

# Abdominal Coarctation and Alagille Syndrome

Swee Chye Quek, MBBS, MMED(PAED), DCH(Lond), FACC, FAMS\*;  
Lenny Tan, MBBS, FRCP, FRACR, FAMS‡; Swee Tian Quek, MBBS, FRCP‡;  
William Yip, MBBS, MD, FRCP, FAMS\*; Marion Aw, MBBS, MMED(PAED), MRCP\*; and  
Seng Hock Quak, MBBS, MD, FRCP(Glasg), FRCPCH\*

**ABSTRACT.** Structural cardiac defects such as peripheral pulmonary stenosis are well-described in Alagille syndrome (AS), which is transmitted in an autosomal dominant inheritance. The genetic defect, with incomplete penetrance and variable expression, is localized to the short arm of chromosome 20. Abdominal coarctation is an uncommon congenital anomaly, with a spectrum of symptoms that may range from hypertension, intermittent claudication to abdominal pain. The association of abdominal coarctation with AS is rarely described. We report such a patient who also had aberrations of the visceral vascular supply involving the celiac, splenic, and superior mesenteric arteries. The indications to treat the coarctation, and in the context of a patient with AS, in whom liver transplantation may be contemplated at some stage, merit discussion. *Pediatrics* 2000;106(1). URL: <http://www.pediatrics.org/cgi/content/full/106/1/e9>; *Alagille syndrome, abdominal coarctation.*

ABBREVIATION. AS, Alagille syndrome.

Alagille syndrome (AS)<sup>1,2</sup> is a genetic disorder<sup>3</sup> inherited in an autosomal dominant fashion. It is characterized by triangular facies<sup>4</sup> and abnormalities of the liver,<sup>5</sup> eyes,<sup>6</sup> heart,<sup>7</sup> and spine.<sup>1,2</sup> Cholestasis is commonly present attributable to a paucity of intrahepatic bile ducts. The spinal defect usually comprises a butterfly-shaped vertebra as a result of fusion of the vertebral arches. In the eyes, posterior embryotoxon is a known complication. The most commonly associated cardiac abnormality is peripheral pulmonary artery stenosis,<sup>8</sup> although few reports of tetralogy of Fallot and ventricular septal defects have been described.<sup>9</sup>

Abdominal aortic coarctation<sup>10-12</sup> is an uncommon anomaly. It may be complicated by varying degrees of involvement of the visceral vasculature and is a cause of hypertension in the young. The severity and extent of this narrowing primarily accounts for the presence of symptoms, such as hypertension, intermittent claudication, or abdominal pain. We describe

the unusual association of abdominal coarctation in a child with AS.

## CASE REPORT

An 8-year-old Indian girl was diagnosed with AS. She presented with cholestatic jaundice at 2 months of life, and liver biopsy showed paucity of intrahepatic bile ducts. She thrived well and was symptom-free except for pruritus. She had the characteristic triangular facies described. Cardiac examination revealed normal upper limb pulses but weak lower limb pulses. Her blood pressure was 111/54 mm Hg (right upper limb), 110/61 mm Hg (left upper limb), 90/60 mm Hg (right lower limb), and 100/65 mm Hg (left lower limb). Auscultatory findings included a grade 3/6 ejection systolic murmur at the infraclavicular region consistent with branch pulmonary artery stenosis that is commonly associated with this condition. Her erythrocyte sedimentation rate and C-reactive protein were not elevated.

Echocardiography demonstrated normal cardiac connections. Bilateral hypoplastic branch pulmonary arteries were noted. Doppler interrogation confirmed a gradient of 31 mm Hg and 24 mm Hg along the left and right pulmonary arteries, respectively. The aortic arch was right-sided, but no abnormality of the proximal descending aorta was noted on echocardiography. However, pulsation of the abdominal descending aorta was noted to be diminished.

Cardiac catheterization was performed to delineate angiographically the abdominal aorta based on the clinical suspicion of abdominal aortic coarctation and to document the right heart hemodynamics. The right ventricular systolic pressure was mildly elevated at 35/4 mm Hg and is a reflection of mild bilateral branch pulmonary artery stenosis.

Most of the abnormal findings were demonstrated in the abdominal aortogram. The upper abdominal aorta was within normal limits, but its lumen narrowed significantly at the level below the origin of the renal arteries (Fig 1). Both renal arteries were catheterized, and hand injections indicated good flow in these. The celiac axis was also entered, which continued on to become the splenic artery. The superior mesenteric artery gave off the hepatic artery, the gastric artery, as well as the right gastroepiploic artery (Fig 2). Although the superior mesenteric artery seemed to fill quite normally, stenosis at its origin is implied from the presence of a large collateral vessel in the mesentery (Fig 3). Immediately below the origin of the renal arteries, there was diffuse narrowing of the abdominal aorta.

## DISCUSSION

AS is an autosomal dominantly transmitted genetic condition with a high mutation rate, incomplete penetrance, and variable expression.<sup>13</sup> The genetic defect has been localized to the short arm of chromosome 20.<sup>14-17</sup>

This patient is the only 1 in our series of AS to have an associated abdominal coarctation. Literature search confirms that this is indeed a rare association, with only 1 described by Shefler et al<sup>18</sup> as is thoracic coarctation.<sup>19</sup> In the patient of Shefler et al, there were symptoms of abdominal pain and intermittent

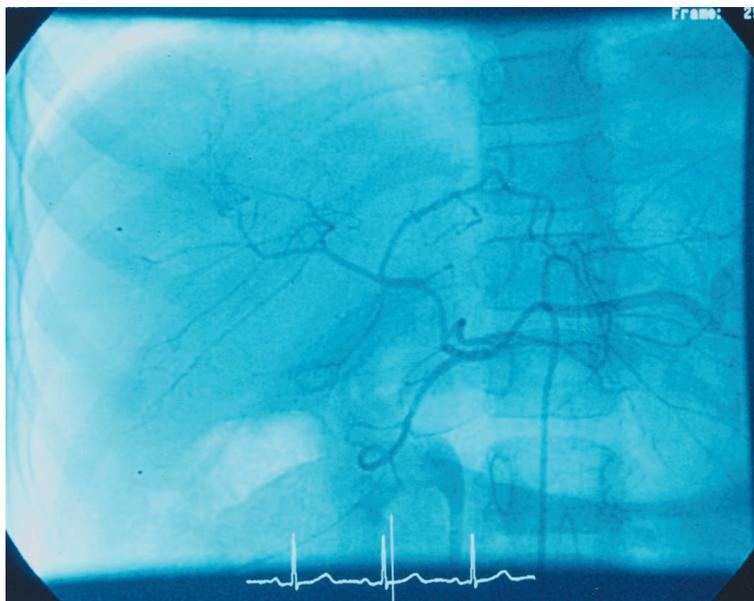
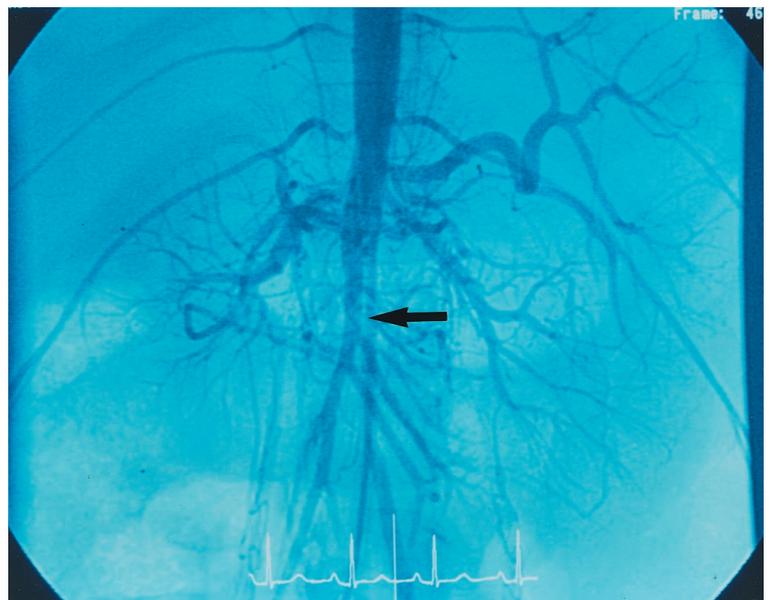
From the \*Department of Pediatrics, Division of Cardiology, National University of Singapore, and ‡Department of Diagnostic Imaging, National University Hospital, Singapore, Singapore.

Received for publication Nov 23, 1999; accepted Feb 18, 2000.

Reprint requests to (S.C.Q.) Department of Pediatrics, National University of Singapore, 5 Lower Kent Ridge Rd, Singapore, 119074, Singapore. E-mail: [paqsc@nus.edu.sg](mailto:paqsc@nus.edu.sg)

PEDIATRICS (ISSN 0031 4005). Copyright © 2000 by the American Academy of Pediatrics.

**Fig 1.** Descending aortogram showing significantly decreased caliber of the abdominal aorta beyond the origin of the renal arteries. The gradient obtained on pullback between the segment was 30 mm Hg.



**Fig 2.** The superior mesenteric artery giving off the hepatic artery, gastric artery, and gastroepiploic artery.

claudication. These necessitated surgery and the symptoms were relieved after surgical correction. Our patient differed in that the aortic narrowing began after the origin of the renal arteries and hypertension, which is usually a significant problem in these patients.

There was a difference between the volume of the upper limb pulses compared with the lower limbs clinically. The result of the pull-back pressure on catheter study was 30 mm Hg. The patient did not complain of intermittent claudication but it is uncertain if this would be a feature when she becomes increasingly more active in her physical activities in future.

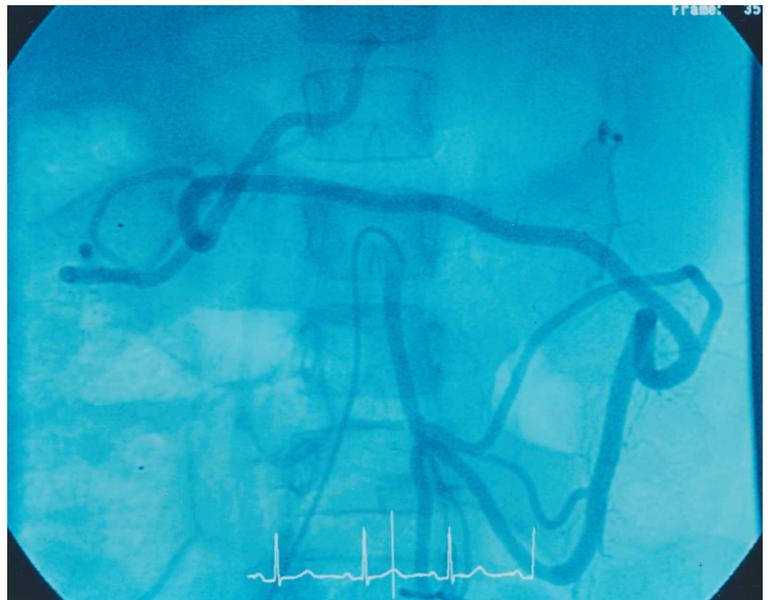
The need for surgical intervention,<sup>11,12,20,21</sup> in the middle aortic syndrome has to be carefully evaluated against the risks. Surgical morbidity may be substantial because of the frequently extensive nature of the vascular abnormality and the difficulty in making an appropriate graft. Percutaneous transluminal angio-

plasty<sup>22</sup> has not resulted in long-term success. In general, the indications of surgery are reserved for those in whom medical control of blood pressure is unsatisfactory or where there are intolerable side effects arising from this condition.

At the moment, it was believed that surgery was not indicated in our patient because she was asymptomatic. Her renal arteries were of normal caliber and there was no upper limb hypertension. The fact that there was no evidence of left ventricular hypertrophy on the electrocardiogram and echocardiogram was a good indicator that there was no severe secondary effect on the heart. To repair the abdominal aorta would be a major undertaking at this stage, technical difficulty notwithstanding, because the narrowing involved a diffusely hypoplastic segment.

Detailed mapping of the visceral supply<sup>23</sup> was important because the patient may have required liver transplantation for AS.<sup>24,25</sup> It is imperative that the surgical team be aware of any abnormalities in the

**Fig 3.** A large collateral vessel feeding the superior mesenteric distribution suggesting stenosis of the latter at its origin.



vascular supply, especially to the liver, before the transplant. Although this aberrant vascular circulation would not in any way preclude a liver transplantation, it may potentially complicate the transplant and/or increase the risks.

The cause of the abdominal vascular aberration is uncertain. Differential diagnoses include Takayasu's arteritis,<sup>26</sup> neurofibromatosis, and mucopolysaccharidosis,<sup>27</sup> which may result in narrowing of the abdominal aorta and vessels. In the former, the use of antiinflammatory agents may be useful in treatment. The inflammatory markers in our patient were negative and the clinical picture did not suggest Takayasu's arteritis or the other differential diagnoses that may lead to narrowing of the abdominal aorta.

It remains to be seen if this abdominal vascular abnormality is a progressive disorder in our patient. The association between AS and peripheral pulmonary artery stenosis is certain and it is plausible that a defect in vascular growth, transmitted on a genetic basis, may be responsible. Yet, the aortic abnormality does not occur with nearly the same incidence as the pulmonary artery narrowing save for the possibility that milder cases are often missed. Bearing this in mind, it would be useful for physicians caring for patients with AS to look out for this anomaly.

### CONCLUSION

This report highlights the presence of abdominal aortic narrowing and the associated abnormalities in the visceral vascular supply in a child with AS. There is a spectrum of symptoms in relation to the extent of the vascular abnormality. The indications to treat and the options available for the optimal treatment of the vascular problem are discussed. Apart from the fact that this may contribute to our better understanding of the pathogenesis of this condition, there are practical management issues to consider in a patient with AS. The bearing of these findings would be even more pronounced in the symptomatic child or where liver transplantation is being considered.

### REFERENCES

1. Alagille D, Odievre M, Gautier M, Dommergues JP. Hepatic ductular hypoplasia associated with characteristic faces, vertebral malformations, retarded physical, mental, and sexual development, and cardiac murmur. *J Pediatr.* 1975;86:63-71
2. Watson GH, Miller V. Arteriohepatic dysplasia, familial pulmonary arterial stenosis with neonatal liver disease. *Arch Dis Child.* 1973;48:459-466
3. Elmslie FV, Vivian AJ, Gardiner H, et al. Alagille syndrome. *J Med Genet.* 1995;32:264-268
4. Sokol RJ, Heubi JE, Balistreri WF. Intrahepatic "cholestatic faces": is it specific for Alagille syndrome? *J Pediatr.* 1983;103:205-208
5. Alagille D, Estrada A, Hadchouel M, et al. Syndromic paucity of interlobular bile ducts (Alagille syndrome or arteriohepatic dysplasia): review of 80 cases. *J Pediatr.* 1987;119:115-200
6. Johnson BL. Ocular pathologic features of arteriohepatic dysplasia (Alagille's syndrome). *Am J Ophthalmol.* 1990;110:504-512
7. Greenwood RD, Rosenthal A, Crocker AC, Nadas AS. Syndrome of intrahepatic biliary dysgenesis and cardiovascular malformations. *Pediatr.* 1976;58:243-247
8. Levin Se, Zarvos P, Milner S, Schmaman A. Arteriohepatic dysplasia: association of liver disease with pulmonary arterial stenosis as well as facial and skeletal abnormalities. *Pediatrics.* 1980;66:876-883
9. Silberbach M, Lashley BA, Rellar MD, et al. Arteriohepatic dysplasia and cardiovascular malformations. *Am Heart J.* 1994;127:695-699
10. Cohen JR, Birnbaum E. Coarctation of the abdominal aorta. *J Vasc Surg.* 1988;8:160-164
11. Graham LM, Zelenock GB, Erlandson EE, et al. Abdominal aortic coarctation and segmental hypoplasia. *Surgery.* 1979;86:519-529
12. Sumboonnanonda A, Robinson BL, Gedroyc WMW, et al. Middle aortic syndrome: clinical and radiological findings. *Arch Dis Child.* 1992;67:501-505
13. Elmslie FV, Vivian AJ, Gardiner H, et al. Alagille syndrome: family studies. *J Med Genet.* 1995;32:264-268
14. Anad F, Burn J, Matthews D, et al. Alagille syndrome and deletion of 20p. *J Med Genet.* 1990;27:729-737
15. Legius E, Fryns JP, Eyskens B, et al. Alagille syndrome (arteriohepatic dysplasia) and del (20p11.2). *Am J Med Genet.* 1990;35:532-535
16. Zhang F, Deleuze JF, Aurias A, et al. Interstitial deletion of the short arm of chromosome 20 in arteriohepatic dysplasia (Alagille syndrome). *J Pediatr.* 1990;116:73-77
17. Rand EB, Spinner NB, Piccoli DA, et al. Molecular analysis of 24 Alagille syndrome families identifies a single submicroscopic deletion and further localizes the Alagille region within 20p12. *Am J Hum Genet.* 1995;57:1068-1073
18. Shefler AG, Chan MKH, Ostman-Smith I. Middle aortic syndrome with arteriohepatic dysplasia. *Pediatr Cardiol.* 1997;18:230-234
19. Alagille D, Odievre M, Gautier M, Dommergues JP. Hepatic ductular

- hypoplasia associated with characteristic facies, vertebral malformation, retarded physical, mental and sexual development, and cardiac murmur. *J Pediatr*. 1975;86:63–71
20. Gupta S. Surgical and haemodynamic considerations in middle aortic syndrome. *Thorax*. 1979;34:470–478
  21. Poulas GE, Skoutas B, Doundoulakis E, et al. The middle aortic dysplastic syndrome: surgical considerations with a 2 to 18 year follow-up and selective histopathology study. *Eur J Vasc Surg*. 1990;4:75–82
  22. Nanni GS, Hawkins IF Jr, Alexander JA. Percutaneous transluminal angioplasty of an abdominal aortic coarctation. *AJR Am J Roentgenol*. 1983;140:1239–1241
  23. Lewis VD III, Meranze SG, McLean GK, O'Neill JA Jr, Berkowitz HD, Burke DR. The midaortic syndrome: diagnosis and treatment. *Radiology*. 1988;167:111–113
  24. Tzakis AG, Reyes J, Tepetes K, et al. Liver transplantation for Alagille's syndrome. *Arch Surg*. 1993;128:337–339
  25. Cardona J, Houssin D, Gauthier F, et al. Liver transplantation in children with Alagille syndrome—a study of twelve cases. *Transplantation*. 1995;60:339–342
  26. Lande A. Takayasu's arteritis and congenital coarctation of the descending thoracic and abdominal aorta: a critical review. *AJR Am J Roentgenol*. 1976;127:122
  27. Taylor DB, Blaser SI, Burrows PE, Stringer DA, Clarke JTR, Thorner P. Arteriopathy and coarctation of the abdominal aorta in children with mucopolysaccharidosis: imaging findings. *AJR Am J Roentgenol*. 1991; 157:819–823

## Abdominal Coarctation and Alagille Syndrome

Swee Chye Quek, FAMS\*; Lenny Tan, FRACR, FAMS, Swee Tian Quek, William Yip, FAMS\*; Marion Aw and Seng Hock Quak

*Pediatrics* 2000;106:e9

DOI: 10.1542/peds.106.1.e9

### Updated Information & Services

including high resolution figures, can be found at:  
<http://pediatrics.aappublications.org/content/106/1/e9>

### References

This article cites 27 articles, 8 of which you can access for free at:  
<http://pediatrics.aappublications.org/content/106/1/e9#BIBL>

### Subspecialty Collections

This article, along with others on similar topics, appears in the following collection(s):

#### **AAP Abroad**

[http://www.aappublications.org/cgi/collection/aap\\_abroad](http://www.aappublications.org/cgi/collection/aap_abroad)

### Permissions & Licensing

Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:

<http://www.aappublications.org/site/misc/Permissions.xhtml>

### Reprints

Information about ordering reprints can be found online:  
<http://www.aappublications.org/site/misc/reprints.xhtml>

# American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN®



# PEDIATRICS®

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

## **Abdominal Coarctation and Alagille Syndrome**

Swee Chye Quek, FAMS\*; Lenny Tan, FRACR, FAMS, Swee Tian Quek, William Yip, FAMS\*; Marion Aw and Seng Hock Quak

*Pediatrics* 2000;106:e9

DOI: 10.1542/peds.106.1.e9

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://pediatrics.aappublications.org/content/106/1/e9>

Pediatrics is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. Pediatrics is owned, published, and trademarked by the American Academy of Pediatrics, 345 Park Avenue, Itasca, Illinois, 60143. Copyright © 2000 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 1073-0397.

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN®

