichet A, Jouk PS, Loeuillet L, Mechler C, Michot C, Pelluard F, Putoux A, Whalen S, Ghoumid J, Manouvrier-Hanu S, Petit F. TAR syndrome: clinical and molecular characterization of a cohort of 26 patients and description of novel noncoding variants of RBM8A. Hum Mutat. 2020;41:1220-5. PubMed PMID: 32227665.

Brodie SA, Rodriguez-Aulet JP, Giri N, Dai J, Steinberg M, Waterfall JJ, Roberson D, Ballew BJ, Zhou W, Anzick SL, Jiang Y, Wang Y, Zhu YJ, Meltzer PS, Boland J, Alter BP, Savage SA. 1q21.1 deletion and a rare functional polymorphism in siblings with thrombocytopenia-absent radius-like phenotypes. Cold Spring Harb Mol Case Stud. 2019;5:a004564. PubMed PMID: 31836590.

Brunetti-Pierri N, Berg JS, Scaglia F, Belmont J, Bacino CA, Sahoo T, Lalani SR, Graham B, Lee B, Shinawi M, Shen J, Kang SH, Pursley A, Lotze T, Kennedy G, Lansky-Shafer S, Weaver C, Roeder ER, Grebe TA, Arnold GL, Hutchison T, Reimschisel T, Amato S, Geragthy MT, Innis JW, Obersztyn E, Nowakowska B, Rosengren SS, Bader PI, Grange DK, Naqvi S, Garnica AD, Bernes SM, Fong CT, Summers A, Walters WD, Lupski JR, Stankiewicz P, Cheung SW, Patel A. Recurrent reciprocal 1q21.1 deletions and duplications associated with microcephaly or macrocephaly and developmental and behavioral abnormalities. Nat Genet. 2008;40:1466-71. PubMed PMID: 19029900.

Camitta BM, Rock A. Acute lymphoidic leukemia in a patient with thrombocytopenia/absent radii (Tar) syndrome. Am J Pediatr Hematol Oncol. 1993;15:335-7. PubMed PMID: 8328649.

Chuang TW, Lu CC, Su CH, Wu PY, Easwvaran S, Lee CC, Kuo HC, Hung KY, Lee KM, Tsai CY, Tarn WY. The RNA processing factor Y14 participates in DNA damage response and repair. iScience. 2019;13:402-15. PubMed PMID: 30901577.

Coccia P, Ruggiero A, Mastrangelo S, Attina G, Scalzone M, Pittiruti M, Zampino G, Maurizi P, Riccardi R. Management of children with thrombocytopenia-absent radius syndrome: an institutional experience. J Paediatr Child Health. 2012;48:166-9. PubMed PMID: 21771154.

da Rocha LA, Pires LVL, Yamamoto GL, Magliocco Ceroni JR, Honjo RS, de Novaes França Bisneto E, Oliveira LAN, Rosenberg C, Krepischi ACV, Passos-Bueno MR, Kim CA, Bertola DR. Congenital limb deficiency: genetic investigation of 44 individuals presenting mainly longitudinal defects in isolated or syndromic forms. Clin Genet. 2021;100:615-23. PubMed PMID: 34341987.

Diep RT, Arcasoy MO. Pregnancy in patients with thrombocytopenia and absent radii (TAR) syndrome. Ann Hematol. 2017;96:1589-90. PubMed PMID: 28730453.

Ding L, Huang YZ, Qian YQ, Dong MY. [Genetic study and prenatal diagnosis of a family with thrombocytopenia-absent radius (TAR) syndrome]. Sichuan Da Xue Xue Bao Yi Xue Ban. 2021;52:711-5. PubMed PMID: 34323054.

Espinoza AF, Krispin E, Cortes MS, Kirk S, Hui SK, Wagner KB, Despotovic J, Shamshirsaz AA. Prenatal diagnosis and management of thrombocytopenia-absent radius syndrome. Neoreviews. 2022;23:e429-e433. PubMed PMID: 35641461.

Fadoo Z, Naqvi SM. Acute myeloid leukemia in a patient with thrombocytopenia with absent radii syndrome. J Pediatr Hematol Oncol. 2002;24:134-5. PubMed PMID: 11990700.

Farlett R, Kulkarni A, Thomas B, Mydam J. Thrombocytopenia with absent radii syndrome with an unusual urological pathology: a case report. Cureus. 2022;14:e23991. PubMed PMID: 35463560.

Faurholm B, Millar RP, Katz AA. The genes encoding the type II gonadotropin-releasing hormone receptor and the ribonucleoprotein RBM8A in humans overlap in two genomic loci. Genomics. 2001;78:15-8. PubMed PMID: 11707068.

Fiedler J, Strauss G, Wannack M, Schwiebert S, Seidel K, Henning K, Klopocki E, Schmugge M, Gaedicke G, Schulze H. Two patterns of thrombopoietin signaling suggest no coupling between platelet production and thrombopoietin reactivity in thrombocytopenia-absent radii syndrome. Haematologica. 2012;97:73-81. PubMed PMID: 21933853.

Giordano P, Cecinati V, Grassi M, Giordani L, De Mattia D, Santoro N. Langerhans cell histiocytosis in a pediatric patient with thrombocytopenia-absent radius syndrome and 1q21.1 deletion: case report and proposal of a rapid molecular diagnosis of 1q21.1 deletion. Immunopharmacol Immunotoxicol. 2011;33:754-8. PubMed PMID: 21428712.

Go RS, Johnston KL. Acute myelogenous leukemia in an adult with thrombocytopenia with absent radii syndrome. Eur J Haematol. 2003;70:246-8. PubMed PMID: 12656750.

Goldfarb CA, Wustrack R, Pratt JA, Mender A, Manske PR. Thumb function and appearance in thrombocytopenia: absent radius syndrome. J Hand Surg Am. 2007;32:157-61. PubMed PMID: 17275588.

Greenhalgh KL, Howell RT, Bottani A, Ancliff PJ, Brunner HG, Verschuuren-Bemelmans CC, Vernon E, Brown KW, Newbury-Ecob RA. Thrombocytopenia-absent radius syndrome: a clinical genetic study. J Med Genet. 2002;39:876-81. PubMed PMID: 12471199.

Griesinger G, Dafopoulos K, Schultze-Mosgau A, Schroder A, Felberbaum R, Diedrich K. Mayer-Rokitansky-Kuster-Hauser syndrome associated with thrombocytopenia-absent radius syndrome. Fertil Steril. 2005;83:452-4. PubMed PMID: 15705390.

Hedberg VA, Lipton JM. Thrombocytopenia with absent radii. A review of 100 cases. Am J Pediatr Hematol Oncol. 1988;10:51-64. PubMed PMID: 3056062.

Hipólito LN, Mendoza-Cembranos MD, Villaescusa MT, Jo-Velasco M, Requena L, Alegría-Landa V. Langerhans cell histiocytosis and multiple reticulohistiocytomas in a patient with TAR syndrome: an association not previously described. J Cutan Pathol. 2019;46:609-12. PubMed PMID: 31006900.

Houeijeh A, Andrieux J, Saugier-Veber P, David A, Goldenberg A, Bonneau D, Fouassier M, Journel H, Martinovic J, Escande F, Devisme L, Bisiaux S, Chaffiotte C, Maux M, Kerckaert JP, Holder-Espinasse M, Mouvrier-Hanu S. Thrombocytopenia-absent radius (TAR) syndrome: a clinical genetic series of 14 further cases. Impact of the associated 1q21.1 deletion on the genetic counseling. Eur J Med Genet. 2011;54:e471-7. PubMed PMID: 21635976.

Idahosa C, Berardi TR, Shkolnikov R, Stoopler ET. Thrombocytopenia absent radius (TAR) syndrome: a case report and review for oral health care providers. Spec Care Dentist. 2014;34:251-8. PubMed PMID: 25346959.

Jameson-Lee M, Chen K, Ritchie E, Shore T, Al-Khattab O, Gergis U. Acute myeloid leukemia in a patient with thrombocytopenia with absent radii: a case report and review of the literature. Hematol Oncol Stem Cell Ther. 2018;11:245-7. PubMed PMID: 28259746.

Klopocki E, Schulze H, Strauss G, Ott CE, Hall J, Trotier F, Fleischhauer S, Greenhalgh L, Newbury-Ecob RA, Neumann LM, Habenicht R, König R, Seemanova E, Megarbane A, Ropers HH, Ullmann R, Horn D, Mundlos S. Complex inheritance pattern resembling autosomal recessive inheritance involving a microdeletion in thrombocytopenia-absent radius syndrome. Am J Hum Genet. 2007;80:232-40 PubMed PMID: 17236129.

Kumar C, Sharma D, Pandita A, Bhalerao S. Thrombocytopenia absent radius syndrome with Tetralogy of Fallot: a rare association. Int Med Case Rep J. 2015;8:81-5. PubMed PMID: 25908903.

Manukjan G, Bösing H, Schmugge M, Strauß G, Schulze H. Impact of genetic variants on haematopoiesis in patients with thrombocytopenia absent radii (TAR) syndrome. Br J Haematol. 2017;179:606-17. PubMed PMID: 28857120.

McLaurin TM, Bukrey CD, Lovett RJ, Mochel DM. Management of thrombocytopenia-absent radius (TAR) syndrome. J Pediatr Orthop. 1999;19:289-96. PubMed PMID: 10344309.

Mefford HC, Sharp AJ, Baker C, Itsara A, Jiang Z, Buysse K, Huang S, Maloney VK, Crolla JA, Baralle D, Collins A, Mercer C, Norga K, de Ravel T, Devriendt K, Bongers EM, de Leeuw N, Reardon W, Gimelli S, Bena F, Hennekam RC, Male A, Gaunt L, Clayton-Smith J, Simonic I, Park SM, Mehta SG, Nik-Zainal S, Woods CG, Firth HV, Parkin G, Fichera M, Reitano S, Lo Giudice M, Li KE, Casuga I, Broomer A, Conrad B, Schwerzmann M, Räber L, Gallati S, Striano P, Coppola A, Tolmie JL, Tobias ES, Lilley C, Armengol L, Spysschaert Y, Verloo P, De Coene A, Goossens L, Mortier G, Speleman F, van Binsbergen E, Nelen MR, Hochstenbach R, Poot M, Gallagher L, Gill M, McClellan J, King MC, Regan R, Skinner C, Stevenson RE, Antonarakis SE, Chen C, Estivill X, Menten B, Gimelli G, Gribble S, Schwartz S, Sutcliffe JS, Walsh T, Knight SJ, Sebat J, Romano C, Schwartz CE, Veltman JA, de Vries BB, Vermeesch JR, Barber JC, Willatt L, Tassabehji M, Eichler EE. Recurrent rearrangements of chromosome 1q21.1 and variable pediatric phenotypes. N Engl J Med. 2008;359:1685-99. PubMed PMID: 18784092.

Miertuš J, Maltese PE, Hýblová M, Tomková E, Ďurovčíková D, Rísová V, Bertelli M. Expanding the phenotype of thrombocytopenia absent radius syndrome with hypospadias. J Biotechnol. 2020;311:44-8. PubMed PMID: 32109542.

Morgan A, Dipresa S, Turolla L, La Bianca M, Faletra F, Girotto G. A new case of TAR syndrome confirms the importance of noncoding variants in the etiopathogenesis of the disease. Hum Mutat. 2021;42:213-5. PubMed PMID: 33559987.

Nicchia E, Giordano P, Greco C, De Rocco D, Savoia A. Molecular diagnosis of thrombocytopenia-absent radius syndrome using next-generation sequencing. Int J Lab Hematol. 2016;38:412-8. PubMed PMID: 27320760.

Papoulidis I, Oikonomidou E, Orru S, Siomou E, Kontodiou M, Eleftheriades M, Bacoulas V, Cigudosa JC, Suela J, Thomaidis L, Manolakos E. Prenatal detection of TAR syndrome in a fetus with compound inheritance of an RBM8A SNP and a 334-kb deletion: a case report. Mol Med Rep. 2014;9:163-5. PubMed PMID: 24220582.

Rao VS, Shenoi UD, Krishnamurthy PN. Acute myeloid leukemia in TAR syndrome. Indian J Pediatr. 1997;64:563-5. PubMed PMID: 10771890.

Schnur RE, Eunpu D, Zackai E. Thrombocytopenia with absent radius in a boy and his uncle. Am J Med Genet. 1987;28:117-23. PubMed PMID: 3314504.

Tassano E, Gimelli S, Divizia MT, Lerone M, Vaccari C, Puliti A, Gimelli G. Thrombocytopenia-absent radius (TAR) syndrome due to compound inheritance for a 1q21.1 microdeletion and a low-frequency noncoding RBM8A SNP: a new familial case. Mol Cytogenet. 2015;8:87. PubMed PMID: 26550033.

Travessa AM, Dias P, Santos A, Custódio S, Sousa A, Sousa AB. Upper limb phocomelia: A prenatal case of thrombocytopenia-absent radius (TAR) syndrome illustrating the importance of chromosomal microarray in limb reduction defects. Taiwan J Obstet Gynecol. 2020;59:318-22. PubMed PMID: 32127157.

Ward RE, Bixler D, Provisor A, Bader P. Parent to child transmission of the thrombocytopenia absent radius (TAR) syndrome. Am J Med Genet Suppl. 1986;2:207-14. PubMed PMID: 3146292.

Wax JR, Crabtree C, Blackstone J, Pinette MG, Cartin A. Maternal thrombocytopenia-absent radius syndrome complicated by severe pre-eclampsia. J Matern Fetal Neonatal Med. 2009;22:175-7. PubMed PMID: 19253167.

Yassaee VR, Hashemi-Gorji F, Soltani Z, Poorhosseini SM. A new approach for molecular diagnosis of TAR syndrome. Clin Biochem. 2014;47:835-9. PubMed PMID: 24769264.

License