Enlargement of Cavernous Haemangioma Associated with Exogenous Administration of Oestrogens

J. E. MORLEY, J. B. MYERS, F. S. SACK, F. KALK, E. E. EPSTEIN, J. LANNON

SUMMARY

A cavernous haemangioma of the liver which enlarged rapidly while the patient was receiving exogenous oestrogens is reported. A dramatic decrease in the size of the tumour was produced by ligating the right hepatic artery and portal vein.

The literature on large haemangiomas of the liver is reviewed.

S. Afr. Med. J., **48**, 695 (1974).

Haemangiomas were first recognised and described by Dupuytren and Cruveilhier, and were first carefully examined by Rokitansky and Virchow.[1]

Haemangiomas are found more commonly in the liver than in any other viscera,[2] and are the commonest benign tumours of the liver.[3]

CASE REPORT

A 57-year-old woman was found to have an enlarged liver at a routine gynaecological check-up after a hysterectomy 15 years previously. The liver had been noted to be minimally enlarged 18 months previously. She had been on Premarin 1,25 mg daily for one month, and then on alternate days for the second month, since her hysterectomy. She had no symptoms of liver failure and no epigastric pain or discomfort.

On examination she was found to have an 11-cm liver with a smooth edge. There was no bruit heard over the liver, the spleen was not enlarged, and there were no stigmata of liver failure.

The bilirubin, serum proteins, liver enzymes and prothrombin index (100%) were all within normal limits. The alkaline phosphatase was raised (26 King-Armstrong units). A liver scan showed a large area of decreased uptake in the right lobe. A liver biopsy was attempted but was unsuccessful. Ultrasound examination showed a semicystic lesion of the liver.

The radiograph of the abdomen showed a very large liver displacing the right kidney into the pelvis. No calcification was observed in the liver area. The angiographic features were diagnostic (Figs 1 - 3), and were demonstrated in both the flush aortogram and the selective coeliac arteriogram. There was considerable downward displacement and stretching of the main hepatic and the right hepatic arteries; a diffuse lesion involving the whole of the right lobe of the liver was shown, with the small hepatic vessels passing directly into clusters of small irregular collections of contrast material (no abnormal vascularity was noted, thus excluding a hepatoma or other malignancy); and the contrast remained pooled in the irregular clustered spaces with the portal hepatogram phase, 10 seconds after commencement of the injection.

There was no definite evidence of similar lesions in the left lobe of the liver or in any extrahepatic location.

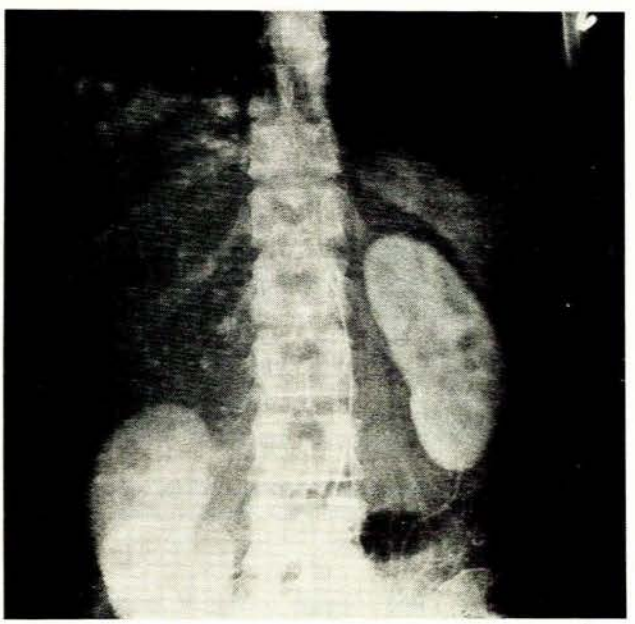

Fig. 1. Late phase after flush aortogram showing multiple contrast-filled spaces.

Johannesburg General Hospital, Johannesburg
J. E. MORLEY, M.B. B.CH.
J. B. MYERS, M.B. B.CH.
F. S. SACK, M.B. B.CH.
F. KALK, M.B. B.CH., F.R.C.S.
E. E. EPSTEIN, M.B. B.CH., D.P.H., D.T.M. & H., D.M.R.D.
J. LANNON, M.B. B.CH., F.R.C.S.

Date received: 25 October 1973.

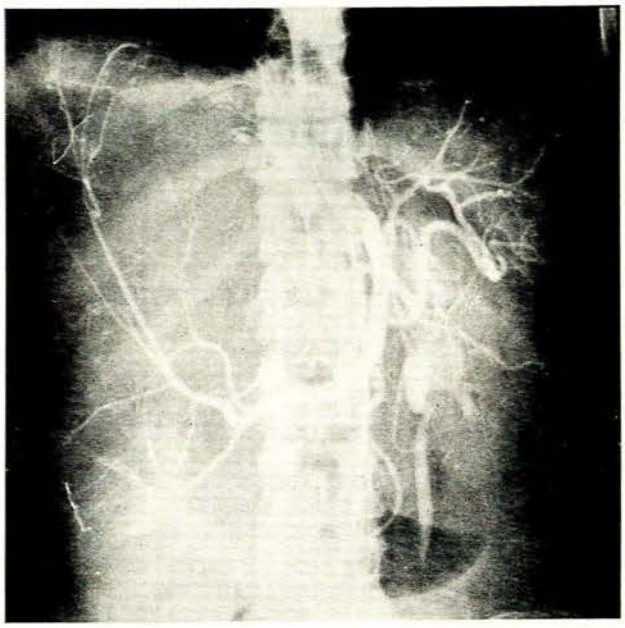

Fig. 2. Selective coeliac angiogram showing thinned, stretched hepatic vessels with early filling of vascular lakes.

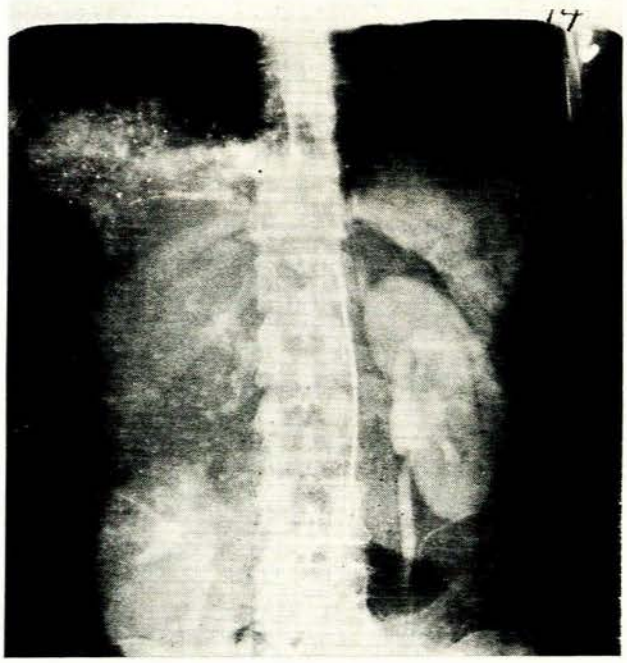

Fig. 3. Delayed phase (18 seconds after injection) of selective coeliac angiogram with vascular lakes showing delayed emptying.

In view of the rapid increase in size of the tumour and the dangers associated with trauma and rupture, it was decided to operate. The operation was performed through a right hypochondrial transverse incision with an angulated thoracic incision to the level of the fourth rib. A large vascular, multinodular mass was found in the right lobe of the liver, extending into the caudate lobe. There were a few scattered haemangiomatous nodules in the left lobe, omentum and on the peritoneum. The diaphragm was not visible from below despite division of the costal margin. The right border of the liver was totally inaccessible and could not be elevated to expose subsidiary hepatic veins entering into the inferior vena cava. The tumour thus appeared to be inoperable.

In view of the vascularity of the tumour as shown on angiography, it was assumed that ligation of the right hepatic artery and portal vein would produce a decrease in its size; which it did dramatically. The liver was dissected off the inferior vena cava and the hepatic veins ligated. The liver was divided at the point of colour demarcation by sharp dissection. Closure was achieved by using collagen tape.

The removed specimen weighed 950 g. Section showed the presence of spongy red tissue surrounded by a rim of relatively normal-looking liver. There were numerous nodules present, the largest measuring 2,5 cm across. Cut sections of the nodules appeared gelatinous.

Histological examination showed the presence of a benign cavernous haemangioma of the liver. The nodules sectioned consisted of loose fibrous connective tissue with myxomatous degeneration. There was no evidence of malignancy in any of the sections studied.

Postoperatively the patient developed a bile leak which decreased from 600 ml to 200 ml/day in 17 days. At the same time, her blood chemistry suggested an obstructive picture with a rise in bilirubin and alkaline phosphatase. By the 22nd day the bile leak had decreased to 50 ml/day and the bilirubin was within normal limits. By the 30th day the bile leak had decreased even further, and the drain was removed. At this stage her alkaline phosphatase had begun to fall. She has been seen subsequently and has no complications.

DISCUSSION

Incidence

Haemangiomas of the liver are found in about 1,4% - 2% of all autopsies,[4,5] most commonly in the third to fifth decades, and are commoner in females.[6] Ochsner and Halpert[5] state that the incidence of left lobe origin is slightly greater than that of right lobe origin.

Symptoms and Signs

The majority of haemangiomas produce no symptoms[12] and symptomatology as a rule only occurs when they have grown to a size where they interfere with the functions of adjacent organs. The commonest symptoms are mild epigastric pain, slight upper abdominal discomfort, a sense of weight and pressure, nausea, vomiting, dyspepsia, anorexia, dysphagia, pain in the back and weakness.[6-8] About half of the patients coming to surgery are aware of a swelling or an enlarging abdomen. Hepatic function is usually unaffected.

The most common physical sign of a liver haemangioma is an abdominal tumour connected to the liver which is smooth and non-tender. The tumour moves with respiration. Occasionally it is compressible and a venous hum or bruit may be heard. Cutaneous haemangiomas may be found in association with liver haemangiomas.

Radiology

Straight X-ray film of the abdomen shows an enlarged liver, rarely with calcification.[19] The angiographic features[20-23] are that the hepatic artery branches taper normally and run directly into abnormal collections of contrast medium, being displaced and crowded; tumour vessels are never present and the vascular spaces are arranged in clusters—ring or C-shaped around avascular areas; and collections of contrast medium persist up to 18 seconds (in the portal hepatogram phase).

These features distinguish cavernous haemangiomas from the more common malignant vascular lesions of the liver, and discourage percutaneous biopsy since surgery or radiotherapy may be required for the larger lesions.

Complications

The most dangerous complication is spontaneous rupture.[9] In infants a large haemangioma of the liver may act as an arteriovenous fistula producing congestive cardiac failure.[10,11,15] There are two cases reported of the Kasabach-Merritt syndrome (thrombocytopenia associated with haemangioma) seen with hepatic haemangioma.

A large pedunculated haemangioma[13,14] has been reported to undergo torsion, obstructing its blood supply with tumour necrosis, pain, fever and collapse.[16] A giant haemangioma has also been known to cause obstruction during childbirth.[17] In addition a fatal haemorrhage immediately after a needle biopsy of a hepatic haemangioendothelioma has been reported.[18]

Treatment

In 1892 Hanks treated a liver haemangioma by galvanism, placing an electrode under the rib margin.[24] The tumour is said to have diminished in size! Five years later Keen exteriorised a haemangioma onto the abdominal wall, placed an elastic tourniquet about its base and excised the lesion 6 days later with recovery of the patient. In 1898 Pfannenstiel removed a haemangioma of the liver weighing 2,5 kg.[25]

Modern treatment consists of surgical excision wherever indicated: viz. rapid enlargement, the presence of symptoms and/or complications, and the possibility of malignancy in very large tumours.

When the tumour is too large to excise, some success has been obtained with radiotherapy.[26-28]

Corticosteroids have also been found to reduce the size of large hepatic haemangiomas.[11] Two mechanisms of action of corticosteroids have been suggested. Steroids maintain arteriolar tone and increase vascular sensitivity to vasoconstrictive agents,[2] especially immature and rapidly proliferating vessels.[30] In addition steroids may significantly alter fibroblasts, ground substance and collagen formation.

Rake *et al.*[31] reported that hepatic artery ligation in an infant with congestive cardiac failure resulted in the disappearance of the failure and a decrease in the size of the liver.

Rubin[17] reported a case of haemangioma of the liver which enlarged rapidly during a woman's tenth pregnancy, possibly due to the hormonal influences. Our case is interesting in that the liver enlarged rapidly over 18 months while using synthetic oestrogens. We could find no other such cases reported in the literature.

Of special interest is the dramatic decrease in size of the right lobe of the liver following the ligation of the right hepatic artery and portal vein. This allows seemingly impossible surgery to be undertaken with relative ease.

REFERENCES

1. Henson, S. W., Gray, M. K. and Docherty, M. B. (1956): Surg. Gynaec. Obstet., **103**, 327.
2. Geschickter, C. F. and Keasbey, L. E. (1935): Amer. J. Cancer, **23**, 568.
3. Adam, Y. G., Hevos, A. C. and Fortner, J. G. (1970): Ann. Surg., **172**, 239.
4. Adami, C. J. (1910): *Principles of Pathology*. Philadelphia: Lea & Febiger.
5. Ochsner, J. C. and Halpert, B. (1958): Surgery, **43**, 577.
6. Shumaker, H. B. (1942): *Ibid.*, **11**, 209.
7. Ecker, J. A. and Doane, W. A. (1969): Amer. J. Gastroent., **52**, 25.
8. Wakeley, C. P. G. (1925): Brit. J. Surg., **12**, 590.
9. Sewell, J. M. and Weiss, K. (1961): Arch. Surg., **83**, 729.
10. De Lorimer, A. A., Simpson, E. B., Baum, R. S. and Carlson, E. (1967): New Engl. J. Med., **277**, 333.
11. Goldberg, S. J. and Fonkalsrud, E. (1969): J. Amer. Med. Assoc., **208**, 2473.
12. Park, W. C. and Phillips, R. (1970): *Ibid.*, **212**, 1496.
13. Behar, A., Moran, E. and Jak, G. (1963): Amer. J. Clin. Path., **40**, 78.
14. Jawes, R. L., Nelson, J. A. and Hyde, G. A. (1971): Surgery, **70**, 782.
15. Berdon, W. E. and Baker, D. M. (1969): Radiology, **92**, 1523.
16. Bockus, M. L. (1965): *Gastroenterology III: Tumours of the Liver*, 2nd ed. Philadelphia: W. B. Saunders.
17. Rubin, I. C. (1918): Amer. J. Obstet., **77**, 273.
18. Karpas, C. M. and Pavon, E. E. (1971): N.Y. Med. J., **71**, 770.
19. Plachta, A. (1962): Radiology, **79**, 783.
20. Pollard, J. J., Nebesar, R. A. and Mattoso, L. F. (1966): *Ibid.*, **86**, 276.
21. Abram, R. M., Bezanbaum, E. R., Santos, J. S. and Lipson, J. (1969): *Ibid.*, **92**, 308.
22. Pantoja, E. (1968): Amer. J. Roentgenol., **104**, 874.
23. McLoughlin, M. J. and Gilday, D. L. (1972): Clin. Radiol., **23**, 377.
24. Wilson, M. and Tyson, W. T. (1952): Amer. Surg., **135**, 124.
25. Bruns Chivig, A. and Smith, R. R. (1952): *Ibid.*, **135**, 124.
26. Ray, B. S. (1939): *Ibid.*, **109**, 373.
27. Shockman, A. J., Wenger, J. A. and Kohn, N. N. (1963): Gastroenterology, **45**, 425.
28. Issa, P. (1968): Brit. J. Radiol., **41**, 26.
29. Zweifach, B. W., Shorr, E. and Black, M. (1953): N.Y. Acad. Sci., **56**, 626.
30. Fort, N. C. and Esterley, N. B. (1968): J. Pediat., **72**, 351.
31. Rake, M. O., Liberman, M. M., Dawson, J. L., Evans, R., Raferty, E. B., Laws, J. and Williams, R. (1970): Gut, **11**, 512.