Case report

Granular cell myoblastoma of the common bile duct treated by biliary drainage and surgery

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SUMMARY A young Caucasian woman is described in whom obstructive jaundice was caused by a granular cell myoblastoma of the common bile duct. She was treated by percutaneous transhepatic biliary drainage for 10 days, before radical removal. Granular cell myoblastomas are benign lesions of disputed histogenesis, rare among biliary neoplasms, the excision of which is curative.

Benign tumours of the extrahepatic biliary tree are rare, and are usually either epithelial (adenomas and papillomas) or have a prominent epithelial component (adenomyomas and polyps).^{1,2} Fibromas, leiomyomas, nerve sheath tumours, and granular cell myoblastomas account for 13%.³ Since the first report of a biliary myoblastoma,⁴ others have been described, usually in negro females (Tables 1 and 2). The only previous case in the British literature was, as in this report, in a young Caucasian woman who presented with obstructive jaundice.⁵

Case report

A 28 year old single Greek woman presented in March 1979 to the Royal Free Hospital, for investigation of jaundice, which was first noted in March 1977. She had previously been well, and had taken an oestrogen/progesterone oral contraceptive since 1970. Between March 1977 and September 1978 she had a variable degree of cholestasis with dark urine and pale stools, and there had been no improvement with a short course of steroids. In September 1978 itching developed and a liver biopsy was reported as consistent with chronic cholestasis.

On examination she was a tall fit young woman, jaundiced with increased pigmentation of exposed areas and skin folds, and scratch marks on her limbs.

There was 10 cm smooth, non-tender hepatomegaly. The tip of the spleen was palpable.

Investigations showed: haemoglobin 10.0 g/dl, white cell count $13 \times 10^9/l$ with a normal differential count. Total bilirubin 220 $\mu\text{mol/l}$, aspartate transaminase 51 IU/l, and alkaline phosphatase 413 IU/l. Serum albumin, gamma globulin, and immunoglobulins were normal. Serum autoantibodies and hepatitis B surface antigens were negative.

Ultrasound of the liver (Fig. 1) showed marked dilatation of the intrahepatic bile ducts and the common hepatic duct. Percutaneous transhepatic cholangiography (PTC) showed complete obstruction of the common hepatic duct (Fig. 2). Endoscopic retrograde cholangiopancreatography (ERCP) showed a normal common bile duct up to the level of the origin of the cystic duct, where there was a tight stricture (Fig. 3). Some contrast medium passed through the stricture and showed the dilated biliary system above the lesion. The pancreatic duct was normal.

A percutaneous drainage catheter (PTD) was introduced through the liver into the dilated biliary system (Fig. 2). External drainage was done for 10 days and the daily output of bile was between 2 and 5 litres. Sodium and water balance was maintained by intravenous infusion, and there were no complications from the procedure. Over the period of drainage, the serum bilirubin concentration fell from 192 to 78 $\mu\text{mol/l}$ (Fig. 4) and elective surgery was then performed.

At operation there was an apparently intraluminal tumour in the common bile duct with proximal dilatation of the duct. The common bile

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Table 1 Granular cell myoblastoma of extrahepatic biliary system: common bile duct

Author	Age (yr)	Sex	Race	Symptoms	Follow-up and comment
Coggins ⁴ (1952)	25	F	N	Hepatic coma	Post-mortem finding
Duncan and Wilson ⁶ (1957)	30	F	N	1/12 obstructive jaundice	Resected. Discharged from follow-up
Whitmore <i>et al.</i> ³⁷ (1969)	37	F	N	Obstructive jaundice	Resected. Discharged from follow-up well
	61	F	N	—	Incidental finding at post-mortem
LiVolsi <i>et al.</i> ³¹ (1973)	30	F	U/S	Abnormal liver function tests	Resected. Cured
Whisnant <i>et al.</i> ³² (1974)	16	M	N	Obstructive jaundice	Resected. Discharged from follow-up
Dursi <i>et al.</i> ¹⁰ (1975)	35	F	N	Jaundice, RUQ pain	Resected. Well 1 yr later
Savage and Devitt ⁵ (1977)	30	F	C	Obstructive jaundice	Resected. Good recovery
Zvargulis <i>et al.</i> ³⁸ (1978)	11	F	U/S	Jaundice, epigastric pain	Resected. Good recovery
Assor ³³ (1979)	33	F	N	Jaundice, abdominal pain	Resected. Good recovery
	31	F	N	Epigastric pain	Resected
	37	F	C	Chest pain	Resected
Jain <i>et al.</i> ³⁹ (1979)	46	F	N	Abdominal pain	Resected. Good recovery
Farris and Faust ⁴⁰ (1979)	23	F	N	Jaundice, epigastric pain	Resected. Well

N: Negroid. C: Caucasoid. M: Mongoloid. U/S: Unspecified, RUQ: right upper quadrant.

duct was divided below the tumour. The gall bladder, cystic duct, and tumour, with a rim of common hepatic duct, were removed, together with local lymphatics and nodes. A hepaticojejunostomy and enteroanastomosis were constructed.

Her postoperative course was uncomplicated and she was discharged 10 days later. She remains well and free from jaundice 10 months later.

PATHOLOGICAL FINDINGS

The resected specimen (Fig. 5) was of gall bladder and cystic duct with 1.0 cm of dilated common bile duct. A firm solitary mass 1.2 cm in axial length with a yellow cut surface obliterated the lumen of the common bile duct without involvement of the serosa.

Histologically the tumour consisted of large eosinophilic cells in strands or solid clumps with uniform small dark nuclei and distinct margins (Fig. 6). The cytoplasm contained granules, closely packed and varying in size, which were strongly positive with the periodic acid-Schiff reaction after

amylase digestion. Faint Sudan Black positivity was found on frozen section. No cross-striations or fibrillary processes were seen. The stroma between tumour cells was collagenous and occasionally myxoid. The edges of the lesion were ill-defined, the granular cells singly or in groups infiltrating, but not destroying, muscle. Occasionally, cells were arranged in whorls around small nerve bundles (Fig. 7), a finding frequently noted in relation to biliary myoblastomas.^{5,6}

The ultrastructural findings (Fig. 8) were of membrane-bound vesicles of various sizes with moderate to dense osmophilia, together with many myelin figures and much electron dense material in mitochondria and Golgi apparatus. These appearances are characteristic of myoblastomas.^{7,8} No axons were found within tumour cells, nor evidence of transition from tumour cells to small nerves or myofibers.

Immunoperoxidase studies on paraffin-embedded tissue sections did not demonstrate carcinoembryo-

Table 2 Granular cell myoblastoma of extrahepatic biliary system: cystic duct and gall bladder

Author	Age (yr)	Sex	Race	Symptoms	Follow-up and comment
<i>Cystic duct</i>					
Fialho and Hilario ⁴⁰ (1952)	21	F	N	RUQ pain	Resected. Well
Serpe <i>et al.</i> ⁴¹ (1960)	34	F	N	RUQ pain	Resected. Well
Goldman <i>et al.</i> ⁴² (1967)	14	F	N	RUQ pain	Resected. Well
Mackay <i>et al.</i> ⁴³ (1968)	34	F	U/S	RUQ pain	Resected. Well at 9 m
Christensen and Ishak ⁴⁴ (1970)	34	F	C	RUQ pain	U/S
Abt <i>et al.</i> ⁴⁵ (1971)	44	F	N	RUQ pain	Resected
LiVolsi <i>et al.</i> ³¹ (1973)	40	F	U/S	RUQ pain	Died of myocardial infarction at 4 yr.
Kittredge and Baer ⁴⁶ (1975)	41	F	U/S	Jaundice and pain	Post-mortem no recurrence or spread
Farris and Faust ⁴⁰ (1979)	31	F	N	Epigastric pain	Conservative procedure
Reul <i>et al.</i> ⁴⁶ (1975)	39	F	N	RUQ pain	Resected. Well
					Resected
<i>Gall bladder</i>					
Ishii <i>et al.</i> ⁴⁷ (1977)	39	F	M	Epigastric pain	

Abbreviations as in Table 1.

Fig. 1 *Gray scale ultrasound of liver showing dilated intrahepatic ducts (arrowed).*

Fig. 2 *PTC with dilated intrahepatic ducts, obstruction of the common hepatic duct (h), and the drainage catheter in the biliary system (arrowed).*

mic antigen (CEA). Myoblastomas occurring in breast have been found to be CEA positive.⁹

Discussion

Benign tumours of the extrahepatic bile ducts are rare⁸ and less than 10% are granular cell myoblastomas (GCM).¹⁰ Review of the literature has shown 25 previous reports of GCMs involving the biliary tract (Tables 1 and 2). The clinical features on presentation depended on the anatomical site of the tumour. Common bile duct tumours presented with jaundice and those in, or at the origin of, the cystic duct with abdominal pain. These clinical features and the preoperative investigations were of no specific value in the diagnosis, this being made in almost every case on histological examination. Resection was curative, but the biliary surgery was often followed by complications including stricture, requiring additional operations.

Our patient presented with an unusual history of two years of cholestasis. The history was non-specific, though the occurrence of jaundice before itching was more consistent with extrahepatic obstruction rather than intrahepatic cholestasis, as, for example, primary biliary cirrhosis, when itching usually occurs before jaundice.¹¹

Ultrasound examination demonstrated bile duct dilatation, and PTC and ERCP showed the site of

Fig. 3 ERCP showing normal common bile duct (a), and pancreatic duct (b), with dilation of the common hepatic duct above a stricture (c) at the origin of the cystic duct. Gall bladder (gb).

obstruction. The cholangiographic appearances were consistent with cholangiocarcinoma, but at surgery the lesion was thought to be benign. Histological examination confirmed this.

Several techniques can now be used to drain obstructed bile ducts before or in place of surgery.¹² Preoperative external bile drainage was done in this case. Nakayama *et al.*¹³ have claimed a reduc-

tion in postoperative mortality using this technique in patients with obstructive jaundice, and for this reason, and also to decompress an unusually tense biliary system after PTC, external drainage was done. The flow of bile was five times that expected and remains unexplained. Internal bile drainage, although preferable, was not possible.

Strict fluid balance, necessary in all cases with bile drainage, was critical, with parenteral replacement of salt and water. Serum bilirubin fell as expected, but whether such a reduction before surgery reduces the operative risk is not established.

Granular cell myoblastomas arise more frequently in the oral cavity, in skin and subcutaneous tissues, than in the biliary tract. They have also been described in other sites including breast,^{14 15} female genital tract,¹⁶ bronchus,^{17 18} and in the gastrointestinal tract. So far as is known, this patient had

Fig. 4 Fall in serum bilirubin concentration during preoperative external biliary drainage.

Fig. 5 Resected specimen showing tumour (m) at the origin of the cystic duct (c), with common hepatic duct (h) above, and common bile duct (b) below. Gall bladder (gb).

only one myoblastoma, but these tumours can be multiple^{19 20} and, of the 22 biliary cases, one patient²¹ had multiple tumours in the biliary tree, and four had myoblastomas elsewhere.²¹⁻²³

The nature and histogenesis of these tumours is uncertain. It has been argued that the lesion is neoplastic,²⁴ a storage disorder,²⁵ and a degenerative change.⁸ The cell of origin is also unknown. Embryonic muscle, Schwann cells, perineural fibroblasts, phagocytic histiocytes, and modified astrocytes in the pituitary²⁶ have all been suggested.

Embryonic striated muscle cells were suggested in the original description,²⁷ and this has received support.^{28 29} The characteristics of the cells in tissue culture also suggest a myogenic origin.³⁰ The lesion has been called a granular cell perineural fibroblastoma³¹ and a lipid thesaurismosis,²⁵ a local metabolic disorder in which histiocytes store lipid material and appear granular.

The most widely accepted view at present is that these tumours arise from neuroectoderm. The lesions could develop from Schwann cells,^{32 8} from undifferentiated mesenchymal cells³³ which are the precursors of Schwann cells,⁷ or from cells of the nerve sheath, like neurofibromas.³⁴ In this patient granular cells were seen within and closely surrounding nerve bundles (Fig. 7).

The proliferative nature of this tumour does not rule out a Schwann cell origin, but, as Schwann cells may assume phagocytic properties in tissue culture³⁵ and possibly in Wallerian degeneration,⁸ a neoplastic change would not necessarily be implicated. Thus the lesion may be more in the nature of a histiocytic response as suggested by Azzopardi²⁵ than a true neoplasm.³⁶

Granular cell myoblastomas are benign, surgically curable, and unlikely to recur. When local recurrence occurs the presence of multifocal tumours is

Fig. 6 Submucosal area showing tumour cells (two arrowed). Mucosa of bile duct (M).

Fig. 7 Tumour cells (arrowed) in whorls around small nerve trunk (N).

Fig. 8 Electron micrograph showing membrane bound vesicles (v) and myelin figures (f).

likely. If aggressive local invasion or metastasis occurs, large cell sarcomas such as rhabdomyosarcomas must be considered. Cadotte²⁴ accepts a total of 22 malignant granular myoblastomas in the literature, none in the biliary tree, mainly arising subcutaneously and spread by lymphatics or the blood system.

We report this patient as a rare case with bile duct obstruction due to a benign tumour. Granular cell myoblastomas are probably of Schwann cell origin. Our patient is well at follow-up 10 months after radical surgery.

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References

- ¹Dowdy GS, Olin WG, Shelton EL, Waldron GW. Benign tumours of the extrahepatic bile ducts. *Arch Surg* 1962; **85**: 503–13.
- ²Hossack KF, Heron JJ. Benign tumours of the common bile duct. *Aust NZ J Surg* 1972; **42**: 22–6.
- ³Chu PT. Benign neoplasms of the extrahepatic biliary ducts. *Arch Pathol Lab Med* 1950; **50**: 84–97.
- ⁴Coggins RP. Granular cell myoblastoma of the common bile duct; a report of a case with autopsy findings. *Arch Pathol Lab Med* 1952; **54**: 398–402.
- ⁵Savage A, Devitt P. Granular cell myoblastoma of the biliary tree. *Postgrad Med J* 1977; **53**: 574–7.
- ⁶Duncan JT, Wilson H. Benign tumours of the common bile duct. *Ann Surg* 1957; **145**: 271–4.
- ⁷Sobel HJ, Schwarz R, Marquet E. Light and electron microscope study of the origin of granular-cell myoblastoma. *J Pathol* 1973; **109**: 101–11.
- ⁸Fisher ER, Wechsler H. Granular cell myoblastoma—a misnomer. *Cancer* 1962; **15**: 936–54.
- ⁹Shousha S, Lyssiotis T. Correlation of carcinoembryonic antigen in tissue sections with spread of mammary carcinoma. *Histopathology* 1978; **2**: 433–47.
- ¹⁰Dursi JF, Hirschl S, Gomez R, Mersheimer WL. Granular cell myoblastoma of common bile duct; report of a case and review of the literature. *Rev Surg* 1975; **32**: 305–10.
- ¹¹Sherlock S, Scheuer PJ. The presentation and diagnosis of 100 patients with primary biliary cirrhosis. *N Engl J Med* 1973; **289**: 674–8.
- ¹²Dooley JS, Dick R, Olney J, Sherlock S. Non-surgical treatment of biliary obstruction. *Lancet* 1979; **2**: 1040–44.
- ¹³Nakayama T, Ikeda A, and Okuda K. Percutaneous transhepatic drainage of the biliary tract. *Gastroenterology* 1978; **74**: 554–9.
- ¹⁴Mulcare R. Granular cell myoblastoma of the breast. *Ann Surg* 1968; **168**: 262–8.
- ¹⁵Vidarthi SC. Granular cell myoblastoma of the breast. *Arch Surg* 1969; **98**: 662–7.
- ¹⁶Hertig AT, Gore H. Tumors of the female sex organs. *Atlas of tumor pathology* Washington, DC: Armed Forces Institute of Pathology, 1960: part 2.
- ¹⁷Campbell DC, Smith EP, Hood RH. Benign granular cell myoblastoma of the bronchus. Review of the literature and report of a case. *Chest* 1964; **46**: 729–33.
- ¹⁸Roje CI. Multiple endobronchial myoblastomas. *Arch Otolaryngol* 1965; **82**: 652–5.
- ¹⁹Moscovic EA, Azar HS. Multiple granular cell tumours (myoblastomas). *Cancer* 1967; **20**: 2032–47.
- ²⁰Vance SF, Hudson RP. Granular cell myoblastoma. Clinicopathologic study of 42 patients. *Am J Clin Pathol* 1969; **52**: 208–11.
- ²¹LiVolsi VA, Perzin KH and Badder EM. Granular cell tumours of the biliary tract. *Arch Pathol Lab Med* 1973; **95**: 13–7.
- ²²Whisnant JD, Bennett SE, Huffman SR, Weiss DL, Parker JC, Griffin WO. Common bile duct obstruction by granular cell tumour (Schwannoma). *Dig Dis Sci* 1974; **19**: 471–6.
- ²³Assor D. Granular cell myoblastoma involving the common bile duct. *Am J Surg* 1979; **137**: 673–5.
- ²⁴Cadotte M. Malignant granular cell myoblastoma. *Cancer* 1974; **33**: 1417–22.
- ²⁵Azzopardi JG. Histogenesis of the granular cell myoblastoma. *J Pathol* 1956; **71**: 85–94.

- ²⁶Burston J, John R, Spencer H. Myoblastoma of the neurohypophysis. *J Pathol* 1962; **83**: 455–61.
- ²⁷Abrikossoff AI. Über myome, ausgehend von der quergestreiften willkürlichen muskulatur. *Virchows Arch (Pathol Anat)* 1926; **260**: 215–33.
- ²⁸Willis RA. *Pathology of tumours*, London: Butterworths 1967: 752.
- ²⁹Stout AP, Lattes R. *Tumours of soft tissues* AFIP. Fascicle 1, 2nd Series, 1967: 94–8.
- ³⁰Murray MR. Cultural characteristics of three granular cell myoblastomas. *Cancer* 1951; **4**: 857–65.
- ³¹Pearse AGE. The histogenesis of granular cell myoblastoma. (?granular cell perineural fibroblastoma). *J Pathol* 1950; **62**: 351–62.
- ³²Garancis JC, Komorowski RA, Kuzma JF. Granular cell myoblastoma. *Cancer* 1970; **25**: 542–50.
- ³³Aparicio SR, Lumsden CE. Light and electron-microscope studies on the granular cell myoblastoma of the tongue. *J Pathol* 1969; **97**: 339–55.
- ³⁴Fust JA, Custer RP. On the neurogenesis of the so-called granular cell myoblastoma. *Am J Clin Pathol* 1949; **19**: 522–35.
- ³⁵McCormack LJ, Hazard JB, Dickson JA. Malignant epithelioid neurilemoma (schwannoma). *Cancer* 1954; **7**: 725–8.
- ³⁶Ashley DJB. In: *Evans' histological appearances of tumours*. Livingstone: Churchill: 1978: 50–2.
- ³⁷Whitmore JT, Whitley JP, LaVerde P, Cerda JJ. Granular cell myoblastoma of the common bile duct. *Dig Dis Sci* 1969; **14**: 516–20.
- ³⁸Zvargulis JE, Keating JP, Askin FB, Ternberg JL. Granular cell myoblastoma: a cause of biliary obstruction. *Am J Dis Child* 1978; **132**: 68–70.
- ³⁹Jain KM, Hastings OM, Rickert RR, Swaminathan AP, Lazaro EJ. Granular cell tumour of the common bile duct. *Am J Gastroenterol* 1979; **71**: 401–7.
- ⁴⁰Fialho F, Hilario J. Rabdomioma granuloso do cystico. *AMB* 1952; **9**: 616–8.
- ⁴¹Serpe SJ, Todd D, Barcu H. Cholecystitis due to granular cell myoblastoma of the cystic duct. *Dig Dis Sci* 1960; **5**: 824–26.
- ⁴²Goldman LI, Lemole G, Ellis R, Rosemond G. Granular cell myoblastoma of the cystic duct. *JAMA*, 1967; **200**: 1185–6.
- ⁴³Mackay G, Elliott GB, MacDougall JA. Granular cell myoblastoma of the cystic duct: report of a case with electron microscopic observations. *Can J Surg* 1968; **11**: 44–51.
- ⁴⁴Christensen AH and Ishak KG. Benign tumours and pseudo-tumours of the gall bladder. Report of 180 cases. *Arch Pathol Lab Med* 1970; **90**: 423–32.
- ⁴⁵Abt AB, Geinberg E, Kaunitz S. Granular cell myoblastoma of the extrahepatic biliary tree. *Mt Sinai J Med (NY)* 1971; **38**: 457–61.
- ⁴⁶Reul GJ, Rubio PA, Berkman NL. Granular cell myoblastoma of the cystic duct. A case associated with hydrops of the gall bladder. *Am J Surg* 1975; **129**: 583–4.
- ⁴⁷Ishii T, Iri H, Yamamoto S, Shinozawa Y, Sudoh M. Granular cell myoblastoma of the gall bladder. *Am J Gastroenterol* 1977; **68**: 38–44.
- ⁴⁸Farris KB, Faust BF. Granular cell tumours of biliary ducts. *Arch Pathol Lab Med* 1979; **103**: 510–2.
- ⁴⁹Kittredge RD, Baer JW. Percutaneous transhepatic cholangiography. *AJR* 1975; **125**: 35–46.