The FDA approved the AVP I and AVP II for use in 2004 and September 2007, respectively. In Japan, AVP I and AVP II were approved in 2013, and AVP IV was approved in 2014. AVP as a single device is highly effective for PAVM occlusion. Usually, the AVP diameter should be at least 20% larger than the diameter of the feeding vessel. At a diameter of 4–16 mm, 3–22 mm, and 4–8 mm for AVP I, II, and IV, respectively, PAVM with large feeding arteries can be rapidly occluded with a low risk of migration. Compared with coils, AVP for embolization of PAVM is associated with a significantly lower rate of re-canalization of feeding vessels. There have been few reports on lobar embolization for PAVM. In the present case, use of AVP successfully achieved safe and minimally invasive complete occlusion of the left lower lobar arteries in a 10-year-old boy with diffuse PAVM, which are considered to be indications for surgical lobectomy.

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Disclosure

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Discrimination of Diamond–Blackfan anemia from parovirus B19 infection by RBC glutathione

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Key words Diamond–Blackfan anemia, erythrocyte adenosine deaminase, erythrocyte reduced glutathione.

Diamond–Blackfan anemia (DBA) is a rare blood disorder characterized by a failure of the bone marrow to produce enough red blood cells (RBC), and various congenital anomalies. DBA must be differentiated from other anemias with low reticulocyte count. Parvovirus B19 infection in utero may be associated with pure RBC aplasia in infancy, and even with hydrops fetalis at birth, but it is difficult to discriminate between the two disorders in infants born to mothers with intrauterine parovirus B19 infection. In the present case we were able to distinguish DBA from parvovirus B19 infection using erythrocyte-reduced glutathione (GSH).

A 26-day-old Japanese girl was referred with anemia. At 24 weeks of gestation, her mother had a mild fever and slapped cheek rash, which occurred 10 days after the development of erythema infectiosum in the patient’s 3-year-old development, 2-10-1 Okura, Setagaya-ku, Tokyo 157-8535, Japan.

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Author contributions

K.M. wrote the manuscript. T.F. was involved with all stages of patient management. M.O. treated the patient and performed catheter intervention. M.K. supervised the treatment of the patient. T.S. collaborated on the final draft and the manuscript’s methodology. All authors read and approved the final manuscript.

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sister. At 25 weeks of gestation, parvovirus B19 IgM antibody was detected in the mother’s serum. Hydrops fetalis did not develop during the pregnancy. The patient was born at 37 weeks 5 days of gestation with a birthweight of 2,398 g. Although parvovirus B19 IgM antibody was not detected in the serum or umbilical cord blood, the patient had macrocytic anemia at birth (leukocyte count, 7,150/µL; hemoglobin [Hb], 9.3 g/dL; platelet count, 101,000/µL; mean corpuscular volume [MCV], 109.8 fL; reticulocyte count, 66,500/µL). Lactate dehydrogenase and bilirubin were not increased, and there was no physical anomaly.

When the baby was born, it was considered that the anemia was caused by intrauterine parvovirus B19 infection, and would resolve spontaneously within 1 month. At 26 days of age, however, the anemia progressed (Hb, 5.7 g/dL). The patient was admitted to hospital at 40 days of age with severe anemia (Hb, 4.0 g/dL; MCV, 107.2 fL; reticulocyte count, 22,500/µL; iron, 111 µg/dL; ferritin, 250 ng/mL). Bone marrow examination at 45 days of age showed normocellularity, but erythroid precursors were notably decreased without megaloblasts, intranuclear inclusion bodies or leukemic cells (Fig. 1a). Polymerase chain reaction for parvovirus B19 in bone marrow cells was negative. DBA was considered as a probable diagnosis for the cause of pure RBC aplasia but it was difficult to distinguish DBA from pure RBC aplasia caused by parvovirus B19 infection, because the patient had no congenital physical anomalies, family history of DBA, or elevation of fetal Hb. After that, the anemia persisted and she required periodic RBC transfusion (Fig. 1b). She developed short stature, macrocephaly and developmental retardation. Therefore, it was vital that DBA be differentiated in this patient.

Elevated erythrocyte adenosine deaminase (eADA) activity, a critical enzyme in the purine salvage pathway, is characteristic of DBA erythropoiesis and can be found in 80–89% of cases. GSH, the most important antioxidant in erythrocytes, can be an additional biomarker for diagnosis of DBA. Also, the simultaneous assessment of eADA and GSH is more informative than eADA alone. Therefore, we examined eADA and GSH at 4 months of age. Although eADA was normal (1.49 IU/gHb), GSH concentration was increased (110 mg/dL RBC). Because these data were strongly suggestive of DBA, we further examined the ribosomal protein genes at 6 months of age. A heterozygous mutation was identified in RPL5 (p.Lys41*, c.121A>T), which encodes a large ribosomal subunit protein. DBA was therefore confirmed.

In this case, it was difficult to diagnose the cause of pure RBC aplasia because the patient was born to a mother with parvovirus B19 infection and did not have either congenital physical anomalies or a family history of DBA. If we had checked eADA alone, we might not have noted the genetic alteration of the ribosome. We propose that assessment of both GSH and eADA concentration is an effective tool for distinguishing DBA from parvovirus B19 infection before confirming ribosomal gene mutations.

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Disclosure

The authors declare no conflict of interest.

Author contributions

J.N. wrote the manuscript; H.K. examined eADA and GSH; Y.C. diagnosed the patient; E.I. analyzed genetic abnormality; A.I. designed the study; H.K., Y.C., E.I. and A.I. critically reviewed the manuscript. All authors read and approved the final manuscript.

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Novel PRKAR1A mutation in Carney complex with cardiac myxoma

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Key words Carney complex, myxoma, PRKAR1A.

A 14-year-old Japanese boy was referred with a heart murmur. Two years before this admission, he had complained of dyspnea on exertion. There was no family history of myxoma. On admission, pulse rate was 100 beats/min and blood pressure was 100/60 mmHg. Chest examination indicated a grade III/VI systolic murmur and a grade IV/VI diastolic murmur. Physical examination, he had spotty skin pigmentation on the face and lip (Fig. 1a). Mild cardiomegaly and mild congestion were seen on chest radiography. Electrocardiogram showed left atrial hypertrophy and left ventricular hypertrophy. Transthoracic echocardiography (Fig. 1b,c) indicated a large mobile 50 x 50 mm mass attached to the mitral anterior leaflet and protruding into the left ventricle during diastole, thereby leading to severe mitral stenosis and regurgitation. Further evaluations showed bilateral calcification on testicular ultrasonography and no cerebral infarction on computed tomography.

The patient underwent median sternotomy and cardiopulmonary bypass using aortic and bicaval cannulation with cardiac arrest. A massive polyoid tumor with a gelatinous appearance attached to the mitral anterior leaflet via a stalk was observed on left atriotomy. A divided mass (74 x 45 x 27 mm and 55 x 40 x 8 mm) was completely removed during surgery. The patient also underwent mitral valve annuloplasty. On pathology the myxoma was not malignant. The postoperative course was uneventful. Postoperative echocardiography documented no residual tumor, and normal mitral valve function. Follow-up echocardiography 1 year after surgery showed no evidence of recurrence. Genomic sequencing of the patient’s DNA identified a novel heterozygous frameshift mutation in cAMP-dependent protein kinase type 1-α regulatory subunit (PRKAR1A) exon 2 (c.4_13del10). Absence of the mutation in the parental DNA suggested its de novo occurrence (Fig. 1d). The functional effects of the mutation were investigated using MutationTaster (http://mutationtaster.org/). The mutation was predicted to be disease-causing because the frameshift would cause splice site changes that might affect the protein function and lead to nonsense-mediated mRNA decay (NMD).

Discussion

In general, cardiac myxomas appear sporadically in middle-aged women as an isolated left atrial mass attached to the fossa ovalis, and most do not recur after surgical resection. Some myxomas, however, occur as part of a syndrome known as Carney complex (CNC). This is an autosomal dominant disorder characterized by myxoma, spotty skin pigmentation, and endocrine overactivity/tumors. CNC has two diagnostic guidelines. In the first, a clinical diagnosis of CNC can be made if there are at least two major manifestations of disease. In the second, the diagnosis requires one major manifestation and either an affected first-degree relative or an inactivating PRKAR1A mutation. Carcinoid myxomas associated with CNC occur in families, and frequently appear at an early age, with an atypical, multicentric location. Recurrence rates for cardiac myxoma are 4–7% for sporadic cases and 10–21% for familial cases. The present patient is at high risk for recurrence, and will need careful long-term monitoring.

Carney complex is usually (in approx. 70% of cases) caused by mutations in PRKAR1A on chromosome 17q22-24. This is a tumor suppressor gene that encodes a protein kinase A (PKA) regulatory 1-α (R1α) subunit. Most PRKAR1A mutations are reported to be frameshift, nonsense, and splice site, in which the mRNA undergo NMD with resultant haploinsufficiency. PKA is the primary mediator of cAMP, which is