

Mitral Valve Repair in a Patient with Thrombocytopenia-Absent Radius Syndrome: Case Report

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ABSTRACT

Thrombocyte level and functions are vital factors during cardiac surgery. Thrombocytopenia-absent radius syndrome (TAR) is a rare genetic disorder consisting of skeletal abnormalities and thrombocytopenia. In this report, we present the management strategy for a 23-year-old female patient with TAR syndrome who underwent mitral valve repair.

INTRODUCTION

Thrombocytopenia-absent radius (TAR) syndrome is a rare autosomal recessive disorder characterized by neonatal onset of thrombocytopenia and bilateral absence or hypoplasia of the radii with normal or poorly developed hands and thumbs [Hall 1969; Hedberg 1988; Gounder 1989; Greenhalgh 2002; Klopocki 2007]. Although similar to congenital rubella caused by intrauterine injury during the developmental stage of the involved systems, a common etiologic agent has not been established [Hedberg 1988; Greenhalgh 2002; Klopocki 2007]. This syndrome may also include abnormalities of the gastrointestinal, hematologic, and cardiac systems, as well as other parts of the skeletal system [Gounder 1989; Greenhalgh 2002]. Cardiac anomalies occur in one third of TAR syndrome patients and can include tetralogy of Fallot and atrial and ventricular septal defects [Barkagan 1986; Greenhalgh 2002]. Only 1 case of mitral valve prolapse presenting with TAR syndrome has been described in the literature [Barkagan 1986].

TAR syndrome associated with mitral valve prolapse leading to severe mitral regurgitation requiring intervention is an exceedingly rare combination [Barkagan 1986]. In this report, we present our strategy for the management of mitral valve disease in a patient with TAR syndrome.

O. Gurer and A. Kirbas collected the data. O. Gurer, A. Kirbas, and M. Ugurlucan interpreted the data and wrote the manuscript. O. Isik designed the study and performed critical revision of the manuscript.

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CASE REPORT

A 23-year-old woman with a short stature and radius aplasia of both extremities was admitted for dyspnea and fatigue. A physical examination revealed a 4/6 mid-systolic murmur in the mitral area; there were no other abnormalities except for skeletal findings. An echocardiographic examination showed a 5-mm prolapse of the anterior leaflet of the mitral valve during systole, leading to mitral regurgitation of grade 3 to 4+. The patient had anemia and thrombocytopenia (hypomegakaryocytic thrombocytopenia) (Table).

At birth, the patient had bilateral micromelia of the upper limbs; hypoplastic and radially curved forearms with poorly formed hands were observed. X-ray films revealed bilateral radial aplasia and radial curving of the left ulna, which were also visualized on chest radiographs taken during the operative period (Figures 1 and 2). Other systems were normal. The clinical diagnosis of TAR syndrome was confirmed a few days after birth when thrombocytopenia, without hemorrhages, was discovered. The mother and father are non-consanguineous, and the patient had no family history of the disease. The family had refused upper-extremity prostheses for the patient at a young age. The patient is able to perform tasks by approximating her body close enough to an object to use her own hands.

In preparation for mitral valve surgery, the hematology service was consulted, because thrombocytopenia may increase the risk of bleeding and thereby complicate the peri- and postoperative courses. Thrombopheresis was recommended by the hematology service.

The operation was performed through a median sternotomy with aortic and bicaval cannulations with the patient under general anesthesia. Myocardial protection was achieved with systemic cooling to 32°C, topical ice slush, and antegrade cold blood cardioplegia. After cross-clamping and cardioplegic arrest, the mitral valve was inspected via a left atriotomy. The valve apparatus was healthy except for prolapse of the anterior leaflet secondary to chordal elongation (type 2 mitral insufficiency). Chordal plication and ring annuloplasty were performed with a CarboMedics 27-mm ring (CarboMedics, Austin, TX, USA). At the end of cardiopulmonary bypass (CPB), a transesophageal echocardiographic examination showed trivial mitral regurgitation. CPB and cross-clamp times were 80 minutes and 64 minutes, respectively.

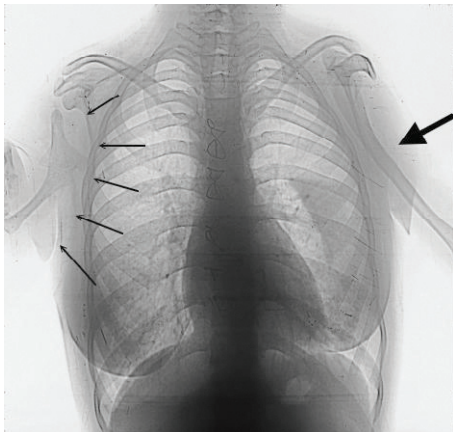


Figure 1. Note bilateral absent radii and the left-side ulna.

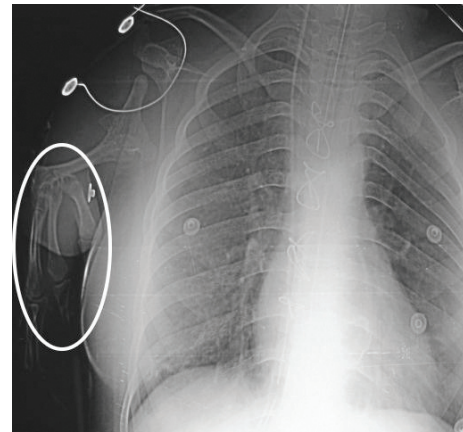


Figure 2. Note hand deformity and absent radius.

Hematologic studies were performed at the 10th minute of midsternal incision, after 5 minutes of heparinization, after the 15th minute of CPB, at the fifth minute after the end of CPB, and at the fifth minute after the surgery. Thrombopheresis was started concomitantly with heparinization. The activated clotting time was 422 seconds, and 1.5 units of thrombocyte suspension was infused into the patient. From the fifth minute of CPB to the end of surgery, 2 more units of thrombocytes, 2 units of fresh blood, and 1 unit of fresh frozen plasma suspension were administered as well.

In the intensive care unit, the patient received transfusions of 1 unit of fresh blood and 1 unit of fresh frozen plasma. The total volume of chest drainage was 350 cm³ in 24 hours. On postoperative day 3, she received another unit of erythrocyte suspension. Hematologic parameters became normalized in the follow-up (Table). The patient was discharged home on day 7. Because the patient was in sinus rhythm and owing to the thrombocytopenia, anticoagulation therapy with warfarin was not used. After 9 months of follow-up, the patient is well.

DISCUSSION

TAR syndrome is a congenital disorder characterized by thrombocytopenia and bilateral radius aplasia. The disorder has an autosomal recessive inheritance pattern [Hall 1969; Hedberg 1988; Gounder 1989; Greenhalgh 2002; Klopocki 2007]. Although the expression may be variable, the syndrome may include abnormalities in the gastrointestinal,

skeletal, hematologic, and cardiac systems [Barkagan 1986; Hedberg 1988; Greenhalgh 2002]. Affected children usually have a short stature accompanied by aplasia or hypoplasia of the ulnae; defects in the hands, legs, and/or feet; congenital dislocation of the hips; subluxation and stiffness of the knees; and musculoskeletal manifestations, such as dislocated patellae [Hedberg 1988]. Systemic involvement is common with various cardiac anomalies [Barkagan 1986] and gastrointestinal disorders, such as hepatomegaly and splenomegaly [Hedberg 1988; Greenhalgh 2002]. The incidence of TAR syndrome in some series has been reported to be approximately 1 in 100,000 [Gounder 1989; Fromm 1991].

The syndrome was first noted by Greenwald and Sherman in 1929 [Smith 1982]. Hall et al coined the acronym in 1969 after describing 4 affected sisters [Hall 1969]. The authors further classified the syndrome as the association of hypomegakaryocytic thrombocytopenia with absent radii [Hall 1969]. Since then, however, no gene causing this disorder has been identified. TAR syndrome is closely similar to congenital rubella, suggesting an intrauterine injury during the development of the involved systems. A common etiologic agent has not been identified [Hedberg 1988; Greenhalgh 2002; Klopocki 2007]. The defective gene, or teratogenic injury, most probably appears in early gestation (between 4 and 8 weeks), because the association of seemingly disparate skeletal and hematologic abnormalities is related to the simultaneous development of the heart, the radii, and megakaryocytes at 4 to 8 weeks of gestation [Letestu 2000; Greenhalgh 2002].

Patient's Hemoglobin, Hematocrit, and Platelet Measurements*

	Preoperative	After				Postoperative			
		Heparinization	Before CPB	During CPB	After CPB	Postoperative	Day 2	Ward, Day 3	Ward, Day 6
Hemoglobin, g/dL	12.0	9.3	7.5	6.4	7.9	10.2	10.4	11	12.6
Hematocrit, %	35.5	29	21.7	19.1	23.5	30.2	30.8	31.4	37.7
Platelets, $\times 10^9/L$	86	119	110	58	71	127	121	102	95

*CPB indicates cardiopulmonary bypass.

In addition to the musculoskeletal manifestations and thrombocytopenia [Hedberg 1988; Greenhalgh 2002], cardiac disorders are also encountered in patients with TAR syndrome at an incidence of 15% to 33% [Barkagan 1986; Greenhalgh 2002]. Tetralogy of Fallot and atrial and ventricular septal defects are the most common [Barkagan 1986; Greenhalgh 2002]. A literature search revealed only a single case of mitral valve prolapse in a patient with TAR syndrome [Barkagan 1986]. This particular case [Barkagan 1986] featured a low platelet count and a high tendency for bleeding.

The major cause of mortality and morbidity during the course of TAR syndrome is known to be hemorrhage due to the thrombocytopenia [Hall 1969; Smith 1982; Barkagan 1986; Hedberg 1988; Gounder 1989; Fromm 1991; Letestu 2000; Greenhalgh 2002; Klopocki 2007]. In our patient, the thrombocyte count was $86 \times 10^9/L$ at the time of admission. Elective surgery was performed with the support of preoperatively prepared whole blood, thrombocyte solution, and fresh frozen plasma. The aim was to transfuse thrombocytes when the platelet level fell to $<80 \times 10^9/L$ and to discontinue transfusion when the count became $>100 \times 10^9/L$. This management strategy allowed uneventful surgical and postoperative courses.

Other than the thrombocytopenia and a tendency for bleeding, cardiac surgery itself is associated with certain amount of blood loss. Systemic hypothermia leads to thrombocytopenia and disorders of thrombocyte function [Levy 2010]. Thrombocytopenia has long been a challenging issue for cardiac surgery teams. Cardiac surgery patients are at high risk for mortality and morbidity. Follow-up of these patients requires close monitoring, especially for the development of thrombocytopenia [McLaurin 1999; Vanderschueren 2000; Crowther 2005; Shalansky 2006]. Thrombocytopenia may have various etiologies. Heparin itself is known to decrease thrombocytes. Moreover, cooling interferes with thrombocyte aggregation and coagulation pathways [Levy 2010]. Anticoagulants may further impair hemostasis. Thus, normal thrombocyte function is vital during and after cardiovascular surgery procedures [McLaurin 1999; Vanderschueren 2000; Crowther 2005; Shalansky 2006; Levy 2010].

Other than classic systemic hypothermic cardiac surgery, alternatives could be intermittent warm blood cardioplegia [Calafiore 1995] or continuous perfusion of the heart with the aorta unclamped and a beating heart technique [Salerno 2007]. Both methods are free from the side effects of hypothermia on thrombocyte functions and offer the benefit of normothermia with respect to platelet activity.

In conclusion, we have presented our management strategy for a patient with TAR syndrome who underwent mitral valve repair. There is no uniform consensus for treating patients who have TAR syndrome and a low platelet count and who are to undergo cardiac surgery [Barkagan 1986].

Transfusion of thrombocytes when the level fell to $<80 \times 10^9/L$ was successful in our patient.

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