Virchows Arch (1998) 433:93–96

CASE REPORT

Dirk Theegarten · Anke Reinacher · Ulrich Graeven
Stathis Philippou

Mixed malignant germ cell tumour of the liver

Received: 21 November 1997 / Accepted: 20 February 1998

Abstract Germ cell tumours of the liver are rare neoplasms, with fewer than 20 cases reported in the literature following presentation as teratomas, choriocarcinomas or yolk sac tumours. We report a 52-year-old patient who complained of upper abdominal pain and anorexia. Ultrasonography and computed tomography of the abdomen revealed a large hepatic mass. Among the laboratory values we found elevated levels of alpha-fetoprotein and beta-chorionic gonadotropin. Repeated biopsies via CT scan, laparoscopy and laparotomy disclosed a poorly differentiated adenocarcinoma. Subsequently liver function deteriorated and, on the basis of clinical data highly suggestive of a malignant germ cell tumour, a modified chemotherapeutic protocol (PEI) was initiated. The elevated levels of alpha-fetoprotein and beta-chorionic gonadotropin declined rapidly, but the patient died 10 days later of liver dysfunction and bronchopneumonia. Subsequent autopsy confirmed the initial clinical diagnosis of a multilocular extragonadal malignant germ cell tumour of the liver with components of choriocarcinoma and embryonal carcinoma.

Key words Neoplasms of the liver · Extragonadal germ cell tumour · Choriocarcinoma · Embryonal carcinoma

Introduction

Extragonadal germ cell tumours originate from the primitive germ cell and may be found along the embryonal germ line, that is the midline of the body [7, 10]. Preferred tumour locations are the mediastinum, the retroperitoneum and the pineal and sacrococcygeal regions [6, 8, 19–21]. Germ cell neoplasms rarely develop in visceral organs [4]. Within the liver, teratomas [18, 25], choriocarcinomas [1, 5, 9, 12–14, 26] and yolk sac tumours [11, 17, 22, 23] have been described.

D. Theegarten (✉) · S. Philippou
Department of Pathology, Ruhr-University Bochum,
Universitätsstrasse 150, D-44780 Bochum, Germany
Tel.: (+49)-234-7006-760, Fax:(+49)-234-7094-200

A. Reinacher · U. Graeven
Department of Medicine, Knappschaftskrankenhaus,
University Hospital,
Bochum, Germany

Clinical history

A 52-year-old patient first came to our attention with a 6 week history of upper abdominal pain and anorexia. On physical examination a large epigastric mass was detected. Ultrasonography and CT scan of the abdomen revealed a multilocular hepatic tumour measuring 10.8×7.2 cm in maximum diameter and perigastric and mediastinal lymph node enlargement (Fig. 1). Laboratory findings included elevated levels of α-fetoprotein (AFP) of 1391.17 ng/ml (normal range 0–4) and β-human chorionicgonadotropin (β-HCG) of 6565 mU/ml (normal range <2), which are highly suggestive of extragonadal or metastatic germ cell tumour.

Ultrasonography of the testes and further CT scans revealed no signs of a primary testicular tumour. Laparoscopic liver biopsy, CT-guided biopsy and a diagnostic laparotomy with wedge exci-

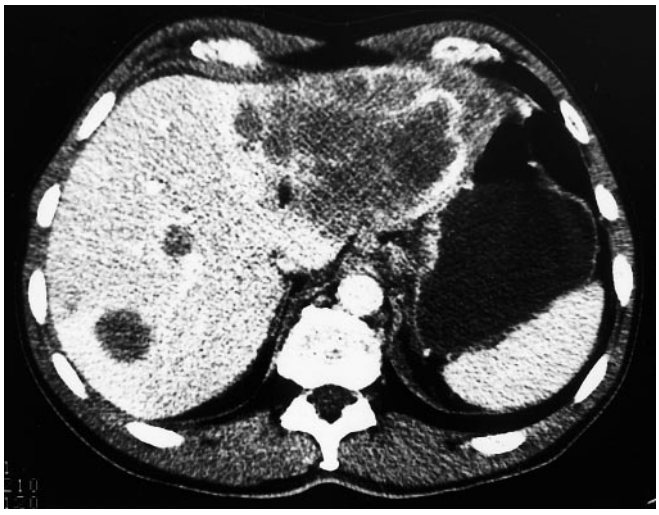


Fig. 1 Computed tomography of the abdomen, revealing a multilocular hepatic tumour measuring 10.8×7.2 cm in maximum diameter

sion were performed. Surprisingly, the clinical diagnosis of extragonadal germ cell tumour of the liver could not be confirmed histopathologically. Subsequently liver function deteriorated (bilirubin level 3.2 mg/dI), with levels of the tumour markers AFP and β-HCG rising steadily. On the basis of a clinical diagnosis of extragonadal germ cell tumour of the liver a modified chemotherapeutic protocol for germ cell neoplasms (PEI) was initiated. The levels of AFP (2729 to 329 ng/ml) and β-HCG (14.286 to 3536 m1 U/ml) subsequently declined rapidly. Progressive liver failure could not be prevented, however, and the patient died 10 days later of tumour cachexia and bronchopneumonia.

Materials and methods

Immunohistochemistry was done in addition to conventional staining (haematoxylin-eosin, elastica van Gieson, periodic acid-Schiff) using formalin-fixed, paraffin-embedded tissue. Monoclonal antibodies to human AFP (Dako, Glostrup, Denmark, dilution 1:100), β-HCG (BioGenex San Ramon, Calif., prediluted), placental alkaline phosphatase (PLAP, Dako, dilution 1:25), CD 30 (Dako, dilution 1:20) and cytokeratin (CK) subtypes (Progen, Heidelberg, Germany) 7 (dilution 1:50), 8 (dilution 1:10), 18 (dilution 1:20), 19 (dilution 1:10) and 20 (dilution 1:10) were applied using the avidin-biotin complex method.

Pathological findings

Histology of the first biopsies revealed tumour tissue with a partly tubulopapillary architecture in better differentiated areas (Fig. 2). Immunohistochemically, under l% of the malignant cells were positive for AFP. Staining for β-HCG and PLAP was completely negative.

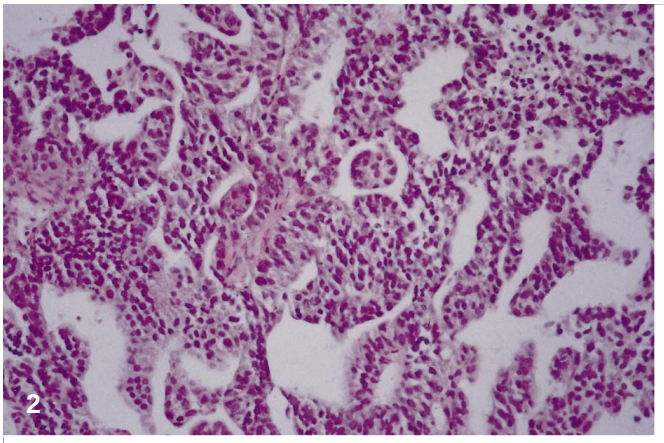
Although the mass was morphologically similar to a germ cell tumour, the negative immunohistochemical reactions led to the diagnosis of poorly differentiated adenocarcinoma. Two other pathologists were consulted, but a definite and consistent pathological diagnosis was not made.

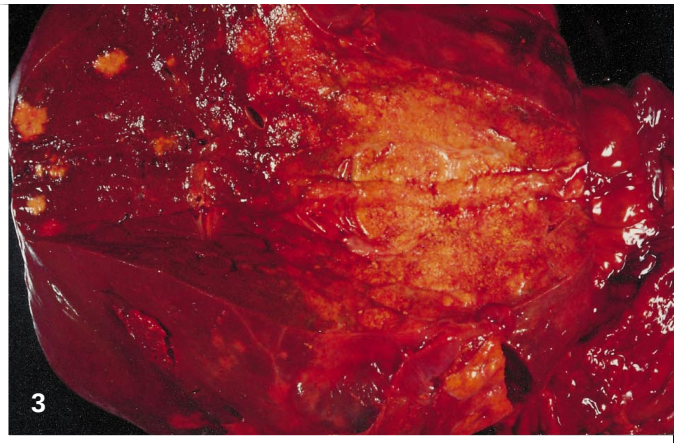
Autopsy revealed a large hepatic mass measuring 14×9×8 cm in diameter in the left lobe of the liver, with multiple intrahepatic metastases (Fig. 3) and an intramural metastasis at the oesophagogastric junction. Multiple perigastric, parapancreatic, para-aortic, and paratracheal lymph node metastases with a maximum diameter of 4 cm, and focal lymphangiosis carcinomatosa of the lung were seen. In addition, thrombosis of the portal vein was

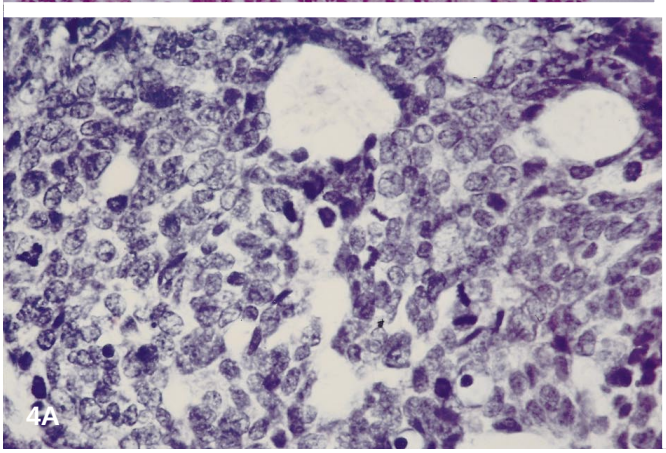
Fig. 2 Diagnosis of poorly differentiated adenocarcinoma is made from the wedge resection. Haematoxylin-eosin, original magnification ×100

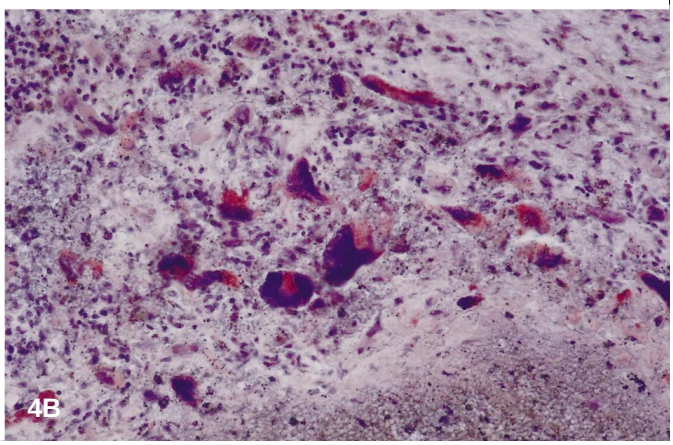
Fig. 3 Autopsy reveals a large yellow tumour in the left lobe of the liver, with a crumbly cut and multiple intrahepatic metastases

Fig. 4 **A** Histology of the autopsy samples shows large areas of a solidly structured carcinoma of the embryonal type without formation of mucus. Periodic acid-Schiff, ×200. **B** Immunohistochemically multinucleated giant cells of syncytiotrophoblast type and cytotrophoblast cells express β-HCG. Avidin-biotin complex, original magnification ×200









present and the immediate cause of death was bilateral purulent bronchopneumonia. No primary extrahepatic tumour was seen at autopsy, and examination of the testes revealed no tumour or scars.

Histopathologically the tumour consisted of two different components. In one part areas with adenoid differentiation resembling that of embryonal carcinoma were found, with focal immunohistochemical expression of AFP, PLAP and CD 30 (Fig. 4A). Secondly, multinucleated giant cells of syncytiotrophoblast type and cytotrophoblast cells positive for β-HCG and large areas of necrosis, haemorrhage and intrahepatic cholestasis were seen (Fig. 4B).

Intrahepatic metastases showed adenoid differentiation like that of embryonal carcinoma, while all other extrahepatic metastases revealed biphasic differentiation side by side. These different areas had been missed by repeated biopsy. Thus, the final diagnosis of an extragonadal mixed germ cell tumour of the liver with components of choriocarcinoma and embryonal carcinoma was made at autopsy. After this final diagnosis was made, CK subtypes were analysed: CK 8 was strongly positive, CK 18 and 19 were focally positive, and CK 7 and 20 were negative.

Histology of the testes showed extensive spermatogenic hypoplasia, probably as an effect of chemotherapy. No atypical germ cells or scars were found.

Discussion

Extragonadal germ cell tumours originate from the primitive germ cell and present with the same histological differentiation as gonadal germ cell tumours [7, 10]. Extragonadal germ cell neoplasms are mainly located along the midline of the body [6, 8, 19–21] but may also be found in various visceral organs [4]. Germ cell tumours of the liver are extremely rare, with fewer than 20 cases described in the literature [3]. The age range of the patients reported is 3 weeks to 67 years.

Tumours frequently consist of different pathological components such as yolk sac tumours, teratoma and chorionic carcinoma [20, 21]. A combination tumour made up of an embryonal carcinoma and a chorionic carcinoma of the liver has not previously been described in the literature.

In this case the morphological appearance and the presence of a choriocarcinomatous component argued against adult hepatoblastoma, which might be suspected in case of an exclusively adenoid differentiation [2]. Focal expression of β-HCG is occasionally seen in hepatocellular carcinoma [15, 16]. Only CK 8, the CK type universally present in all adenocarcinomas, was strongly expressed. CK 7, typically seen in cholangiocellular carcinomas, was negative. Together with focal expression of CK 18 and 19, the reactions of CK subtypes do not allow the diagnosis of hepatocellular or cholangiocellular carcinoma [3].

Laboratory findings with elevated levels of AFP and β-HCG, rapidly decreasing after initiation of chemotherapy, and the morphology of autopsy specimens and immunohistochemistry with expression of AFP, PLAP, CD30 and β-HCG strongly favour the diagnosis of mixed extragonadal germ cell tumour of the liver [24].

This case demonstrates that although a firm histopathological diagnosis is crucial before treatment of any malignant neoplasm, in rare cases chemotherapy for potentially curable disease should be initiated on the basis of clinical data alone, especially if other therapeutic options are lacking.

References

1. Alonso FJ, Saez C, Perez P, Montano A, Japon MA (1992) Primary pure choriocarcinoma of the liver. Pathol Res Pract 188:375–377
2. Altmann HW (1992) Epithelial and mixed hepatoblastoma in the adult. Histological observations and general considerations. Pathol Res Pract 188:16–26
3. Anthony PP (1994) Tumours and tumour-like lesions of the liver and biliary tract. In: MacSween RNM, Anthony PP, Scheuer PJ, Burt AD, Portmann BC (eds) Pathology of the liver. Churchill Livingstone, Edinburgh, pp 635–711
4. Atkinson JB, Foster CE, Lally KP, Isaacs H, Siegel SE (1992) Primary endodermal sinus (yolk sac) tumour of the falciform ligament. J Pediatr Surg 27:105–107
5. Belchis DA, Mowry J, Davis JH (1993) Infantile choriocarcinoma. Re-examination of a potentially curable entity. Cancer 72:2028–2032
6. Bukowski RM, Wolf M, Kulander G, Montie J, Crawford ED, Blumenstein B (1993)Alterning combination chemotherapy in patients with extragonadal germ cell tumours. A Southwest Oncology Group study. Cancer 71:2631–2638
7. Chaganti RSK, Rodriquez E, Mathew S (1994) Origin of adult male mediastinal germ-cell tumours. Lancet 343:1130–1132
8. Delgado FG, Tjulandin SA, Garin AM (1993) Long term results of treatment in patients with extragonadal germ cell tumours. Eur J Cancer 29:1002–1005
9. Fischer B (1913) Primäres Chorionepitheliom der Leber. Frankfurter Z Pathol 12:462–480
10. Friedman FB (1951) The comparative morphogenesis of extragenital and gonadal teratoid tumours. Cancer 4:265–276
11. Hart WR (1975) Primary endodermal sinus (yolk sac) tumour of the liver. First reported case. Cancer 35:1453–1458
12. Heaton GE, Matthews TH, Christopherson WM (1986) Malignant trophoblastic tumours with massive hemorrhage presenting as liver primary. A report of two cases. Am J Surg Pathol 10:342–347
13. Hongo T, Fujii Y, Fukuoka T, Iijima S, Matsusita T, Nakagawa Y, Igarashi Y (1992) Long-term treatment in infantile choriocarcinoma. Acta Paediatr Jpn 34:52–59
14. Kim SN, Chi JG, Kim YW, Dong ES, Shin HY, Ahn HS, Kim CW (1993) Neonatal choriocarcinoma of the liver. Pediatr Pathol 13:723–730
15. Nakagawara A, Ikeda K, Tsuneyoshi M, Daimaru Y, Enjoji M, Watanabe I, Iwafuchi M, Sawada T (1985) Hepatoblastoma producing both alpha-fetoprotein and human chorionic gonadotropin. Cancer 56:1636–1642
16. Nakanuma Y, Unoura M, Noto H, Ohto G (1986) Human chorionic gonadotropin in primary liver carcinoma in adults. An immunohistochemical study. Virchows Arch [A] 409:365–73
17. Narita T, Moriyama Y, Ito Y (1988) Endodermal sinus (yolk sac) tumour of the liver. A case report and review of the literature. J Pathol (Lond) 155:41–47

18. Robinson RA, Nelson L (1986) Hepatic teratoma in an anencephalic fetus. Arch Pathol Lab Med 110:655–657
19. Rosado-de-Christenson ML, Temleton PA, Moran CA (1992) Mediastinal germ cell tumours: radiologic and pathologic correlation. Radiographics 12:1012–1030
20. Taccagni GL, Parafioriti A, Dell'Antonio G, Crespi G (1989) Mixed germ cell tumour of the mediastinum (seminoma, embryonal carcinoma, choriocarcinoma and teratoma). Light and electron microscopic cytology and histological investigation. Pathol Res Pract 185:506–510
21. Talerman A (1985) Germ cell tumours. Ann Pathol 5:145–157
22. Villaschi S, Balistreri P (1991) Endodermal sinus tumour of the liver. Histopathology18:86–88
23. Wakely PE, Krummel TM, Johnson DE (1991) Yolk sac tumour of the liver. Mod Pathol 4:121–125
24. Wick MR, Swanson PE, Manivel JC (1987) Placental-like alkaline phosphatase re-activity in human tumours: an immunohistochemical study of 520 cases. Hum Pathol 18:946–954
25. Yarbrough SM, Evashwick G (1956) Case of teratoma of the liver with fourteen-year postoperative survival. Cancer 9:848–850
26. Zalka E de (1928) Concerning ectopic chorionepithelioma. Report of two cases. Am J Pathol 4:59–73