of arterial origin^{3,4} although one in the inferior vena cava also contained undifferentiated small cells¹ and a case in the superior vena cava was epithelioid with only moderate pleomorphism.² Intimal sarcomas show immunopositivity for vimentin, most are positive for smooth muscle actin,¹ some for factor VIII related antigen^{2,6,7} and one for cytokeratin² but all are negative for desmin. Burke and Virmani¹ suggest that the tumours arise from intimal myofibroblastic cells and the immunohistochemistry in this case supports such a suggestion, markers of endothelium being negative. Factor VIII related antigen positivity and adjacent endothelial atypia have lead to the suggestion of a possible endothelial origin.^{6,7} However, in 10 cases of intimal sarcoma there was no factor VIII related antigen positivity.¹

Here, we described an uncommon tumour, intimal sarcoma, arising in a previously unreported site, the right brachiocephalic vein. It had caused obstruction of the superior vena cava, an extremely rare cause of this syndrome. Most intimal sarcomas arise in arteries and

show a variety of histological and immunohistochemical appearances. This venous tumour had features similar to most arterial neoplasms, showing evidence of myofibroblastic lineage and an MFH-like morphology. Despite palliative radiotherapy, survival after presentation was short, reflecting the generally poor prognosis of intimal sarcomas.¹

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- 1 Burke AP, Virmani R. Sarcomas of the great vessels. A clinicopathological study. *Cancer* 1993;71:1761-73.
- 2 Downes AJ, Jones TJ, Wilson RSE. Intimal sarcoma of the superior vena cava. *Postgrad Med J* 1993;69:155-6.
- 3 Kaiser LR, Urmacher C. Primary sarcoma of the superior pulmonary vein. *Cancer* 1990;66:789-95.
- 4 Khan MA, Davidson RC. Malignant fibrous histiocytoma of the pulmonary vein with prolapse through the mitral valve orifice. *Postgrad Med J* 1992;68:680-2.
- 5 Enzinger FM, Weiss SW (eds). Miscellaneous sarcomas of vascular origin. In: *Soft tissue tumours*. 3rd edn. St Louis: Mosby, 1995:508.
- 6 Fitzmaurice RJ, McClure J. Aortic intimal sarcoma: an unusual case with pulmonary vasculature involvement. *Histopathology* 1990;17:457-62.
- 7 Haber LM, Truong L. Immunohistochemical demonstration of the endothelial nature of aortic intimal sarcoma. *Am J Surg Pathol* 1988;12:798-802.

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Alpha-fetoprotein production by a malignant mixed müllerian tumour of the uterus

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Abstract

A case of α -fetoprotein production by a uterine malignant mixed müllerian tumour is described. The patient was a 68 year old woman who developed intra-abdominal recurrence of a stage 1 uterine tumour which had been treated surgically seven years previously. Her serum α -fetoprotein was raised at 21 000 $\mu\text{g/l}$ (normal <10 $\mu\text{g/l}$) and staining with immunoperoxidase confirmed that the tumour was the site of α -fetoprotein production. The patient was treated with combination chemotherapy but died two weeks after the first course. This is believed to be only the second such case reported.

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Keywords: α -fetoprotein, malignant mixed mesodermal tumour, uterus.

Alpha-fetoprotein is an important tumour marker in germ cell tumours and hepatocellular carcinoma and occasionally may be raised in other cancers. In 1985, Kawagoe reported a case in which a malignant mixed müllerian tumour (MMMT) produced α -fetoprotein.¹ Here, we report a second case and discuss the

relevance to the histogenesis of MMMT and the possibility of using serum α -fetoprotein concentrations to monitor the progress of disease.

Case report

A 68 year old woman presented with a one month history of symptoms of partial small bowel obstruction. A computed tomography scan showed a large heterogeneous intra-abdominal mass and a hyperechoic liver. She had a past history of a stage 1 uterine MMMT which had been treated by total hysterectomy, bilateral salpingo-oophorectomy and pelvic lymphadenectomy seven years previously and a pulmonary carcinoid tumour by left upper lobectomy six years later. Laboratory investigations included a noticeably raised serum α -fetoprotein concentration (21 000 $\mu\text{g/l}$ (normal <10 $\mu\text{g/l}$)) and a raised CA 125 (710 units/l (normal <35 units/l)). The patient underwent a needle core biopsy of the abdominal mass.

PATHOLOGY

The core biopsy specimen, which measured 0.5 $\times$ 0.1 cm, showed metastatic MMMT with sharply demarcated carcinomatous and sar-

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Figure 1 MMT showing strong cytoplasmic α -fetoprotein reactivity in all cells of the carcinomatous component (above), but negative in the sarcomatous component. (Immunoperoxidase $\times 400$.)

comatous components. The carcinomatous component could not be classified beyond poorly differentiated adenocarcinoma, while the sarcomatous component was undifferentiated. Both showed high grade nuclear atypia. Eosinophilic hyaline intracytoplasmic globules were seen in a small number of cells within the carcinomatous component.

IMMUNOHISTOCHEMISTRY

There was strong cytoplasmic reactivity for α -fetoprotein (fig 1) and low molecular weight cytokeratin in the carcinomatous component only. Providing a mirror-image, the spindle cell component showed reactivity for vimentin and focally for desmin, but not for α -fetoprotein or cytokeratin.

REVIEW OF PREVIOUS PATHOLOGY

The original uterine tumour was an intracavity polypoid mass of soft white tumour, measuring $2.5 \times 1.5 \times 1.0$ cm, attached to the posterior wall of the body, with further detached similar tumour measuring $2 \times 2 \times 1$ cm. On histological examination, there was a homologous type MMT confined to the endometrium and with no evidence of spread to the Fallopian tubes, ovaries, pelvic, common iliac, or para-aortic lymph nodes. There were no hyaline globules and α -fetoprotein was not detected on staining with immunoperoxidase.

The lung tumour was a 2.1 cm circumscribed firm white mass, decending 0.1 cm into the pleura in the left upper lobe. Histology showed a carcinoid tumour characterised by sheets, trabeculae and ribbons of ovoid neoplastic cells with generally mild pleomorphism, stippled chromatic and small nucleoli. Alpha-fetoprotein was not detected on staining with immunoperoxidase.

FOLLOW UP

The patient was treated with carboplatin and adriamycin chemotherapy, but developed worsening hypoalbuminaemia and ascites requiring paracentesis and intravenous albumin. She died two weeks after the first course of chemotherapy. A necropsy was not carried out.

Discussion

MMMT is an uncommon high grade, biphasic tumour characterised by carcinomatous and sarcomatous elements. It occurs as a primary tumour of the endometrium, ovary, tube, cervix, and peritoneum.² Recent evidence suggests that the sarcomatous element in MMT is metaplastic carcinoma rather than true sarcoma.²

Alpha-fetoprotein is the main fetal serum protein and is produced by the yolk sac and liver, and, subsequently, after the yolk sac has involuted, by the liver alone.³ Trace amounts are also produced by the fetal gastrointestinal tract. Alpha-fetoprotein is synthesised only to a very limited extent in normal adult tissues. When α -fetoprotein was discovered in large concentrations in hepatocellular carcinoma, it became the first of a new class of substances, the oncofetal antigens. These substances are synthesised by the fetus and in neoplastic conditions, but not in normal adult tissues. Oncofetal antigens reflect the re-expression of fetal genes in malignant cells and serve as markers for the diagnosis and progression of neoplasia.

The tumours that characteristically express α -fetoprotein are those whose histogenesis reflects the sites of fetal α -fetoprotein production—that is, yolk sac tumours and hepatocellular carcinomas. Hepatoid carcinomas are a rare group of extrahepatic tumours and have been found in the stomach, pancreas, kidney, bladder, and ovary. These tumours show liver differentiation and produce α -fetoprotein.⁴ Occasionally, upper gastrointestinal tract cancers and ovarian mucinous adenocarcinomas of intestinal type express α -fetoprotein.⁵ While all of these tumours show a link with the sites of α -fetoprotein production in the fetus, α -fetoprotein is expressed rarely by tumours which seem to be histogenetically unrelated, including lung and renal carcinoma and rhabdomyosarcoma.³ MMT, with only one previously reported case with α -fetoprotein production, falls into this last category.¹ In our case α -fetoprotein expression was probably focal, as it was not seen in the samples of the primary uterine MMT.

Alpha-fetoprotein can be used as a convenient tumour marker, regardless of the type of tumour which expresses it. It is easily measured in the serum and has a known half-life of four to six days. It is effective in germ cell tumours where it is an important prognostic factor at diagnosis and, when present at raised concentrations, provides an accurate means of monitoring tumour activity and response to treatment.

The clinical importance of α -fetoprotein production in the case reported here is uncertain. It

may suggest a separate histogenesis compared with other cases of MMT. Alpha-fetoprotein may provide a useful marker for monitoring response to treatment in cancers other than germ cell tumours. This case also provides an important lesson in diagnosis—the presence of a raised α -fetoprotein concentration in association with a pelvic tumour does not necessarily indicate the presence of a germ cell tumour.

- 1 Kawagoe KA. A case of mixed mesodermal tumour of the uterus with alphafetoprotein production. *Jpn J Clin Oncol* 1985;15:577–83.
- 2 Zaloudek C, Norris HJ. Chapter 13. Mesenchymal tumors of the uterus. In: Blaustein's *Pathology of the female genital tract*. New York: Springer-Verlag, 1994:487–528.
- 3 Jalanko H. Alpha-fetoprotein in cancer. *Ann Chir Gynaecol* 1989;78:27–31.
- 4 Ishikura H, Scully RE. Hepatoid carcinoma of the ovary. *Cancer* 1987;60:2775–84.
- 5 Nomura K, Miyasaka Y, Murae M, Terashima Y, Aizawa S. Ovarian mucinous cystadenocarcinoma producing alpha-fetoprotein. A case report. *Acta Pathol Jpn* 1992;42:372–5.

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An unusual association of Felty syndrome and TCR $\gamma\delta$ lymphocytosis

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Abstract

Felty syndrome, comprised of neutropenia, rheumatoid arthritis and splenomegaly, occurs in approximately 1% of patients with rheumatoid arthritis. Up to one third of these patients have an increased number of large granular lymphocytes. The usual immunophenotype of these cells is CD3+, CD8+, CD57+, T cell receptor (TCR) $\alpha\beta$. A patient with Felty syndrome and large granular lymphocytosis, who had an unusual immunophenotype CD3+, CD4–, CD8–, TCR $\gamma\delta$, is described. Her neutropenia responded to treatment with granulocyte colony stimulating factor (G-CSF), which was given in order to raise her neutrophil count prior to bilateral knee replacement surgery. Thus, Felty syndrome with large granular lymphocytosis is a heterogeneous condition, one in which TCR $\gamma\delta$ large granular lymphocytosis may be found, and also shows a response to treatment with G-CSF.

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form of T cell lymphocytosis, in which the expanded lymphocytes have a large granular morphology.³ These proliferations of large granular lymphocytes (LGL) may be found in up to one third of patients with Felty syndrome, and may be clonal in nature, representing a form of LGL leukaemia.^{4,5} The usual immunophenotype of these cells is CD8+, CD57+, T cell receptor (TCR) $\alpha\beta$. The nature of the role of these expansions, whether occult or overt, in the pathophysiology of Felty syndrome (and rheumatoid arthritis in general) is not clear.

Some patients with Felty syndrome and neutropenia may be troubled by recurrent infections, which may further add to the disability imposed by active or longstanding arthritis. Furthermore, the risk of infection due to associated neutropenia may be a relative contraindication to elective orthopaedic surgery indicated in these groups of patients. Treatment of patients with Felty syndrome and noticeable neutropenia in these situations remains unclear and unsatisfactory in many cases, although recent interest has focused on the use of granulocyte colony stimulating factor (G-CSF).⁶

Case report

This patient, a woman, was first diagnosed as having seropositive rheumatoid arthritis in 1961 when aged 40 years. The arthritis initially affected her small joints but gradually became more severe such that by April 1993, fixed flexion deformities were present in both knee joints. She was also found to have splenomegaly at this time. A full blood count revealed a haemoglobin of 1.1 g/l, with a total white cell count of $3.6 \times 10^9/l$, and a significant neutropenia of $0.8 \times 10^9/l$, consistent with a diagnosis of Felty syndrome. A small ulcer by the right ankle was also noted at this time. The neutropenia remained at this level, and gen-

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