Anomalous Origin of the Subclavian Artery Associated with Phocomelia*

R. L. VAN DER HORST, M.B., CH.B., M.MED. (PAED.) AND M. S. GOTSMAN, M.D., M.R.C.P., D.T.M. & H., *Cardiac Unit, Wentworth Hospital and the University of Natal, Durban*

SUMMARY

A hitherto unreported association between anomalous origin of the right subclavian artery and phocomelia of the right arm is described. The aetiology of phocomelia is briefly reviewed and the possible casual relationship or association between phocomelia and the disturbance in vascular supply to the limb is discussed.

S. Afr. Med. J., **45**, 1397 (1971).

Anomalous origin of the right subclavian artery is a well-known anomaly; in most instances it is not responsible for symptoms and is an incidental finding at angiography, surgery or autopsy.[1-3] If symptoms of tracheal compression occur, surgical relief of the abnormal vascular ring is necessary.

It is the purpose of this report to describe a symptomatic infant who had anomalous origin of the subclavian artery with phocomelia of the right arm. The symptoms of tracheal compression were relieved by surgery. We can find no published report in which is described phocomelia of a limb in which the associated subclavian artery has an anomalous origin.

*Date received: 1 June 1971.

Reprint requests to Professor M. S. Gotsman, Wentworth Hospital, P.O. Jacobs, Natal.

CASE REPORT

A Bantu male infant, aged 2 weeks, was admitted to hospital with a history of progressive cough, stridor and respiratory distress which dated from birth. He weighed 3·3 kg and was 58·4 cm tall. The baby had inspiratory stridor, slight cyanosis, mild respiratory distress with tachypnoea and rib recession. There were no stigmata of known chromosomal disorders. The right upper limb showed features which were typical of phocomelia (Fig. 1). An X-ray of the chest showed no abnormality but the barium-filled oesophagus was indented in the typical position by a right subclavian artery which arose anomalously as the third branch of the aorta (Fig. 2). The haemoglobin concentration was 15·0 g/100 ml and the blood count and smear were normal. On clinical, electrocardiographic and radiological grounds the heart was normal, but to exclude any associated cardiovascular disease and to confirm the abnormality of the subclavian vessel, right and left heart catheterization were performed. The intracardiac pressures were normal and a shunt could not be demonstrated. Selective aortography showed that the right subclavian artery had its origin from the descending aorta and passed behind the oesophagus before supplying the right arm. Selective catheterization of the anomalous right subclavian artery, with injection of contrast medium into the axillary artery of the

phocomelic limb, showed the features in Fig. 3 in which the abnormal arterial supply to the limb is demonstrated.

Analysis of the chromosomal pattern* showed a normal male karyotype; fragments, deletions, ring formation or satellites were not evident.

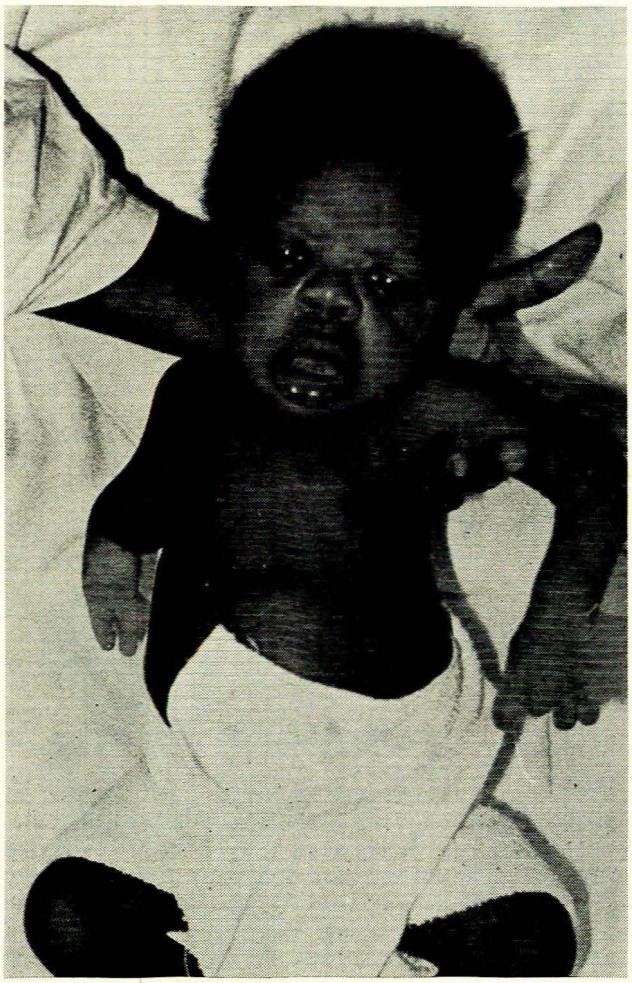

Fig. 1. The patient with phocomelia of the right upper limb.

The infant remained in respiratory distress, ate poorly and had a constant nasorespiratory purulent discharge. After 22 days in hospital, an operation was performed to divide the abnormal right subclavian artery at its origin and thereby to relieve the obstructive symptoms. During the postoperative period, there was marked clinical improvement in the baby's condition. At the age of 10 weeks he weighed 4·1 kg and was discharged from hospital. Some months later he developed gastro-enteritis, was admitted to another hospital and died from severe dehydration. Permission for autopsy was refused.

*Performed by the Cytologic Division of the Natal Blood Transfusion Service.

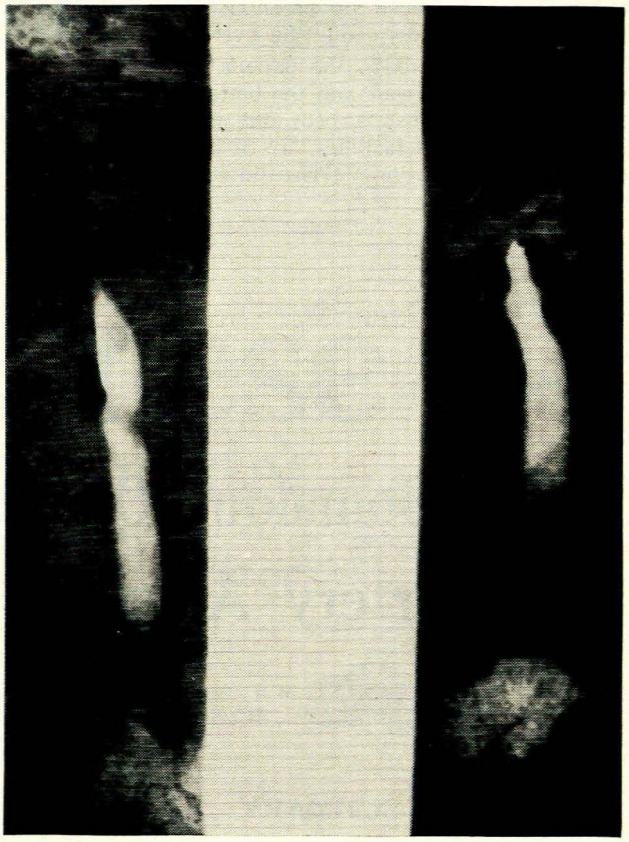

Fig. 2. X-ray with the oesophagus filled with barium showing the indentation produced by the anomalous right subclavian artery (arrow).

DISCUSSION

In phocomelia of the arm, the hand is often vestigial and arises from a short upper extremity like the flipper of a seal. The characteristic features are a short upper limb in which the radius is absent, the ulna shortened or absent and the carpal bones rudimentary. The thalidomide epidemic induced multiple congenital abnormalities which affected various systems in different infants: skeletal and cardiovascular malformations were common. In none of these cases was an anomalous origin of the subclavian artery reported although phocomelia was an almost constant finding. Phocomelia has been reported to be an associated feature in infants with trisomy 18,[4] and in an infant with multiple cardiovascular malformations who also had deletion of the long arm of chromosome 4.[5] Others, with phocomelia, have had normal chromosomes.[6] Phocomelia has not been reported as part of the syndrome with trisomy 13 - 15 or with trisomy 21, although

in patients with the latter condition anomalous origin of the subclavian artery occurs more commonly than in the general population.[7]

Phocomelia can be hereditary and several forms have been described.[8] Many environmental factors have been incriminated to account for the aetiology of phocomelia, including chemicals such as thalidomide, stelazine and trifluoperazine. Thallium, insulin, sulphonamides and other compounds as well as lack of riboflavine produce phocomelia-like malformations in experimental animals while maternal infection such as rubella is teratogenic in humans, but evidence that it causes phocomelia is not well established.

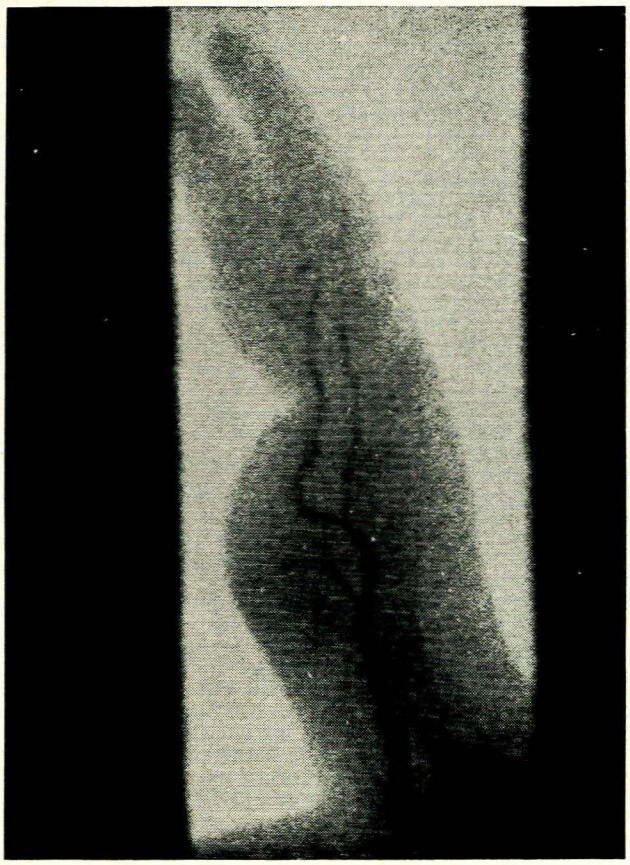

Fig. 3. Arteriogram with injection of contrast medium into the anomalously arising right subclavian artery.

The association between phocomelia and anomalous origin of the subclavian artery in this patient may be a coincidental event, but it is of great interest since a teratogenic insult in the 4th week of embryological development can alter normal development of an upper limb and its associated vascular supply. The theory of vascular insufficiency as a cause of congenital malformations is based on the assumption that interruption of the blood supply to a segment of bowel (and possibly a limb) may lead to an arrest of growth and atrophy of the affected portion. This aetiological mechanism, applicable to the intestine and reproducible experimentally, is responsible for a wide variety of intestinal anomalies of different grades of severity.[9] This author suggested that the principle of vascular insufficiency may be a primary factor in the genesis of anomalies of other systems. Furthermore, there is good experimental evidence that structural defects which are secondary to anoxia may be responsible for permanent impairment of the blood supply to a specific area.[10] The hypothesis of vascular insufficiency as the underlying mechanism responsible for phocomelia is feasible. The blood flow through an aberrant subclavian artery has not been measured but if such flow is reduced during intra-uterine life it may be responsible for maldevelopment of the limb with phocomelia as a consequence.

The exact mechanism of thalidomide-induced deformities is not known although it has been attributed to abnormal intracellular chemical competition interfering with limb development.[11] Intestinal atresia (oesophageal, duodenal, jejunal and ileal) are common features of thalidomide embryopathies where phocomelia is almost always present.[12] The abnormalities of the bowel may be due to vascular insufficiency and this might also account for the phocomelia.

Few angiographic studies of the blood vessels in phocomelic limbs have been reported,[13] so that we are uncertain whether the abnormal pathway taken by the subclavian artery is a result of the same embryological abnormality responsible for maldevelopment of the limb or whether the phocomelia is a result of a reduction in blood supply consequent upon the abnormal anatomical route taken by the right subclavian artery.

This study was supported by a grant from the Ethical Drug Foundation of South Africa.

REFERENCES

1. Klinkhamer, A. C. (1966): Amer. J. Roentgenol., **97**, 438.
2. Beabout, J. W., Steward, J. R. and Kincaid, O. W. (1964): *Ibid.*, **92**, 855.
3. Lincoln, J. C. R., Deverall, P. B., Stark, J., Aberdeen, E. and Waterston, D. J. (1969): Thorax, **24**, 295.
4. Warkany, J., Passarge, E. and Smith, L. B. (1966): Amer. J. Dis. Child., **112**, 502.
5. Ockey, C. H., Feldman, G. V., McCaulay, M. E. and Delaney, M. J. (1967): Arch. Dis. Childh., **42**, 428.
6. Falek, A., Heath, C. W., Ebbin, A. J. and McClean, W. R. (1968): Pediatrics, **73**, 910.
7. Goldstein, W. B. (1965): Amer. J. Roentgenol., **95**, 131.
8. Zellweger, H., Duff, H. S. and Abbo, S. (1965): Acta Genet. med. (Roma), **14**, 164.
9. Louw, J. H. (1959): Ann. Roy. Coll. Surg. Engl., **25**, 209.
10. Ingalls, T. H. and Curley, F. (1957): New Eng. J. Med., **257**, 1121.
11. Norman, A. P. (1963): *Congenital Abnormalities in Infancy*, p. 370. Oxford: Blackwell Scientific Publications.
12. Spiers, A. L. (1962): Lancet, **1**, 303.
13. Maier, W. A. (1965): Arch. Dis. Childh., **40**, 154.