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Interatrial septal aneurysm associated with patent foramen ovale in a dog – case report

[*Aneurisma de septo interatrial associado a forame oval patente em cão – relato de caso*]

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ABSTRACT

Atrial septal aneurysm (ASA) is a rare congenital deformity of variable clinical relevance, often reported in association with patent foramen ovale (PFO). Transthoracic Doppler echocardiography (TTE) is the first choice for diagnosis, but complementary techniques, such as microbubble contrast, should be used. Despite its importance, in Veterinary Medicine, there is little information related to the subject, and the present study is the second report of this condition in dogs. The objective was to report a case of ASA type IV LR associated with PFO in a Shar Pei bitch, diagnosed by a combined approach of transthoracic echocardiography backed by agitated saline solution (microbubbles). During clinical care, the owners reported episodes of seizures as their main complaint. Echocardiographic examination revealed a type 4 LR atrial septal aneurysm and left ventricular systolic dysfunction. The use of microbubble contrast showed right-to-left shunt, confirming PFO. The recommended treatment was medication. It was concluded that the rarity of ASA in dogs may be due to incomplete diagnoses and the transthoracic echocardiographic examination allows its analysis and classification. Furthermore, ASA can be found in animals with or without evidence of heart disease and it should be investigated in patients with neurological alterations.

Keywords: cardiology, echocardiography, congenital heart disease, small animals

RESUMO

O aneurisma do septo atrial (ASA) é uma rara deformidade congênita, de relevância clínica variável, frequentemente relatado em associação a forame oval patente (PFO). O ecodopplercardiograma transtorácico (TTE) é a primeira escolha para o diagnóstico, mas técnicas complementares, como o contraste por microbolhas, devem ser utilizadas. Apesar da importância, em medicina veterinária existe uma carência de informações relacionadas ao tema, sendo esse o segundo relato dessa condição em cão. Objetivou-se relatar um caso de ASA tipo IV LR, associado a PFO, em uma cadela Shar Pei, diagnosticado por uma abordagem combinada por ecodopplercardiograma transtorácico e costrastado com solução salina agitada (microbolhas). Ao atendimento clínico, os proprietários relataram, como queixa principal, episódios de crises convulsivas. O exame ecocardiográfico revelou aneurisma de septo atrial tipo 4 LR e disfunção sistólica em ventrículo esquerdo. A utilização de contraste por microbolhas constatou shunt direita-esquerda, confirmando PFO. O tratamento recomendado foi medicamentoso. Concluiu-se que a raridade do ASA em cães pode ser devido a diagnósticos incompletos, e o exame ecocardiográfico transtorácico permite sua análise e classificação. Ainda, ASA pode ser encontrado em animais com ou sem evidências de cardiopatia e sua investigação deve ser feita em pacientes com alterações neurológicas.

Palavras-chave: cardiologia, ecocardiografia, cardiopatia congênita, pequenos animais

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INTRODUCTION

Interatrial septal aneurysm (ASA) is a rare congenital deformity located in the interatrial septum, usually at the level of the fossa ovale, characterized by redundancy or saccular deformation, which projects into the right or left atrium, or both (Lin *et al*., 2020).
Its clinical relevance is quite variable, and, in some cases, it has no important repercussion, being just an incidental finding in routine echocardiographic examination. However, this condition is often reported in association with other congenital or acquired heart diseases, such as mitral and tricuspid regurgitation. Furthermore, it can act as an arrhythmogenic focus. In addition, arterial embolism is another possible complication, due to the tendency to cause blood stasis within the left atrium, predisposing to thrombus formation and/or pulmonary embolism (Mügge *et al*., 1995). The most common abnormality associated with ASA is patent foramen ovale (PFO), which can lead to significant blood pressure changes, requiring therapeutic intervention (Cabanes *et al*., 1993).

Transthoracic echocardiography (TTE) with Doppler is the first choice for ASA diagnosis but for PFO detection this technique is not always possible. In these cases, transesophageal echocardiography (TEE) or the use of microbubble contrast should be used to confirm PFO (Mirode *et al*., 1993). Through these tests, it is also possible to classify ASA according to the incursion into the atria, according to the most current classification criteria, as follows: types 1R (bulging only to the right atrium), type 2L (bulging only to the left atrium), type 3RL (bulging to both atria, but greater to the right), type 4LR (bulging to both atria, but greater to the left) and type 5 (bidirectional bulging equidistant to both atria) (Olivares-Reyes *et al*., 1997).

Several cases of ASA associated with other cardiovascular conditions have been described for humans (Sun *et al*., 2018; Qin *et al*., 2019; Lin *et al.*, 2020) and there are larger, multicenter studies involving many patients (Mügge *et al*., 1995; Fang *et al*., 2021; Atak *et al*., 2019). However, in Veterinary Medicine, this condition is not well identified, with a single report in the literature of an ASA mimicking cor triatriatum in a Cavalier King Charles Spaniel dog (Çolakoğlu *et al*., 2016).

Thus, for dogs, there is a notorious lack of information related to the subject, making additional studies and the publication of new cases necessary, to emphasize the importance of ASA, as well as its correct identification, investigation and classification, in order to identify possible related clinical repercussions, as well as direct treatment in canine patients.

This study aimed to report a case of a type IV LR interatrial septal aneurysm associated with a patent foramen ovale in a Shar Pei dog, diagnosed by a combined approach of transthoracic echocardiography backed by microbubbles.

CASUISTRY

A 4-year-old female dog of the Shar Pei breed, weighing 12.7 kg, was treated at the University Veterinary Hospital at the Federal University of Piauí - HVU/UFPI, in an elective consultation.

In the anamnesis, the tutor reported as the main complaint that the animal had had three episodes of seizures, always after intense stress (fights with other dogs) in the three months before the consultation. After the sudden onset, the seizures lasted an average of 20 seconds and the animal returned dyspneic and lethargic. The convulsions returned after a few minutes and the interval between them became longer with time, but they only ceased definitively when the animal was referred to the emergency department for administration of anxiolytic intravenous anticonvulsants (Diazepan, 6,35mg).

The owner claims that the dog showed normal behavior, that she ate good quality food and was offered water ad libitum. He denies easy tiredness, syncope, cough, vomiting and a history of parasitic and infectious diseases. The animal was vaccinated and had recently tested negative for leishmaniasis.

On physical examination, the animal was conscious, agitated and normohydrated. Heart rate was measured at 170 beats per minute (bpm), respiratory rate at 35 and rectal temperature at 38 ^{o} C. Ocular and oral mucosa were normal-stained and capillary refill time was

approximately 1 second. The palpable lymph nodes were of normal size and consistency for the patient, and it did not have any noticeable neurological and locomotor deficits.

Pulmonary auscultation showed aerated lung fields, with no crackles. Cardiac auscultation revealed a regular, tachycardic rhythm, absence of murmur in heart valves and synchronous beats with the pulse in the femoral artery. An echocardiogram, electrocardiogram, and abdominal and pelvic ultrasound were requested.

The ultrasound report presented a result within normal parameters. The electrocardiogram showed sinus tachycardia and increased P wave duration, suggesting left atrial overload. In addition, there was a T wave of increased amplitude and peaked morphology, suggesting disturbance of ventricular repolarization, suggestive of myocardial hypoxia or electrolyte imbalance (Fig. 1).

The transthoracic echocardiogram revealed laminar flow in the mitral, tricuspid, aortic and pulmonary valves, with no evidence that could suggest valvular changes. The left ventricular (LV) ejection fraction was estimated at 53% using the Teichholz method and shortening fraction at 26%. The longitudinal global strain was -17.6% (Fig. 2). As a result, LV systolic dysfunction was diagnosed.

An interatrial septal aneurysm was also observed, characterized by a deformity located in this region, at the level of the oval fossa that projected to both atria, with an incursion of 10 mm from the septal plane to the left atrium, 5.2 mm to the right atrium, and a base width of 1.09 cm, being classified as ASA type 4 LR (Fig. 3). Color Doppler did not reveal a shunt, which could characterize PFO by this technique, due to the difficulty in obtaining the echocardiographic windows. Microbubble contrast was recommended for confirmation.

For the definitive PFO diagnosis, the following dose was applied with agitated saline solution: 8mL saline solution, 1mL of 50% glucose solution and 0.5mL air, mixed (intensively) thoroughly by passing through two syringes and rapid administration, using a three-way stopcock, simultaneously with the echocardiogram (Feigenbaum *et al*., 2005). The passage of contrast was observed from the right atrium to the left atrium, confirming a right-left shunt through a patent foramen ovale (Fig. 4).

The recommended treatment was (drug) medication and aimed at preventing thrombotic events through antiplatelet and anticoagulant therapy, as well as treatment of heart failure due to reduced ejection fraction. The following drugs were prescribed: clopidogrel, at a dose of 0.5 mg/kg, orally, once a day, for continuous use; benazepril, at a dose of 0.5mg/kg, orally, for 12-12 hours, for continuous use; pimobendan, at a dose of 0.25mg/kg, orally, 12-12 hours, for continuous use; spironolactone, at a dose of 2mg/kg, orally, once a day, for continuous use.

Surgical or percutaneous closure of the defect was not initially recommended, but periodic cardiological follow-up was recommended to assess the progression of the disease. Thus, the prognosis was considered good.

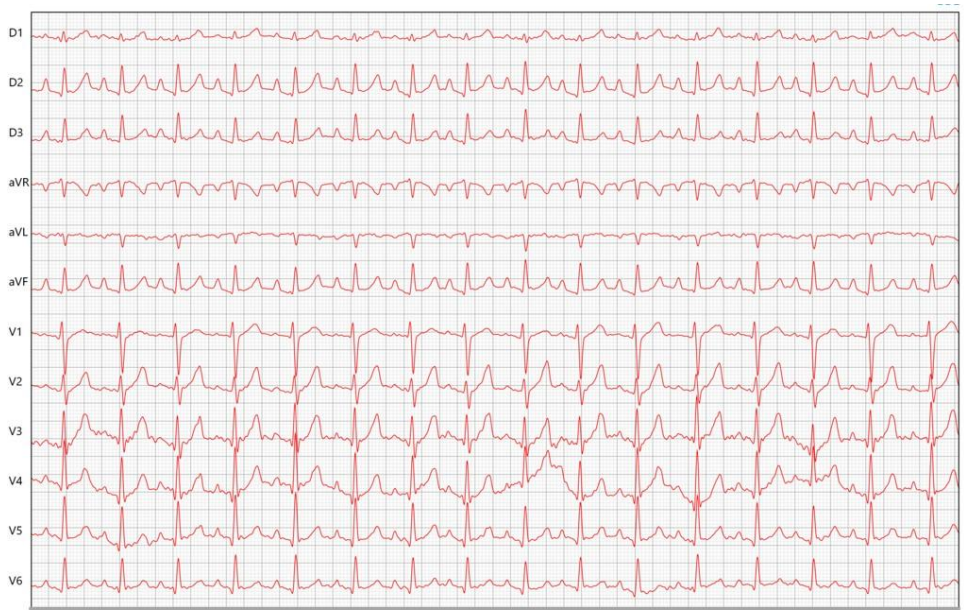

Figure 1. 12-lead electrocardiographic tracing showing sinus tachycardia (170bpm), increased P wave duration (50ms) and T wave showing amplitude greater than 25% of the QRS complex amplitude, in lead DII. Speed 50mm/s, 10mm/mV, (N).

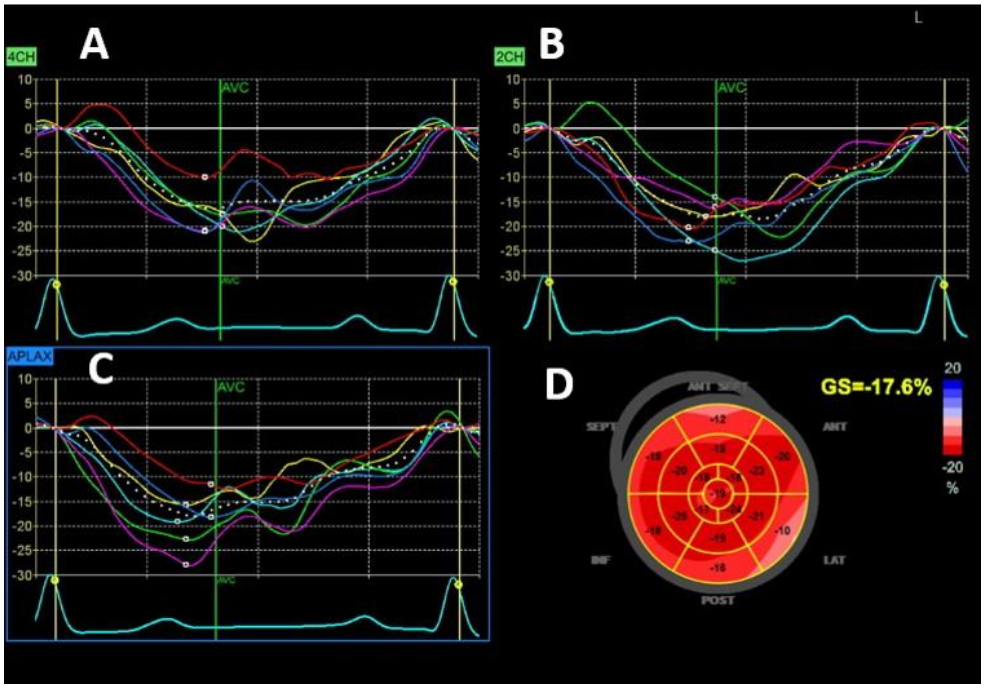

Figure 2. Myocardial deformation curves obtained by tracking all analyzed segments (A, B and C). Note the *bulls eye* showing peak systolic values for each of the 17 analyzed segments, used to calculate the global mean (D).

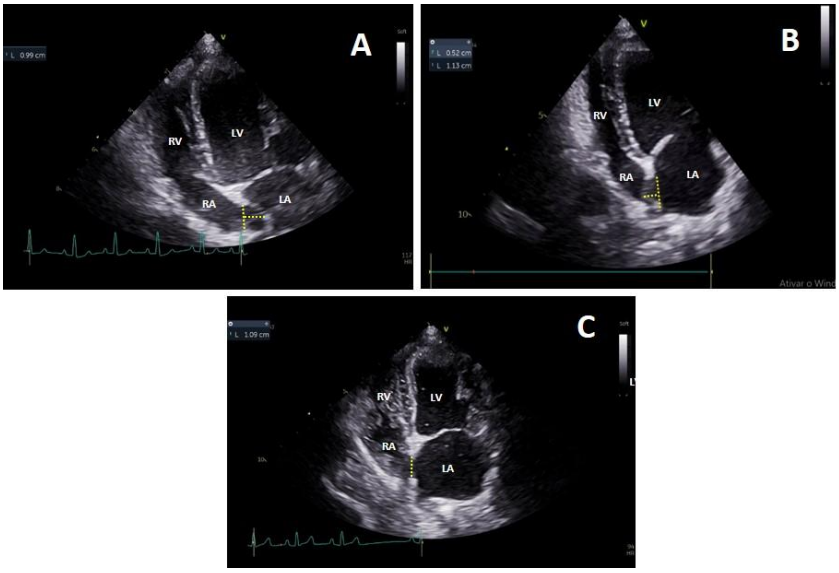

Figure 3. Echocardiographic image of a type 4 LR atrial septal aneurysm in 4-chamber apical view showing a 10mm incursion from the septal plane to the left atrium (A), 5mm to the right atrium (B), and a base width of 1.09cm (C).

LV: left ventricle; RV: right ventricle; LA: left atrium; RA: right atrium

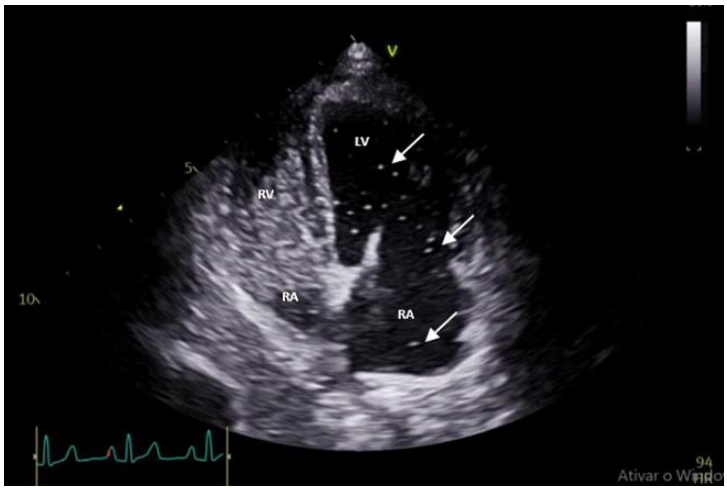

Figure 4. Echocardiographic image obtained in apical four-chamber view, after applying agitated saline solution. Note the contrast-filled right atrium and ventricle and the presence of hyperechogenic points in the left atrium and ventricle (arrows), characterizing the passage of contrast due to a right-left shunt through a patent foramen ovale.

LV: left ventricle; RV: right ventricle; LA: left atrium; AR: right atrium

DISCUSSION

To date, this is the second report of interatrial septal aneurysm associated with patent foramen ovale reported in Veterinary Medicine. A single paper reported an ASA mimicking cor triatriatum in a Cavalier King Charles Spaniel dog with congestive heart failure (CHF) due to association with major mitral and tricuspid regurgitation (Çolakoğlu *et al*., 2016). Thus, most of this discussion will be based on studies in human beings.

In our case, the animal had no clinical signs or echocardiographic findings that could suggest CHF, or clinical signs directly indicative of ASA. According to Mügge *et al*. (1995) ASA is a cardiac abnormality of uncertain clinical significance. It has been reported as an unexpected finding during autopsies in humans, but it is also occasionally diagnosed by echocardiography in living patients with or without clinical symptoms (Silver and Dorsey, 1978; Gondi and Nanda, 1981; Atak *et al*., 2019).

The formation of ASA may occur primarily, by a congenital alteration involving the fossa ovalis region or the entire septum, or it may be secondary to differences in interatrial pressure (Mügge *et al*., 19955). In the latter, it usually occurs in more advanced stages of heart disease with advanced remodeling, where the atrial chambers are subject to intense volume overload, as in degenerative valve diseases (Ilicetus *et al*., 1994). According to this information, given the young age of the animal and absence of significant pressure changes and CHF, it can be inferred that it was a congenital alteration, incidentally reported, similarly to that found in humans, where it is rare and has very low prevalence in adults (Mügge *et al*., 19955).

In the present case, the transthoracic echocardiogram was sufficient for the diagnosis and classification of the heart disease. However, the atrial septum defect was only visible after using contrast with agitated saline solution, as the windows obtained did not allow the correct angulation and detection by means of color Doppler. Corroborating these findings, (Woods and Patel (2019) demonstrated that contrast echocardiography is more sensitive than color Doppler flow imaging for the detection of interatrial shunt, being one of the techniques of choice for confirmation.

ETT echo is considered the main first-line imaging technique for ASA detection, but it requires a good acoustic window. In cases where good transducer alignment is not possible, transesophageal echo (TEE) can provide more detailed morphological information and increase the sensitivity of ASA identification. However, it is important to emphasize that there is no consensus in the literature or a technique that is considered the gold standard (Mügge *et al*., 1995). Despite the greater accuracy of TEE, in the confirmation of ASA by TTE, with shunt study by contrast with microbubbles, both have practically similar sensitivity (Pearson *et al*., 1991).

The cut-off point between a slightly redundant atrial septum and an ASA is somewhat arbitrary. However, the results found in this study are confirmed by the criteria of Silver and Dorsey (1978), reported for a study with autopsies in humans, where a protrusion of the aneurysm greater than 10 mm beyond the plane of the atrial septum into the atrium was defined, right or left. In addition, our findings are confirmed by the American Society of Echocardiography's Guidelines for the Echocardiographic Assessment of Atrial Septal and Patent Foramen Ovale Defects, which considers the septum to be aneurysmal when it has an excursion greater than 10 mm into the left or right atrium or sum of total excursion for both atria greater than 10 mm, with a base width greater than or equal to 15 mm, similar to that found in our study (Silvestry *et al*., 2015). It is important to note, however, that it was a 12.7 kg animal, that is, with cardiac dimensions significantly smaller than those of an adult person, and yet it met the ASA criteria.

According to the new classification for atrial septal aneurysm for adults, the ASA found was classified as type 4LR, due to the incursion to both atria, that was greater to the left. According to Olivares-Reye *et al*. (1997), this may be an isolated finding or may be associated with other congenital or acquired heart diseases. According to the same author, of the 57 patients diagnosed with ASA in this classification, other associated cardiovascular changes were also reported, such as cerebrovascular events, valvular prolapses (mitral and tricuspid), and the majority, 19 patients, had PFO, the latter also being observed in our study. Among these changes, PFO is most common and is present in more than 20% - 25% of adults with ASA, being commonly reported for humans (Hagen *et al*., 1984) and it is also reported in the only case reported for dogs (Çolakoğlu *et al*., 2016**).**

Arrhythmic events are also frequently reported for people with ASA, particularly supraventricular arrhythmias such as atrial fibrillation (AF), atrial flutter, paroxysmal supraventricular tachycardia, and atrial

extrasystoles (Yetkin *et al*., 2016; Atak *et al*., 2019). Despite this, none of these were detected in the case in question, only a sinus tachycardia that was associated with stress from restraint (Tilley, 1992). Similarly, Çolakoğlu *et al*. (2016) reported only an increase in heart rate in the dog with ASA in their study but as a compensatory response to CHF.

ASA is also frequently associated with transient ischemic attacks and strokes, but the nature of this relationship is not well understood (Hanley *et al*., 1985; Giannopoulos, *et al*., 2014). Embolic events have been attributed to thrombus formation within or at the base of the aneurysmal sac (Silver and Dorsey, 1978; Ker, 2017), however, in our case, no thrombi were found in this region, nor in any cardiac chambers or abdominal vessels. However, the possibility of an association between patent foramen ovale and a paradoxical embolus via the right-left shunt has been suggested, which may be related to the reported seizure neurological events for the animal (Grosgogeat *et al*., 1973; Giannopoulos, *et al*., 2014).

In the study by Zabalgoitia-Reyes *et al*. (1990), five of the 20 patients with ASA who had cerebral ischemic events had right-to-left interatrial shunt, as was found in our case. In 2 of these patients, additional underlying heart defects were found (one with AF and one with carotid artery disease) that could explain the neurologic symptoms. In the other 3 patients, an embolic origin was suggested based on clinical presentation, CT scan, or arteriography. An additional patient with PFO and right atrium and right ventricle dilatation had a history of unexplained syncope. No patient had echocardiographic evidence of thrombus in any chamber, including the aneurysmal sac.

Despite this, none of these alterations mentioned were diagnosed in our patient, however, cardiac function was impaired, with reduced ejection and shortening fractions, as well as a global longitudinal strain of -17.6%. Such reduction can be explained by several factors, however, in this case, it would most likely be due to congenital heart disease that, from an anatomo-functional point of view, may potentially lead to ventricular diastolic overloads associated with marked ventricular hypocontractility, resulting in the manifestations observed (Afiune Neto *et al*., 2006).

Thus, the neurological clinical sign of seizure presented by the animal may be related to the previously suggested association between ASA and transient cerebral ischemic events resulting from heart diseases that could lead to the presented condition. However, the evidence is not conclusive, despite their frequent association. Additional neurologic CT studies could provide additional information and/or confirm the hypothesis (Terasaki *et al*., 1997).

Due to the presence of associated neurological events, as well as a patent foramen ovale, the recommended therapeutic option was considered adequate. Antiplatelet and anticoagulant therapy was indicated due to the risk of cerebral events related to thrombus ischemia, common in interatrial septal abnormalities. As the findings found were not related to significant hemodynamic repercussions, including short- and medium-term evolutionary problems, shunt closure through the percutaneous approach was not indicated at this time. Cardiological evaluation with recommended periodic echocardiograms is important for monitoring the animal's general health status and assessing the severity of the aneurysm (Ponikowski *et al*., 2016; Sousa *et al*., 2019; Keene *et al*., 2019).

CONCLUSION

Interatrial septal aneurysm is rare in dogs, perhaps for reasons inherent to the species itself or to incomplete diagnoses. The transthoracic echocardiographic examination was of fundamental importance for the diagnosis of ASA and allowed its analysis and classification. The use of microbubble contrast enabled PFO detection and proved to be a sensitive and easy-to-perform technique. Although little reported in veterinary medicine, ASA can be found in animals with or without evidence of heart disease and may be related to neurological problems. It is important to investigate ASA in patients with clinical neurological signs to confirm or rule out possible relationships. In these patients, whenever possible, further investigation by computed tomography or arteriography should be carried out.

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