REVIEW ARTICLE

Clarifying the anatomy and physiology of totally anomalous systemic venous connection

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ABSTRACT

The description of totally anomalous systemic venous connection is limited to case reports. In this review, we seek to clarify anatomic, physiologic, and hemodynamic aspects of this extremely rare anomaly. We also present findings of two patients in whom connection of all the systemic veins was anomalous. In the first patient, with usual atrial arrangement, all systemic veins, including the coronary sinus, were connected anomalously to the morphologically left atrium. Limited left-to-right shunt across an atrial septal defect provided the only source of blood flow to the lungs. The diagnosis was established by saline contrast echocardiography and cardiac catheterization. Extreme hypoplasia of the right ventricle precluded corrective surgery, so we performed a bidirectional Glenn operation, along with atrial septectomy. The second patient had isomerism of the left atrial appendages, which creates problems in the definition in anatomic terms since the connection of the systemic veins can never be normal anatomically when both atriums possess a morphologically left appendage. Our patient, nonetheless, had all the systemic and pulmonary veins, connected to the left-sided atrial chamber which then connected to the left ventricle, thus producing hemodynamics of totally anomalous systemic venous connection. We propose an algorithm for evaluation of this hemodynamic combination and discuss management options. We also intend to clarify the potential differences between connection and drainage, with particular attention to the arrangement of atrial appendages. Even though the hemodynamics may be comparable, in anatomic terms, both systemic and pulmonary venoatrial connection will always be anomalous with isomeric atrial appendages.

Keywords: Atrial isomerism, saline contrast echocardiography, totally anomalous systemic venous connection

INTRODUCTION

Connection of all systemic veins, along with the pulmonary veins, to morphologically left atrium (LA) is rare, particularly when the atrial arrangement is usual or mirror-image. When present as an isolated anomaly, left-to-right shunt through an atrial septal defect (ASD) or ventricular septal defect (VSD), or patent arterial duct provides blood flow to the lungs, and in turn, determines systemic oxygen saturation. The amount of left-to-right shunt also governs growth and size of the right atrium (RA) and right ventricle (RV).[1] Patients with small shunts have hypoplasia of the right-sided chambers and present with intense cyanosis.[2-9] On the other hand, the presence of a large shunt allows good oxygenation, together with the growth of RV, thus permitting complete surgical repair.[9-19] The presence of cyanosis despite left-to-right shunt across an ASD, in the setting of a hypoplastic RV in hearts with concordant atrioventricular and ventriculoarterial connections, is almost diagnostic of totally anomalous systemic venous connection (TASVC). Unfortunately, even in the

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current era of modern echocardiography, despite many clues, the diagnosis is often delayed.[5,8,11,12,14,15,20] Not uncommonly, the diagnosis is missed completely,[10] and the arrangement is misinterpreted as functionally single ventricle. It is also not uncommon to find that anomalous connection of only one caval vein, generally the superior caval vein (SCV), is correctly identified mainly because saline contrast echocardiography is generally performed only from the upper limb.[10]

In this report, we discuss a stepwise approach that we adopted in two patients in whom we suspected anomalous systemic venous connection. Morphological aspects that influence the choice of surgical repair are also discussed. We have also found many inconsistencies in the description of cases reported earlier, especially with regard to the morphology and nomenclature. Inconsistencies have been particularly more in the setting of isomeric atrial appendages or so-called heterotaxy. The differences in nomenclature, in a large part, stem from the lack of attention to, and variable definitions used for recognition of the atrial chambers. We also noted ambiguity in the use of connection and drainage, almost akin to anomalous pulmonary venous connection. In this review, we summarize our own understanding of TASVC, describing our approach in the settings of both lateralized and isomeric atrial appendages.

CASE PRESENTATIONS

Case 1

A 13-year-old girl, was referred to our outpatient department with the diagnosis of functionally univentricular physiology. At presentation, she had intense cyanosis, was breathless at rest, and had severe fatigue (NYHA functional class IV). The oxygen saturation, measured in room air, was 60%, and grade 3 clubbing was noted. Jugular venous pressure was not elevated. Cardiovascular examination revealed no cardiomegaly, a normal first heart sound and a single second sound. There was no murmur. The liver was right-sided and of normal size.

Laboratory investigation showed hemoglobin concentration of 22 g/dl with a packed cell volume of 72%. The electrocardiogram (ECG) showed sick sinus syndrome with junctional escape (isorhythmic atrioventricular dissociation), and QRS axis of 45° with poor RV forces. Chest radiograph confirmed left-sided heart with normal cardiothoracic ratio and pulmonary oliegmia. Transthoracic echocardiogram showed usual arrangement of the abdominal vessels and atriums, concordant atrioventricular and ventriculoarterial connections, and normally related arterial trunks. All the pulmonary veins were observed to drain into LA. There was no left SCV, and the intrahepatic portion of the inferior caval vein (ICV) was patent. The drainage of the caval veins, however, was not clearly visualized. The RA and RV were both hypoplastic, with tricuspid valve annulus of 13 mm, giving a Z-score of – 2.3 [Figure 1]. The LA and left ventricle (LV) were dilated although with preserved contractile function. The ventricular septum was intact, and the arterial duct was not patent. Despite careful evaluation, it was not possible to identify an ASD. There was no pulmonary stenosis. The pulmonary arteries were confluent, with the left (LPA) and right (RPA) branches measuring 9.5 and 8.5 mm, respectively. The descending thoracic aorta at the diaphragm measured 11.5 mm. The echocardiography findings are summarized in Table 1.

Saline contrast echocardiography with agitated saline injected in a right arm vein showed immediate and intense filling of LA followed by filling of RA [Figure 2a and b; Online Video 1]. A similar pattern of opacification was observed subsequent to injection of agitated saline into the right saphenous vein, confirming anomalous drainage of both SCV and ICV to LA. Late opacification of RA confirmed the presence of an ASD, permitting

Table 1: Echocardiographic findings in our patients

	Case 1	Case 2
TV annulus (mm), z score	13, - 2.3	12.8, –1.52
MV annulus (mm), z score	31, 2.0	23, 2.3
LA diameter (mm), z score	30, 2.5	24, 2.5
LVEDD (mm), z score	43, 2.3	37, 2.9
LVESD (mm), z score	29, 2.5	25, 3.5
LPA size (mm)	9.5	8.5
RPA size (mm)	8.5	7.5
DTA size at diaphragm (mm)	11.5	11
McGoon's ratio	1.56	1.45

DTA: Descending thoracic aorta, LA: Left atrium, LPA: Left pulmonary artery, LVEDD: Left ventricular end diastolic dia, LVESD: Left ventricular end systolic diameter, MV: Mitral valve, RPA: Right pulmonary artery, TV: Tricuspid valve

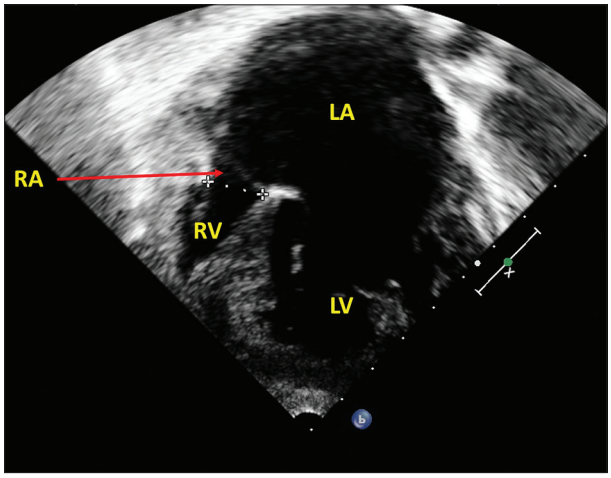

Figure 1: Transthoracic echocardiogram in apical four-chamber view shows severe hypoplasia of the right atrium and right ventricle

left-to-right shunt. The drainage of the coronary veins could not be clarified.

At cardiac catheterization, injection of contrast in the caval veins confirmed that both SCV and ICV, along with hepatic veins [Online Videos 2 and 3], were connected to the posterior atrium, which had an appendage of the left atrial morphology. This morphologically LA was connected to LV and thence to the aorta. We then inserted a 5 French Swan Ganz catheter through the right femoral artery. After crossing the aortic valve retrogradely, we could guide the catheter across the mitral valve to LA and then through an ASD to RA. Further manipulation made it possible to cross tricuspid valve and enter RV. A hand injection of contrast showed hypoplastic RV [Online Video 4]. The same catheter went across the pulmonary valve into the pulmonary arteries (PA) [Figure 3 and Online Video 5]. Additional angiograms showed that the coronary sinus as well as the pulmonary veins were also connected to LA [Online Videos 6 and 7]. LV angiogram confirmed the absence of VSD. Oxygen saturation in femoral artery and all the cardiac chambers was essentially similar and measured at 60%. PA pressure measured 28/14 mmHg, mean 21 mmHg. The calculated indexed pulmonary vascular resistance was 6.5 WU. m^2. Computed tomography (CT) angiography performed subsequently, confirmed the presence of usual arrangement of the atrial appendages and bronchi, along with gross hypoplasia of RA and RV [Figure 4].

Severely hypoplastic tricuspid valve and RV precluded complete surgical repair or even one-and-half ventricular repair. Therefore, we performed bidirectional Glenn anastomosis with atrial septectomy. A dual-chamber epicardial pacemaker was implanted for associated sick sinus syndrome. Following surgical palliation, her arterial oxygen saturation immediately improved to 82% that further improved to 84% at discharge. On follow-up, the child reported marked improvement in her activities and other symptoms.

Case 2

Our second patient is a two and half-year-old girl, who was referred for the evaluation of cyanosis. She had clubbing and cyanosis, with an oxygen saturation of 80% in room air. Her heart was left-sided, and there was no cardiomegaly. A grade 3/6 ejection systolic murmur was audible in the pulmonary area. The first heart sound was normal while the second heart sound was widely split, with a soft pulmonary component. Chest radiograph showed pulmonary oligemia with a normal-sized heart (cardiothoracic ratio 50%). The ECG was quite similar to the first patient and showed sinus node dysfunction with a low atrial rhythm, QRS axis of 0 degree, and RV hypoplasia, although with 1-to-1 atrioventricular conduction. Transthoracic echocardiography revealed interruption of ICV, which

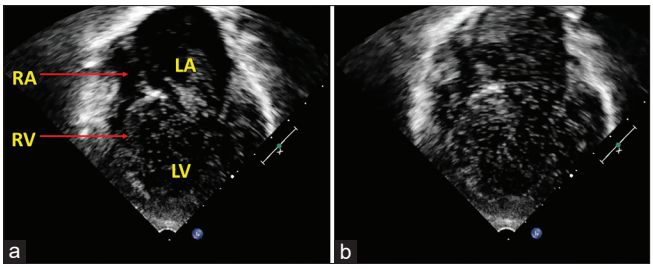

Figure 2: Saline contrast echocardiogram in apical four-chamber view following the injection of agitated saline in a right arm vein shows (a) immediate filling of the left atrium and left ventricle. (b) The right atrium and right ventricle fills late by flow of microbubbles across atrial septal defect

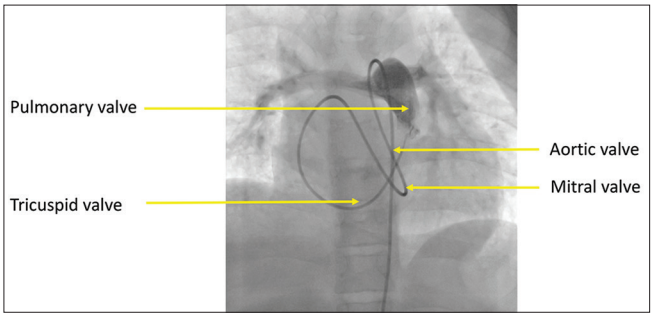

Figure 3: Catheter course during pulmonary artery angiogram. Single balloon floatation catheter placed from the femoral artery crossed all the cardiac valves allowing access to the pulmonary artery

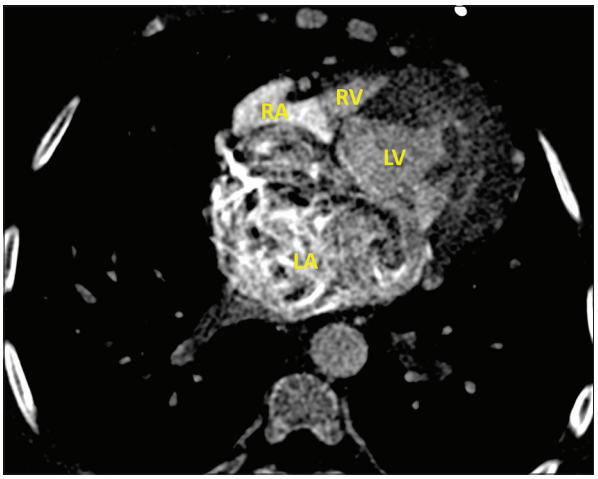

Figure 4: Axial section from computed tomography angiogram shows severe hypoplasia of the right atrium and right ventricle. The right atrial appendage is that of right atrial morphology confirming usual arrangement of atriums

continued through the azygous vein and joined a left-sided SCV. There was a right SCV with no bridging vein. All pulmonary veins could be seen to be connected to the left-sided atrium, but systemic venous connection remained unclear. The images did show, nonetheless, that the right-sided and left-sided atrial chambers were connected to morphologically RV and LV, respectively, with the ventricular mass showing right-handed

topology and concordant ventriculoarterial connections. There was also a large perimembranous VSD with inlet extension. The left-sided atrium and LV were enlarged. The right-sided atrium and RV were both hypoplastic, with tricuspid valve annulus Z score of – 1.52 [Table 1]. There was no tricuspid valve straddling. There was severe infundibular and valvar RV outflow tract obstruction with a peak systolic gradient of 75 mmHg. The PAs were confluent, with LPA and RPA measuring 8.5 and 7.5 mm, respectively.

Given our experience with the first case, inability to clarify systemic venous connections along with unexplained dilation of LA and LV alerted us to the possibility of TASVC. Disproportionate arterial desaturation with a left-to-right shunt across VSD reinforced our belief. Saline contrast echocardiography, as in the first case, was the logical next step. Injection of agitated saline in the right arm vein showed an immediate and intense appearance of microbubbles in LA and LV [Figure 5a and Online Video 8], followed by filling of the right-sided atrium and RV through ASD and VSD, respectively [Figure 5b]. A sequence of appearance of microbubbles , similar to the first case, was then noted after injections made in a leg vein and a left arm vein, confirming anomalous drainage of blood from both arms and both legs to the left-sided atrium. The drainage of the cardiac and hepatic veins, however, was still not clear. Interrupted ICV indicated to the possibility of the left isomerism that could not be confirmed on echocardiography.

CT angiogram revealed isomerism of both the bronchial tree and the atrial appendages [Figure 6 and Online Video 9]. All the pulmonary veins, both SCV, with the left-sided SCV draining the blood from azygous vein, and the hepatic veins connected to the left-sided atrium. There was no coronary sinus, and cardiac veins drained direclty to the atrial chambers. The CT angiogram also confirmed the remainder of the echocardiographic findings.

DISCUSSION

What is totally anomalous systemic venous connection?

It is extremely rare for all the systemic veins to be connected to a site other than the morphologically RA. There has been no study to look at the exact prevalence of this disease. To warrant a diagnosis of TASVC, it is necessary that all the hepatic veins, the coronary sinus, and both caval veins should be connected to morphologically LA.[5] The label of TASVC is not tenable if even one systemic vein connects to RA. It also follows that this should be diagnosed only in the setting of usual or mirror-imaged atrial arrangement[6-8,10,15,21] This is because, if the systemic veins were connected to a left-sided atrium in the setting of right isomerism, they would be anatomically normally connected. In a similar fashion, the systemic veins can never be connected in anatomically normal fashion in the setting of isomeric left atrial appendages.[18] It follows, therefore, that it is illogical, from the anatomic stance, to diagnose TASVC in patients with so-called "heterotaxy," as was the case in our second patient. The hemodynamics, nonetheless, was identical to that in our first patient. This points to the need to provide a precise account of all the venoatrial connections in patients with isomerism of atrial appendages. While the label of TASVC should be reserved for those patients with either usual or mirror-imaged atrial arrangements, it may be justifiable to describe the arrangement in our second patient as quasi-TASVC. In the same way, it is necessary, in many patients with isomeric atrial appendages, to note that the overall venoatrial connections can be quasi-usual or quasi-mirror-imaged although the presence of the isomeric appendages means that these are not accurate anatomic descriptions.

Considering these fallacies, it is not surprising to find ambiguity in the descriptions in previously published case reports of TASVC. The information regarding

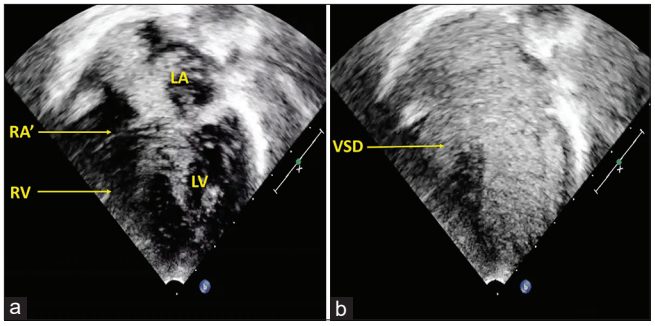

Figure 5: Saline contrast echocardiogram in apical four-chamber view following the injection of agitated saline in the right arm vein shows (a) immediate filling of left-sided atrium (LA) and left ventricle (LV). (b) The right-sided atrium (RA') and right ventricle (RV) fills from flow across atrial septal defect and ventricular septal defect (VSD) respectively

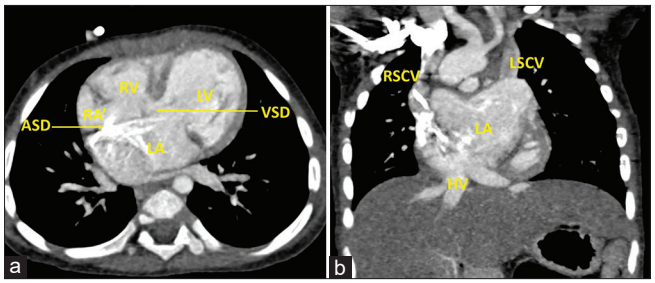

Figure 6: Maximal intensity projection computed tomography angiography images in axial (a) and coronal (b) plane, at the level of left-sided atrium, shows hypoplasia of right-sided atrium and right ventricle with all hepatic veins, right and left superior caval veins connecting anomalously to the left-sided atrium. A small atrial septal defect and a large ventricular septal defect is also seen. The patient also had severe right ventricular outflow tract obstruction (not shown here)

the influence of isomerism is particularly scant in the literature. This has led some authors to conclude that the "presence of totally anomalous systemic venous drainage (TASVD) indicates a strong likelihood of the left isomerism," and to propose that "TASVD be included as a part of the syndrome of the left atrial isomerism."[9] We now know that isomerism within the heart is limited to the atrial appendages.[20] This makes it inappropriate, as emphasized above, to diagnose true TASVC in the setting of the left isomerism. Our review of the literature, together with our current experience, thus shows that TASVC, anatomically, can exist only in the setting of lateralized atrial arrangement [Table 2].[2-27] Hemodynamically, however, it can very well exist in the setting of isomeric atrial appendages. In our opinion, in the later setting, it is best to provide details of connections of systemic veins rather than clubbing under an ambiguous label of TASVC.

Is an anomalous connection always abnormal?

Anomalies of individual systemic venous connection are not uncommon. While such abnormal connection will often produce abnormal venous drainage, this is not always the case. On occasion, systemic venous drainage may be normal despite an abnormal connection. "Connection" and "drainage," therefore, should not be considered as being synonymous. The obvious example of this paradox is persistence of the left SCV, with or without hemiazygous continuation of ICV, with the vein connecting to the coronary sinus, combination that is not uncommon. Despite anomalous connection in this setting, the drainage is to RA, and therefore, is hemodynamically normal. Similarly, when all the systemic veins connect to the coronary sinus, the drainage to RA remains normal, despite abnormal connection and therefore, is not equivalent to typical TASVC described so far. While a label of anomalous connection is justified, they cannot be labeled as having TASVD, as has sometimes been the case.[28-30] Patients with these combinations are unlikely to require surgical correction since the drainage is normal. It is important, therefore, to establish both the connection and drainage of anomalous systemic veins to determine the physiologic significance.

What are the hemodynamic consequences?

When present as an isolated anomaly, TASVC produces complete admixture of oxygenated and deoxygenated blood in LA.[31] A left-to-right shunt is then the only means for the blood to reach the lungs for oxygenation. In the majority, the left-to-right shunt is at atrial level although it can be across a VSD[6,9,13,21,22,27] or a persistently patent arterial duct.[6,7,18] It is the amount of left-to-right shunt that determines the arterial saturation, and hence, the likelihood of survival. In addition, the amount of left-to-right shunt determines the intrauterine growth of RV.[1] In patients with smaller ASD,[4,5] as in our first patient, the limited growth of the RV precludes corrective surgery. Patients with large ASD, on the other hand, can have RV sufficiently large to allow corrective surgery.[8-12,14,15,17,19] A coexisting left-to-right shunt at the level of VSD[6] and or patent arterial duct,[7] however, can also reduce the interatrial shunt, and result in hypoplasia of RV. Irrespective of the amount of left-to-right shunt, systemic arterial saturation is expected to be less than normal. All patients reported thus far, with one exception,[19] have shown visible cyanosis or arterial saturations <90%. This exceptional patient,[19] as with our second case, had left isomerism with a large ASD, which could have allowed good admixture. In addition, since the reported child was only 2 days old, it is likely that the flow between the atrial chambers was sufficient to produce normal arterial saturation at that age.

In the absence of a VSD or patent arterial duct, the pulmonary blood flow is almost always reduced, even when there is no pulmonary stenosis. Although reported in one case,[15] the presence of severe pulmonary hypertension is extremely unlikely in the setting of isolated TASVC. In the reported case, the authors invoked the finding as secondary to hypoxia, but this seems unlikely since the oxygen saturation was 81%, not severe enough to explain hypoxia-related pulmonary hypertension. We suggest it is more likely that the patient had idiopathic pulmonary hypertension coexisting with TASVC.

How and when to suspect anomalous systemic venous connection?

Despite impressive cyanosis in the majority of reported cases, delayed diagnosis in adulthood[8] or even a missed diagnosis,[10,13] is not uncommon, even in the current era of advanced echocardiography. Challenges faced in the visualization of major caval veins, and their sites of drainage, are not uncommon. Based on our experience and the literature review, we suggest certain clinical, radiological, and echocardiographic markers for suspecting TASVC [Figure 7].

Pre echocardiographic evaluation

Central cyanosis with a nearly normal cardiac examination should make one suspect TASVC. Although much rarer than pulmonary arteriovenous fistulous connection, anomalous systemic venous drainage, be it partial or complete, is an important differential diagnosis in these patients. ECG is often abnormal showing poor right ventricular forces and sinus node dysfunction. In cases providing the details of the ECG, the finding of an ectopic atrial rhythm[4-6,14,15,18] junctional rhythm,[12] or right ventricular hypoplasia is common.[32]

Chest radiograph may reveal cardiomegaly owing to dilated LA and LV. In patients with hypoplasia of RA, the right heart border is also less prominent. The lung fields

Table 2: Reported examples of totally anomalous systemic venous connection

S. no	Author	Age	Sex	Systemic vein drainage					RV hypoplasia	Cardiac anatomy source of PBF	Rhythm abnormalities	Surgery
				RSCV	LSCV	ICV	CS	HV				
Morphology of atrial appendages not defined												
1	Taussig HB[2]	NA	NA	LA	NA	LA	NA	NA	Present	VSD, Pulm. atresia	NA	NA
2	Taussig HB[2]	NA	NA	LA	NA	LA	NA	NA	NA	NA	NA	NA
3	Miller GA[23]	5 y	F	Absent	LA	LA	LA	NA	NA	ASD	NA	ASD enlargement, venous rerouting
4	Gasul BM[3]	NA	NA	LA	NA	LA	NA	NA	Present	NA	NA	NA
5	Roberts KD[24]	5 y	F	LA	LA	Interrupted	LA	LA	NA	NA	NA	ASD enlargement
6	de Leval[26]	NA	NA	Absent	LA	Interrupted	NA	LA	NA	NA	NA	NA
7	de Leval[26]	NA	NA	LA	LA	LA	NA	LA	NA	NA	NA	NA
8	Krayenbuhl CU[37]	NA	NA	NA	LA	Interrupted	NA	NA	NA	NA		NA
9	Pearl WR[11]	18 y	F	Absent	LA	Interrupted	LA	LA	Absent	ASD	NA	Complete repair
10	Gueron M[4]	15 y	M	LA	Absent	LA	LA	LA	Present	ASD	Ectopic atrial rhythm	ASD enlargement, venous rerouting
11	Viart P[25]	3.5 y	M	Absent	LA	LA	LA	LA	NA	ASD	NA	ASD enlargement, venous rerouting
12	Mappe JB[5]	15 y	F	LA	LA	LA	LA	LA	Present	SVASD	Ectopic atrial rhythm	BDG, atrial septectomy, venous rerouting
13	Martin DP[13]	4 y	M	LA	LA	LA	LA	LA	NA	ASD, VSD	NA	Complete repair
Lateralised atrial appendages usual arrangement												
1	Lazzarin O[7]	15 m	F	LA	Absent	LA	LA	LA	Present	PDA, ASD	LVH	Complete repair
2	Zhang ZW[21]	33 m	F	LA	LA	LA	LA	LA	NA	ASD, VSD	NA	Venous rerouting
3	Devendran V[8]	27 y	M	LA	Absent	LA	LA	LA	Present	SVASD, OSASD	Normal	Complete repair
4	Mishra A[10]	16 m	M	LA	Absent	LA	LA	LA	NA	ASD	NA	Complete repair
5	Vaidyanathan S[15]	9 y	F	LA	Absent	LA	LA	LA	NA	ASD	Ectopic atrial rhythm	Complete repair
6	Gupta SK	13 y	F	LA	LA	LA	LA	LA	Present	ASD	Isorrhythmic AV dissociation	BDG, ASD enlargement
Mirror image arrangement												
1	Moghadam[6]	14 m	M	LA	Absent	Interrupted	LA	LA	Present	ASD, VSD, PDA	Low atrial rhythm	ASD enlargement
Left isomerism												
1	Danielson GK[16]	NA	NA	Absent	LA	Interrupted	NA	NA	NA	NA	NA	Complete repair
2	Johnson TR[17]	11 y	M	Absent	LA	Interrupted	NA	NA	NA	ASD	NA	Complete repair
3	Turkoz R[27]	7 m	M	Absent	LA	Interrupted	Absent	LA	NA	OPASD, VSD	NA	AVSD repair, venous rerouting
4	Khandenahally RS[12]	11 y	F	LA	Absent	Interrupted	LA	LA	NA	ASD	Isorrhythmic AV dissociation	Complete repair
5	Vallath G[14]	9 y	F	Absent	LA	Interrupted	NA	LA	Absent	OPASD	Low atrial rhythm	Complete repair
6	Yildirim V[19]	2 d	M	Absent	LA	Interrupted	LA	LA	NA	ASD	NA	Complete repair
7	Awasthy N[9]	5 y	F	Absent	LA	Interrupted	LA	LA	NA	ASD	NA	Complete repair
8	Awasthy N[9]	5 y	NA	LA	LA	Interrupted	LA	LA	NA	ASD, DORV, VSD, PS	NA	Complete repair
9	Awasthy N[9]	2 y	M	LA	LA	LA	LA	LA	Present	ASD, VSD	NA	BDG, ASD enlargement, PA band
10	Vo AT[22]	7 y	F	LA	LA	Interrupted	LA	LA	Present	ASD, VSD	NA	Complete repair
11	Talwar S[18]	1 y	F	Absent	LA	Interrupted	NA	LA	NA	ASD, PDA	Ectopic atrial rhythm	Complete repair
12	Gupta SK	2.5 y	F	LA	LA	Interrupted	Absent	LA	Present	ASD, VSD, PS	Ectopic atrial rhythm	Not done

ASD: atrial septal defect, AVSD: Atrioventricular septal defect, BDG: Bidirectional Glenn, CS: Coronary sinus, d: Days, DORV: Double outlet right ventricle, F: Female, HV: Hepatic vein, ICV: Inferior caval vein, LA: Left atrium, LSVC: Left superior caval vein, M: Male, NA: Not available, OPASD: Ostium primum atrial septal defect, PA: Pulmonary artery, PDA: Patent ductus arteriosus, PBF: Pulmonary blood flow, PDA: Patent ductus arteriosus, PS: Pulmonary stenosis, RSCV: Right superior caval vein, RV: Right ventricle, SVASD: Sinus venosus atrial septal defect, VSD: Ventricular septal defect, y: Years

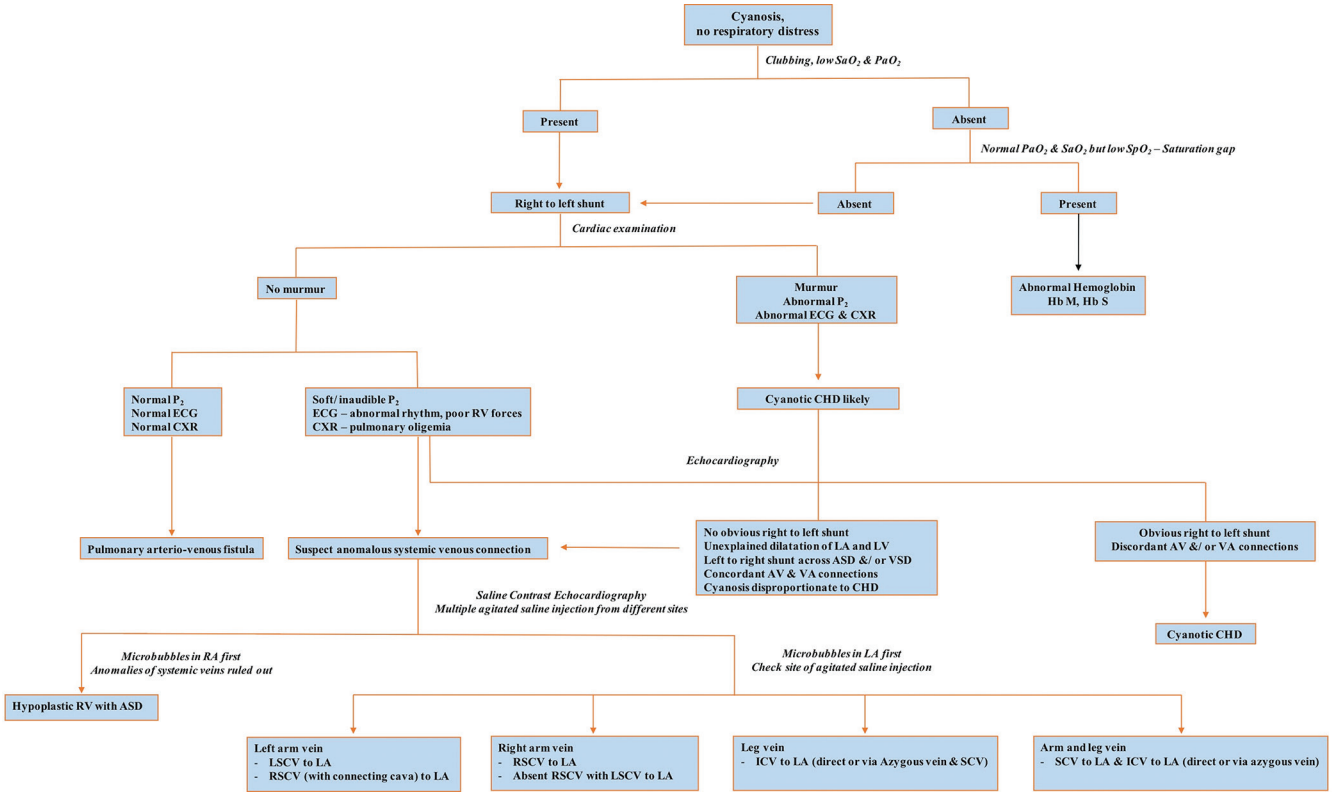

Figure 7: Algorithm for the evaluation of suspected systemic venous anomalies. Saline contrast echocardiography interpretation adapted with permission from Gupta *et al.*[34]

show oligemia although the extent can vary depending on the amount of left-to-right shunt.

RV hypoplasia with an ASD closely resembles TASVC both clinically as well as radiologically. ECG is also quite similar to TASVC with poor RV forces and dominant LV voltages. Hemoglobinopathies, such as methemoglobinemia and sulfhemoglobinemia, wherein cyanosis can exist in the absence of right-to-left shunt, is yet another differential diagnosis. This possibility is ruled out by the absence of clubbing, and normal partial pressures of oxygen and oxygen saturations in the arterial blood gases [Figure 7]. Unlike patients with pulmonary arteriovenous fistulas or those with anomalous systemic venous connection, these patients with abnormal hemoglobin typically show a "saturation gap," having normal oxygen saturations revealed by the blood gas analysis, but reduced saturations by pulse oximetry.[33]

The identification of TASVC is somewhat difficult when it coexists with other cardiac anomalies. Lower than expected saturations, as was seen in our second case, should prompt the clinician to the possibility of systemic venous anomaly. This subtle clue, if missed during the preoperative evaluation, can lead to an incomplete surgical repair.[10,13]

Echocardiographic assessment

Although direct visualization of anomalous venoatrial connections is desirable, it is not always possible. The finding of dilated LA and LV, in association with hypoplasia of right-sided cardiac chambers, should always raise a suspicion for TASVC. Although LV dilation, at first sight, might seem unexplained, it is to be expected since both the systemic and pulmonary venous returns are to the left side of the heart. It is also the case that, in patients with cyanosis, right-to-left shunt is expected at some level, and hence is sought during the echocardiographic interrogation. Demonstration of the right-to-left shunt at atrial level in the presence of hypoplastic RV and dilated LV easily provides clue to the diagnosis of hypoplastic RV with ASD.

When the right-to-left shunt is the consequence of the anomalous systemic venous connection, it may remain undetected. Instead, left-to-right shunt, most commonly across ASD, is always present.[8,9,12,14,15] To reiterate, the presence of the left-to-right shunt at the atrial level appears misplaced in the presence of cyanosis, whereas it is the only means for blood to flow to the lungs and is mandatory for survival in TASVC. It is the identification of these indirect markers that should prompt further evaluation of potential anomalies of systemic venous connection. Once the anomaly is suspected, the diagnosis is not difficult, especially using saline contrast echocardiography. In cyanotic patients with concordant atrioventricular and ventriculoarterial connections and no other abnormality, left-to-right shunt at atrial level is almost diagnostic for TASVC.

How to diagnose totally anomalous systemic venous connection?

Saline contrast echocardiography

Unlike cross-sectional echocardiography with color Doppler, saline contrast echocardiography does not depend on direct visualization. Instead, its diagnostic potential lies in the path followed by the microbubbles after an injection of agitated saline.[34-36] A carefully performed and interpreted saline contrast echocardiogram allows demonstration of hidden right-to-left shunt and therefore, should be performed in all children with unexplained or disproportionate cyanosis. Even when right-to-left shunt is not visible on routine echocardiography, an appearance of microbubbles first in RA strongly suggest hypoplasia of RV as the cause of cyanosis. The diagnosis of RV hypoplsia, however, should not be based on the single injection of agitated saline. Variable degree of RV hypoplasia may be present with partial anomalous systemic venous connection, and therefore, it is crucial to exclude partial anomalous systemic venous connection by repeating agitated saline injection from both arms and leg [Figure 7].

Saline contrast echocardiogram also permits direct identification of anomalies of systemic venous drainage [Figure 7]. The appearance of microbubbles in LA before RA following injection from veins in the arm and leg is almost diagnostic of anomalous drainage of the SCV and ICV, respectively. The drainage of the left SCV, if present, can easily be demonstrated by injection into a vein in the left arm.[34,35] The presence of anomalous drainage of SCV should itself prompt a search for possible anomalous drainage of ICV.[10] The site of venous injection, therefore, is extremely important while performing saline contrast echocardiography. An injection in the right arm may miss anomalous drainage of a LSCV to LA while anomalous drainage of ICV may remain undetected even after injecting in veins in both the arms. It follows that multiple injections in veins in both arms and leg is mandatory for a complete interrogation.[34]

Computed tomographic angiography or catheter angiography?

The diagnosis of TASVC requires unequivocal demonstration of the anomalous drainage not only of both caval veins but also of the coronary sinus and the hepatic veins. This can easily be achieved using computed tomographic angiography. Cardiac catheterisation, however, also permits estimation of PA pressures, an advantage when consideration is being given to the bidirectional Glenn anastomosis, as was the situation in our first patient.

How to treat totally anomalous systemic venous connection?

The surgical approach will be influenced by associated cardiac malformations, but will largely depend on the size of RV when found as an isolated anomaly. A large left-to-right shunt and an adequately sized RV cavity will permit complete repair. In patients with suboptimal RV cavities options are limited to wide atrial septectomy, with or without venous rerouting. Should the RV cavity be deemed too small, as in our first patient, then an additional bidirectional Glenn anastomosis can be performed.

CONCLUSION

We conclude that a careful stepwise evaluation, as shown in Figure 7, will provide the complete diagnosis of TASVC, even when observed in the hemodynamically comparable variant as found in the setting of isomeric atrial appendages. The evaluation will also indicate the most appropriate surgical treatment.

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Conflicts of interest

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REFERENCES

1. Foker JE, Berry J, Setty SP, Harvey BA, Rivard AL, Groot AC, *et al.* Growth and function of hypoplastic right ventricles and tricuspid valves in infants with pulmonary atresia and intact ventricular septum. Prog Pediatr Cardiol 2010;29:49-54.
2. Taussig HB. Congenital Malformations of the Heart. 2nd ed., Vol. 2. Cambridge: Harvard University Press; 1960. p. 953.
3. Gasul BM, Arcilla RA, Lev M. Heart Diseases in Children. Philadelphia: J.B. Lippincott Co.; 1966. p. 514.
4. Gueron M, Hirsh M, Borman J. Total anomalous systemic venous drainage into the left atrium. Report of a successful surgical correction. J Thorac Cardiovasc Surg 1969;58:570-4.
5. Mappe JB, Ludgerio D. A case of TASVC to LA. Philipp Heart Cent J 2002;9:60-9.
6. Moghadam MY, Omrani G, Zanjani KS, Tabae AS. Total anomalous systeic venous return to right sided atrium with left atrium morphology: A case report. Iran Heart J 2004;5:61-4.
7. Lazzarin O, Rossi RD. Total anomalous systemic venous drainage. A case report. Surgical considerations. Rev Argent Cardiol 2009;77:5-6.
8. Devendran V, Varghese R, Gudeboyana K, Jessudian V. Isolated total anomalous systemic venous drainage in an adult: Case report. Pediatr Cardiol 2013;34:1918-21.
9. Awasthy N, Radhakrishnan S, Kaushal S, Sharma R. Total anomalous systemic venous drainage to the left atrium: An entity reviewed and investigated. Ann Pediatr Cardiol 2014;7:98-102.
10. Mishra A, Sharma P, Shah R, Oswal N, Rana Y. Total

anomalous systemic and pulmonary venous connection. Asian Cardiovasc Thorac Ann 2013;23:61-3.

11. Pearl WR, Spicer MJ. Total anomalous systemic venous return. South Med J 1980;73:259-61.
12. Khandenahally RS, Deora S, Math RS. Total anomalous systemic venous drainage in left heterotaxy syndrome. Cardiol Young 2013;23:284-6.
13. Martin DP, Phillips A, Tobias JD. An unusual case of intraoperative hypoxemia in a four-year-old boy. Pediatr Anesth Crit Care J 2013;1:93-7.
14. Vallath G, Gajjar T, Desai N. Total anomalous systemic with partial anomalous pulmonary venous connections. Asian Cardiovasc Thorac Ann 2013;21:720-3.
15. Vaidyanathan S, Kothandam S, Kumar R, Pradhan PM, Agarwal R. Unusual presentation of total anomalous systemic venous connection. Asian Cardiovasc Thorac Ann 2016. pii: 0218492316644355.
16. Danielson GK, McMullan MH, Kinsley RH, DuShane JW. Successful repair of complete atrioventricular canal associated with dextroversion, common atrium, and total anomalous systemic venous return. J Thorac Cardiovasc Surg 1973;66:817-22.
17. Johnson TR, Schamberger MS, Brown JW, Girod DA. Resolution of acquired pulmonary arteriovenous malformations in a patient with total anomalous systemic venous return. Pediatr Cardiol 2002;23:210-2.
18. Talwar S, Ramakrishnan P, Anderson RH, Choudhary SK, Makhija N, Kumar S, *et al.* Left isomerism of the atrial appendages with sinus venosus defect and anomalous systemic venous drainage. World J Pediatr Congenit Heart Surg 2016;7:661-4.
19. Yildirim A, Kosger P, Ozdemir G, Ucar B, Kilic Z. Total anomalous systemic venous drainage with heterotaxia syndrome: A rare case. Case Rep Cardiol 2014;2014: article ID: 392841.
20. Uemura H, Ho SY, Devine WA, Kilpatrick LL, Anderson RH. Atrial appendages and venoatrial connections in hearts from patients with visceral heterotaxy. Ann Thorac Surg 1995;60:561-9.
21. Zhang ZW, Duan QJ, Gao Z, Ru W, Ying LY. Total anomalous systemic venous drainage to the left atrium. Ann Thorac Surg 2009;87:1599-601.
22. Vo AT, Cao KD, Le KM, Nguyen DH. Left isomerism syndrome with total anomalous systemic connection. Asian Cardiovasc Thorac Ann 2017;25:58-61.
23. Miller GA, Ongley PA, Rastelli GC, Kirklin JW. Surgical correction of total anomalous systemic venous connection: Report of case. Mayo Clin Proc 1965;40:532-8.
24. Roberts KD, Edwards JM, Astley R. Surgical correction of total anomalous systemic venous drainage. J Thorac Cardiovasc Surg 1972;64:803-10.
25. Viart P, Le Clerc JL, Primo G, Polis O. Total anomalous systemic venous drainage. Am J Dis Child 1977;131:195-8.
26. de Leval MR, Ritter DG, McGoon DC, Danielson GK. Anomalous systemic venous connection. Surgical considerations. Mayo Clin Proc 1975;50:599-610.
27. Turkoz R, Ayabakan C, Vuran C, Omay O. Intraatrial baffle repair of anomalous systemic venous return without hepatic venous drainage in heterotaxy syndrome. Pediatr Cardiol 2010;31:865-7.
28. Kadletz M, Black MD, Smallhorn J, Freedom RM, Van Praagh S. Total anomalous systemic venous drainage to the coronary sinus in association with hypoplastic left heart disease: More than a mere coincidence. J Thorac Cardiovasc Surg 1997;114:282-4.
29. Barrea C, Biard JM, Hutchings G, Bernard P. Prenatal diagnosis of isolated total anomalous systemic venous return to the coronary sinus. Ultrasound Obstet Gynecol 2010;35:117-9.
30. Agarwal A, Agrawal N, Patra S, Manjunath CN. Total anomalous systemic venous drainage to coronary sinus. BMJ Case Rep 2014;2014. pii: Bcr2013201493.
31. Tharakan JA. Admixture lesions in congenital cyanotic heart disease. Ann Pediatr Cardiol 2011;4:53-9.
32. Furuse A, Mizuno A, Sato F, Hasegawa T, Kotoda T. Coronary sinus rhythm in anomalous systemic venous connection. Jpn Heart J 1968;9:200-7.
33. Gupta SK. Clinical approach to a neonate with cyanosis. Indian J Pediatr 2015;82:1050-60.
34. Gupta SK, Shetkar SS, Ramakrishnan S, Kothari SS. Saline contrast echocardiography in the era of multimodality imaging – Importance of "bubbling it right". Echocardiography 2015;32:1707-19.
35. Shetkar SS, Gupta SK, Gulati GS, Juneja R. Right superior vena cava to left atrium: Importance of "bubbling it right". Echocardiography 2014;31:E161-2.
36. Gupta SK, Gupta A. Saline contrast echocardiography for the detection of anomalous origin of pulmonary artery from aorta. Echocardiography 2017;34:145-6.
37. Krayenbuhl CU, Lincoln JC. Total anomalous systemic venous connection, common atrium and partial atrioventricular canal. A case report of successful surgical correction. J Thorac Cardiovasc Surg 1977;73:686-9.