Coexisting Metastatic Choriocarcinoma and Bladder Adenocarcinoma of Common Germ Cell Origin

Dear Editor,

A 51-year-old post-menopausal Chinese woman developed acute retention of urine and was treated with forceps removal of visibly obstructing friable soft tissue. This was not sent for histology. Imaging showed a 10.1 cm by 5.9 cm irregular heterogenous mass involving the bladder and uterus (Fig. 1), right hydronephrosis and hydroureter, and hypodense lesions in the liver and lungs. A pulmonary lesion biopsy yielded choriocarcinoma (Fig. 2). β-HCG levels were 79,091 IU/L (Normal range <1.2 IU/L). She received 8 cycles of etoposide/methotrexate/d-actinomycin alternating with cyclophosphamide/vincristine[1] with normalisation of β-HCG levels, radiological reduction in masses, and resolution of the right hydronephrosis and hydroureter (Fig. 3). She then underwent a total hysterectomy and bilateral salpingo-oophorectomy with curative intent. Intraoperatively, a full thickness biopsy for gross thickening of the bladder was performed. Histology showed mucinous adenocarcinoma (Fig. 4) of the bladder wall with extensive peritoneal and regional lymph nodal involvement but no evidence of choriocarcinoma. The patient received palliative radiotherapy to the bladder for haematuria. Meanwhile, her β-HCG level rose from undetectable to >200,000 IU/L with a clinically palpable liver within 3 months.

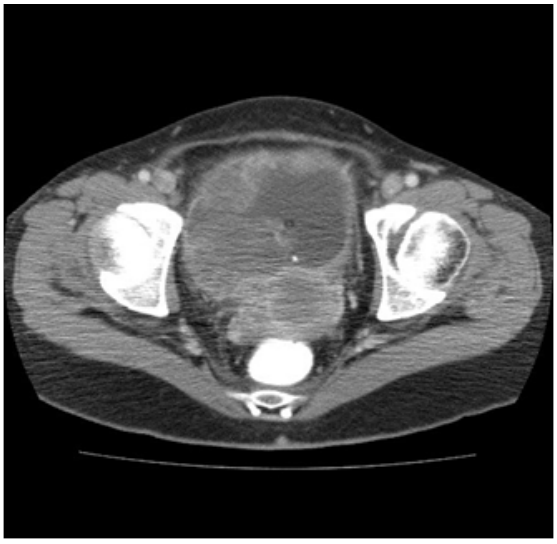

Fig. 1. Imaging pre-treatment showing pelvic mass involving the bladder and uterus, with concomitant liver metastasis.

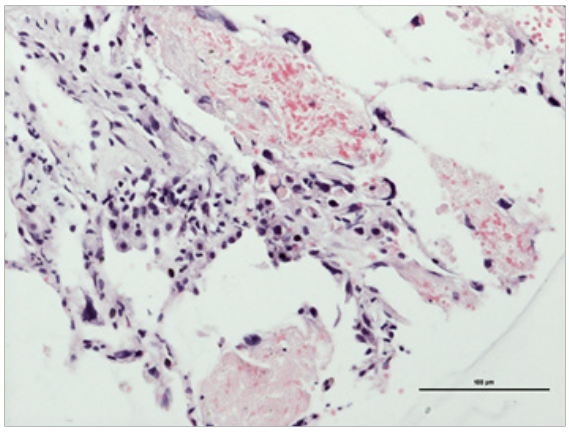

Fig. 2. Metastatic lung mass: choriocarcinomatous component (haematoxylin and eosin staining x20) showed high grade malignant tumour strongly positive for β-HCG, CD10 and CAM5.2.

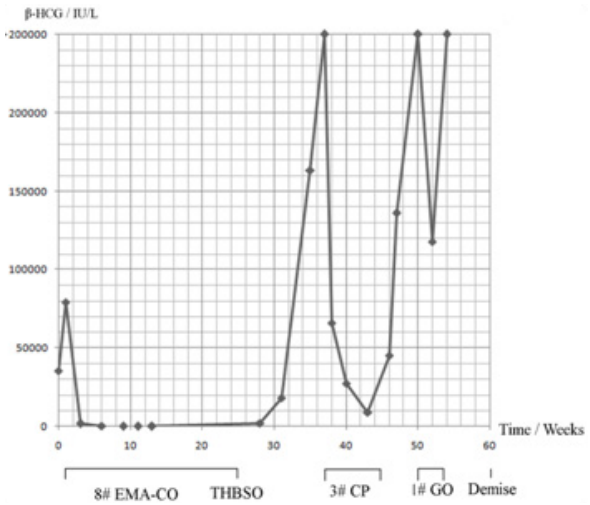

Fig. 3. This figure demonstrates the temporal relationship between β-HCG levels and treatment. The patient received 8 cycles of etoposide/methotrexate/d-actinomycin alternating with cyclophosphamide/vincristine (8# EMA-CO), underwent a total hysterectomy and bilateral salpingo-oophorectomy (THBSO), then received 3 cycles of cisplatin/paclitaxel (3# CP), and finally received 1 cycle of gemcitabine/oxaliplatin (1# GO).

After 3 cycles of cisplatin 750 mg/m^2 and paclitaxel 175 mg/m^2, her β-HCG level was 8660 IU/L. She declined further cycles and her β-HCG level rose to >200,000 IU/L within 7 weeks. FISH analysis of her sampled bladder tissue showed 12p gain in 46% of scored nuclei (Fig. 5). Analysis for 12p gain in the original lung biopsy tissue was unsuccessful due to a low number of cells. The patient agreed to 1 cycle of gemcitabine and oxaliplatin

with a subsequent decrease in β-HCG to 117,611 IU/L. She declined further treatment altogether, deteriorated, and passed away 2 months later.

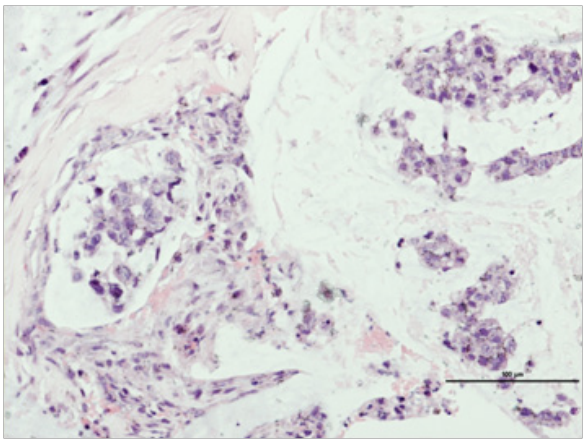

Fig. 4. Primary bladder tumour: adenocarcinomatous component (haematoxylin and eosin staining x20).

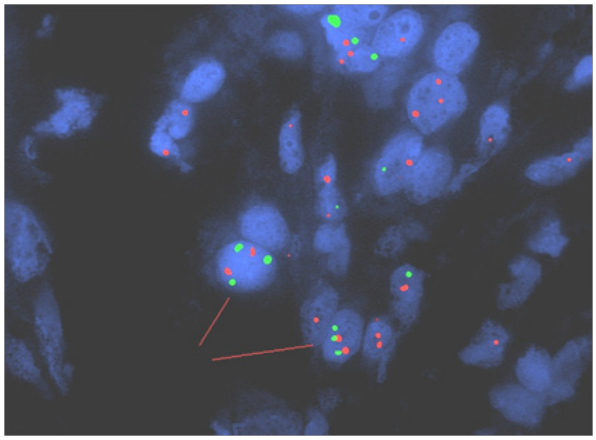

Fig. 5. Fluorescent in-situ hybridization with a TEL/AML1 dual-color translocation probe showing cells with three signals for *ETV6* at 12p13 (green) and two signals for *AML1* at 21q22 (orange) in the bladder mucinous adenocarcinoma as shown by the lines. This was seen in 92 of 200 cells (46%).

Thirty-one papers published since 1971 have described concomitant adenocarcinoma and choriocarcinoma[2] but none described bladder involvement. In our patient, the bladder was likely the concomitant primary site. 12p gain is a consistent feature of germ cell cancers including choriocarcinoma. It is mostly due to isochromosome formation.[3] Its presence in other subtypes of cancer strongly suggest germ cell origin.[4] 12p, the short arm of chromosome 12, contains 40 megabases and about 120 genes. Amplification of 12p11.2 to 12p12.1 is seen in a variety of cancers. *DAD-R* is a potential candidate gene in this region that may account for the pathological effects of 12p gain. Its overamplification leads to a low degree of apoptosis.[5] The pathogenesis of tumour differentiation from choriocarcinoma to adenocarcinoma is not well studied.

REFERENCES

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