Primary Lymphoma of the Gall Bladder

CASE REPORT AND REVIEW OF THE LITERATURE

J. B. C. BOTHA, L. B. KAHN

SUMMARY

A patient with primary lymphocytic lymphoma of the gall bladder is presented, and cases of primary lymphoma of this organ reported in the English literature are reviewed.

Primary lymphoma of the extrahepatic biliary drainage system is a rare cause of obstructive jaundice and has a poor prognosis.

S. Afr. Med. J., **48**, 1345 (1974).

Primary lymphoma of the gall bladder is an exceedingly rare condition and is not mentioned in several standard textbooks of pathology.[1-4] We have been able to find only 11 cases documented in the world literature; and only 4 of these in the English literature.[5,6] They have appeared as isolated case reports or are mentioned in reviews dealing with primary sarcomas of the gall bladder. To the best of our knowledge, there is no other review dealing specifically with lymphoma of the gall bladder.

The most comprehensive surveys of primary sarcoma of the gall bladder are those of Vaittinen[5] and Yasuma and Yanaka.[6] Vaittinen reviewed 92 cases of primary sarcoma of the gall bladder, which included 4 lymphocytic lymphomas. To these he added a further 6 personal cases, 3 of which were lymphocytic lymphomas. Yasuma and Yanaka reviewed 93 cases of primary sarcoma of the gall bladder, including 14 cases reported from Japan. Of these 93 cases, 4 were lymphocytic lymphomas and 4 were reticulum cell lymphomas. Their review included 3 personal cases, one of which was a reticulum cell lymphoma. Lymphomas thus constitute about 10% of all primary sarcomas of the gall bladder.

We wish to document a further case of primary lymphocytic lymphoma of the gall bladder, and to review the cases of primary lymphoma of the gall bladder which have appeared in the English literature.

CASE REPORT

A 54-year-old Moslem male presented at Groote Schuur Hospital with a brief history of progressive shortness of breath. He was found to have a right-sided pleural effusion which was tapped on 2 occasions and clear fluid obtained. The fluid was sterile and no cells could be demonstrated microscopically. It had a specific gravity of 1,017 and a protein content of 3,6 g/100 ml. A needle biopsy of the pleura failed to reveal any abnormality and no acid-fast bacilli were found in the sputum. Before an open pleural biopsy could be performed, the patient developed nausea, anorexia, jaundice and weight loss, and he noticed pallor of his stools and darkening of his urine. He rapidly developed a 6-cm palpable tender hepatomegaly. Examination of his urine showed the presence of much bilirubin but no urobilinogen.

The haemoglobin was 13 g/100 ml, white cell count 10 900/mm^3 with a normal differential count, platelet count 600 000/mm^3 and erythrocyte sedimentation rate 2 mm in the first hour (Westergren). There was no alpha fetoprotein in the serum. The serum protein was 6,8 g/100 ml, albumin 3,4 g/100 ml, cholesterol 250 mg/100 ml, total bilirubin 29,4 mg/100 ml, conjugated bilirubin 21,6 mg/100 ml, creatine phosphokinase 140 units (normal 10 - 110), lactate dehydrogenase 221 units (normal 60 - 145) and amino-aspartic transaminase 71 units (normal 5 - 20). A liver biopsy was done and showed marked centrilobular cholestasis with bile within the hepatocytes, Kupffer cells and canaliculi. Moderate numbers of foamy histiocytes and scanty neutrophils were seen in the portal tracts and a moderate degree of bile duct proliferation was present. There was no evidence of malignancy. The features were those of extrahepatic biliary obstruction.

It was thought that the patient had extensive carcinomatosis with hepatic secondaries, but a peritoneoscopy failed to demonstrate any tumour. A laparotomy was performed and the liver found to be massively enlarged. The gall bladder was collapsed and there was a palpable tumour in the region of the gall bladder neck. No gall stones were palpable. An operative cholangiogram showed a small common bile duct with complete obstruction of the common hepatic duct at its junction with the cystic duct. The gall bladder was removed, the common bile duct opened and the stenosed portion of the common hepatic duct dilated. A biopsy specimen of the stenotic area was submitted for frozen section examination and was interpreted as a poorly-differentiated neoplasm of uncertain histogenesis. A U-tube drainage procedure was done. The rest of the abdominal cavity was essentially normal. The spleen was not enlarged and frozen section biopsy specimens of enlarged porta hepatis and mesenteric lymph nodes showed non-specific reactive changes. A liver specimen again showed features of extrahepatic biliary obstruction.

Immediately postoperatively the patient had cardiac arrest, did not regain consciousness, and died 15 days later of hypostatic pneumonia. Permission for autopsy was refused.

Department of Pathology, University of Cape Town
J. B. C. BOTHA, M.B. CH.B.
L. B. KAHN, M.B. B.CH., M.MED. (PATH.)

Date received: 18 February 1974.

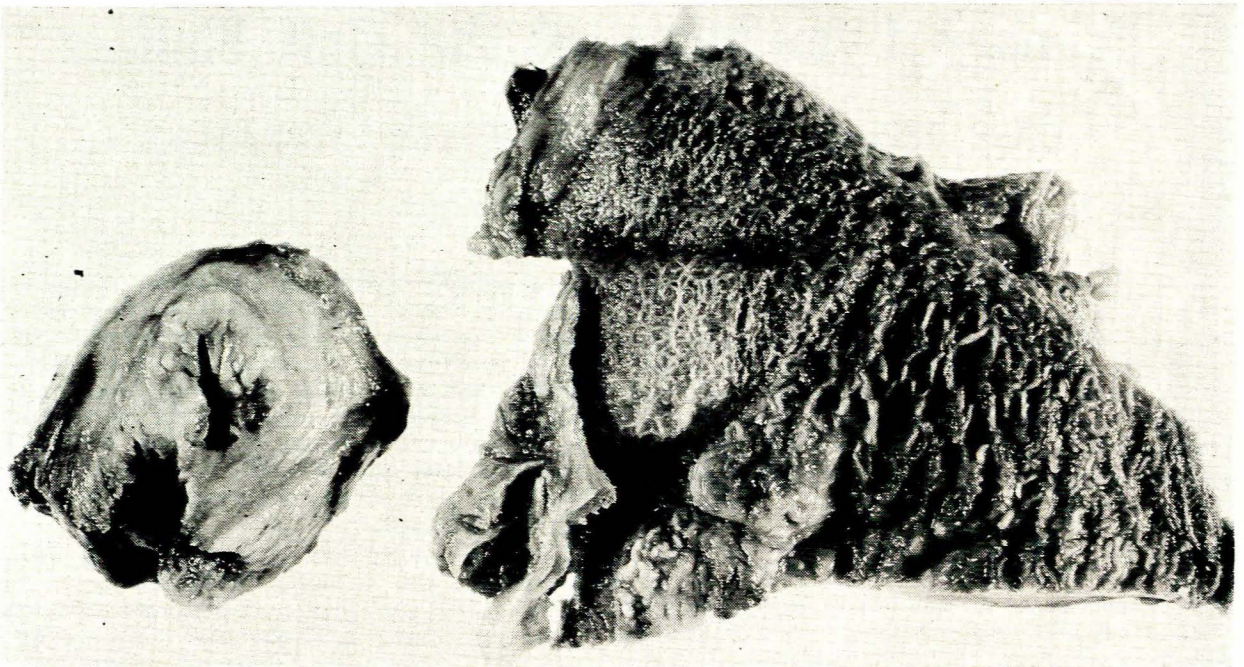

Fig. 1. On the right, mucosal surface of gall bladder show ing coarse, thickened folds; on the left, diffuse lymphomatous infiltration causing severe thickening in the region o f the neck of the gall bladder.

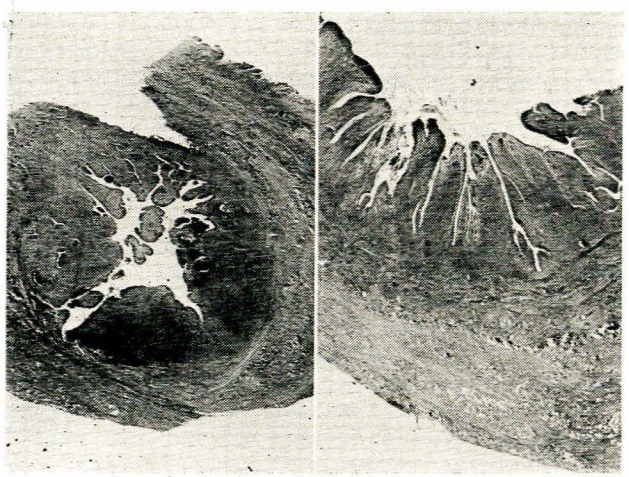

Fig. 2. Low-power photomicrograph showing dense infiltration of the entire thickness of the cystic duct (left) **and of the gall bladder wall** (right). **The thickening of the mucosal villi is well shown (H. and E. × 6).**

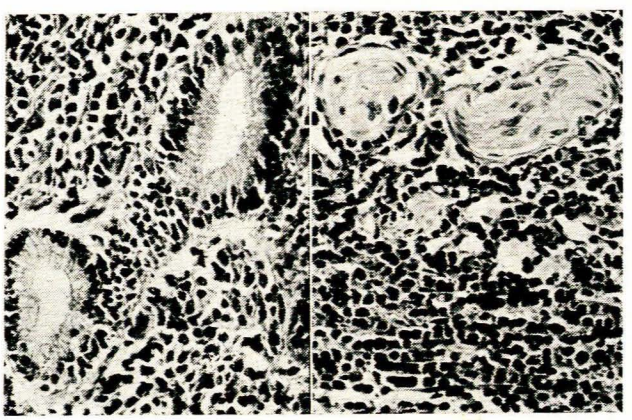

Fig. 3. The lymphoma cells surround mucosal glandular structures (left), **and myelinated nerve bundles** (right) **(H. and E. × 250).**

PATHOLOGY

The gall bladder measured 7 × 3 × 3 cm. The wall was diffusely thickened and the mucosal surface presented coarse villi which imparted a velvety appearance (Fig. 1). The cystic duct had severe thickening of its wall right up to the line of surgical resection. Histological examination proved the entire gall bladder wall, as well as the wall of the cystic duct, to be diffusely infiltrated by poorly-differentiated lymphocytic cells (Figs 2 to 4). A moderate number of mitotic figures were seen. The infiltrate caused considerable distension of the mucosal villi, and the surface epithelium was atrophic but still intact. The features were those of a poorly-differentiated lymphocytic lymphoma.

The mesenteric lymph node showed reactive change as well as a few small foci of early lymphomatous transformation. The lymph node from the region of the common hepatic duct showed coagulative necrosis of the

central portion with lymphomatous transformation peripherally.

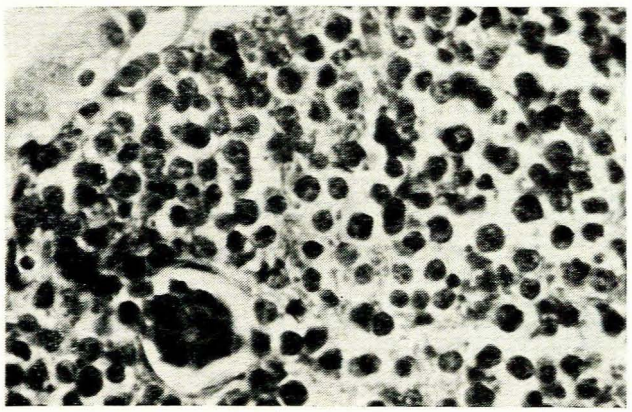

Fig. 4. Tumour infiltrate consisting of sheets of poorly-differentiated lymphocytes underlying intact surface epithelium seen at the upper left hand corner (H. and E. × 600).

DISCUSSION

Cases of primary sarcoma of the gall bladder reported in the literature have shown a varied histological picture; spindle cell tumours are the most common, but bizarre variants such as melanosarcoma, myxosarcoma, leiomyosarcoma, rhabdomyosarcoma and alveolar cell sarcoma are reported.[5,6] Higgs *et al.*[7] reported a malignant mixed tumour of the gall bladder with 4 microscopic components, viz. osteoid, adenocarcinoma, fibrosarcoma and chondrosarcoma. A review of primary lymphoma of the gall bladder is difficult because of the use of terms such as angioreticulum cell sarcoma[5] and round cell sarcoma;[6] some of these may, in fact, have been lymphomas of one or other type. In addition, several examples of lymphoma reported in the foreign language literature have been only briefly alluded to in the larger surveys of gall bladder sarcomas. The only acceptable cases of primary lymphoma of the gall bladder that we have been able to find in the English literature are those of Vaittinen[5] and Yasuma and Yanaka[6] (Table I). Despite the failure to obtain an autopsy, we consider our case an example of primary lymphoma of the gall bladder since there was no clinical, radiological or laboratory evidence of distant dissemination. Findings at laparotomy or on histological examination showed the lesion to be confined to the gall bladder and regional lymph nodes, with no evidence of hepatic or splenic involvement.

The mean age of the 5 patients at the time of diagnosis was 55 years, and is similar to the mean age for all primary sarcomas of the gall bladder. The clinical presentation of primary lymphoma of the gall bladder may be indistinguishable from that of other gall bladder malignancies. Three of the 5 patients presented with biliary symptoms without jaundice and the other 2 with obstructive jaundice resulting from complete obstruction of the

TABLE I. PRIMARY LYMPHOMAS OF THE GALL BLADDER

Author	Age (yrs)	Sex	Clinical presentation	Diagnosis	Gall stones	Treatment	Prognosis
Vaittinen[5]	44	F	Biliary symptoms for 2 years; loss of weight and abdominal swelling; mass in right upper quadrant; no jaundice	Lymphocytic lymphoma	—	Cholecystectomy and radiotherapy	At laparotomy found to have enlarged gall bladder, ascites and regional node involvement; died 3 mo. postoperatively
Vaittinen[5]	73	F	Biliary symptoms for 2 years; abdominal swelling, epigastric tenderness and pyrexia; occult blood in stools; no jaundice	Lymphocytic lymphoma	+	No treatment	At autopsy found to have a gall bladder tumour extending into the liver with involvement of the regional and para-aortic nodes; died 1½ mo. after admission
Vaittinen[5]	75	F	Pain in right upper quadrant; vomiting, abdominal swelling, diarrhoea, fatigue and pyrexia; hepatomegaly and mass in right upper quadrant; no jaundice	Lymphocytic lymphoma	+	No treatment	At autopsy found to have a gall bladder tumour extending into the liver with regional lymph node metastases; died 2 mo. after admission
Yasuma and Yanaka[6]	29	M	Nausea, fatigue and jaundice; tenderness in right upper quadrant and hepatomegaly	Reticulum cell lymphoma	—	Cholecystectomy, radiotherapy, cytotoxic drugs	At laparotomy found to have an enlarged gall bladder with cystic duct obstruction; died 7½ mo. postoperatively
Botha and Kahn	54	M	Dyspnoea, nausea, anorexia, weight loss, jaundice and hepatomegaly	Lymphocytic lymphoma	—	No treatment	At laparotomy found to have gall bladder mass, hepatic duct obstruction and regional node involvement; died 5 days postoperatively

biliary system. Scirrhous carcinoma is the most common intrinsic bile duct tumour causing obstructive jaundice.[8] Primary sarcomas are less likely to cause occlusion of the biliary system, and only 3 of the 14 cases of sarcomas of the gall bladder reported from Japan presented in this way. In this regard, it is worth noting that while neoplastic involvement of the lymph nodes in the porta hepatis is often quoted as a possible cause of obstructive jaundice, this is, in fact, a rare occurrence and is usually associated with actual invasion of the ducts by tumour, causing a desmoplastic reaction.[9] Herbut and Watson[10] reported a case of disseminated lymphocytic lymphoma which had extensively infiltrated the extrahepatic bile duct, causing obstructive jaundice without significant enlargement of the lymph nodes of the porta hepatis.

The prognosis of these few patients with primary lymphoma of the gall bladder has been poor as with other gall bladder sarcomas.[11] Two of the 5 patients were diagnosed only at autopsy, and 2 died 5 days and 3 months respectively after laparotomy. The fifth patient showed no evidence of node involvement and was treated with radiotherapy (1 050 rads) and cytotoxic drugs; this patient died about 7 months postoperatively.

REFERENCES

1. Ackerman, L. V. (1968): *Surgical Pathology*, 4th ed. St Louis: C. V. Mosby.
2. Willis, R. A. (1967): *Pathology of Tumours*, 4th ed. London: Butterworths.
3. Edmondsen, H. A. (1967): *Atlas of Tumor Pathology: Tumors of the Gall Bladder and Extrahepatic Bile Ducts*, section VIII, fasc. 26. Wash.ngton, D.C.: Armed Forces Institute of Pathology.
4. Evans, R. W. (1968): *Histological Appearances of Tumours*, 2nd ed. Edinburgh: E. & S. Livingstone.
5. Vaittinen, E. (1972): Ann. Chir. Gynaec. Fenn., **61**, 184.
6. Yasuma, T. and Yanaka, M. (1971): Acta Path. Jap., **21**, 285.
7. Higgs, W. R., Mocega, E. E. and Jordan, P. W. (1973): Cancer, **32**, 471.
8. Payling-Wright, G. and Symmers, W. St C. (1966): *Systemic Pathology*, 1st ed., p. 655. London: Longmans.
9. Bower, J. S. and Coca Mir, R. (1951): J. Amer. Med. Assoc., **146**, 987.
10. Herbut, P A. and Watson, J. S. (1946): Amer. J. Clin. Path., **16**, 365.
11. Carpentier, Y. and Lambilliotte, J. P. (1973): Cancer, **32**, 493.