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94

ePTFE INFERIOR VENA CAVA PATCH RECONSTRUCTION SURGERY IN DELAYED CAVAL THROMBECTOMY IN A MALE PATIENT WITH PREVIOUS RADICAL NEPHRECTOMY DUE TO RIGHT KIDNEY TUMOR

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Background: Abdominal full vena cava thrombosis, abandoned after right radical nephrectomy, is very rare. We describe the complex surgical technique in a 38-year-old male patient with a full thrombus of the vena cava remaining after right radical nephrectomy. **Case Report:** A 38-year-old male with symptomatic abdominal pain was referred to our hospital one month after right radical nephrectomy due to kidney tumor. A CT scan prior to nephrectomy showed an 8-cm right renal mass with extended thrombosis in the inferior vena cava (IVC) until the iliac cross. No other abdominal mass had been previously described. The patient underwent right radical nephrectomy with abdominal Mercedes incision without caval surgery for thrombectomy. After the operation, the patient was referred to the oncologist for adjuvant therapy. The oncologist referred the patient back to the Urology Department for reconsideration of caval surgery. Xiphoid-pubic surgical abdominal incision was carried out with severe sub-hepatic abdominal viscerolysis of the ileum, right and transverse colon that occupied the previous right retroperitoneal kidney space. An urovascular approach was adopted with a double team. It was impossible to perform the usual incision in the root of the mesentery and Kocker maneuver, allowing the dissection of the aorta and the sub-hepatic IVC, because of the previous surgery. After the approach to the aorta and vena cava, the intra-hepatic vena cava was completely exposed with hepatic rotation. The left renal vein was completely prepared from the IVC through the kidney. A clamp up to the sub-diaphragmatic vena cava was placed; the hepatic vascular support was also prepared and clamped. Subsequently, we proceeded with incision of the IVC until the iliac bifurcation and the extended cavo-iliac thrombus was removed. In the ligated hilum cross of the right kidney vascular support, the thrombus was fixed to the wall of the vena cava and extended for several centimeters. Consequently, a large part of the IVC was removed together with the thrombus. Regular suturing of caval tissue was impossible. Subsequently, polytetraethylene expanded (ePTFE) material was tailored for a reconstruction patch in the vena cava. The ePTFE was much more useful than Dacron material. **Results:** Total operation time was 3.5 h, with a blood

loss of 700 ml and use of two transfusion units. No postoperative complication appeared and the patient was discharged in ten days. The 10-month outcome is excellent and the patient is metastasis-free. **Conclusion:** The multidisciplinary urovascular approach taken in this case is the gold standard, considering the possible outcome indicated by the kidney tumor pathology when the surgery is well done. A one-stage surgery, namely radical nephrectomy and the simultaneous removal of the thrombotic material, should always be considered in order to reduce early embolism phenomenon and early metastasis. Because of high perioperative mortality, it is strongly suggested these cases are referred to the surgical urovascular teams, which are familiar with such surgical procedures.

95

PRELIMINARY STUDY OF THE EFFECTS OF GEFITINIB, AN EGF-RECEPTOR INHIBITOR, ON PROSTATE CANCER STEM CELLS

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Background: Existing therapies for prostate cancer eradicate the bulk of cells within a tumor, but most patients go on to develop androgen-independent disease that remains incurable by current treatments. The progression of the disease seems to be caused by a small population of cells, named cancer stem cells, which show stem cell features: they are self-renewing, can differentiate and are highly tumorigenic *in vivo*. Using neurosphere culture strategies, unattached clusters of cells (prostatespheres) with cancer stem cell properties can be obtained from both malignant and non-malignant prostate tissues. The culture of prostaspheres is useful to obtain a consistent number of cancer stem cells and allows their propagation in an undifferentiated state. The epidermal growth factor receptor (EGFR) and its ligands (EGF, TGF- α) are overexpressed during the progression of benign, localized and metastatic forms of prostatic cancer. The up-regulated activation of EGFR signaling appears to sustain cell proliferation, vascularization, invasion and decrease of cell apoptosis. It has also been reported that the interruption of EGF-EGFR signaling by using a selective EGFR inhibitor, such as gefitinib, leads to growth inhibition and apoptotic death of many cancer cell types, including prostate tumor epithelial cells, both *in vitro* and *in vivo*. Moreover, gefitinib, combined

with cyclopamine, a selective inhibitor of the sonic hedgehog pathway, and docetaxel induced significant antiproliferative and apoptotic effects on side and non-side population cell fractions isolated from the WPE1-NB26 cell line (1, 2). This study investigated the antiproliferative effects of gefitinib on androgen-independent (DU145, PC3) and -dependent (LNCaP-C33) prostate cancer cell lines and on U285 non-malignant prostatic hyperplastic cells used as control. *Materials and Methods:* DU145, PC3 and LNCaP cell lines were cultured according to the supplier's instructions. U285 were cultured in RPMI medium with 10% FBS and 10% HS. Adherent cells of bulk cell lines were treated with gefitinib at different concentrations. After 24, 48 and 72 h of incubation, neutral-red and kenacid-blue stains on DU145, PC3 and U285 cells, and MTS assay on LNCaP cells were performed. *Results:* Data obtained from proliferation assays showed that gefitinib inhibited the cell growth in a concentration-dependent manner. IC_{50} values were obtained from the dose-response curves. The IC_{50} value after 48 h of incubation with gefitinib was higher than those after 24 h and 72 h of treatment in the LNCaP cell line. The IC_{50} value obtained using neutral-red staining revealed no significant differences in DU145 cells, whereas higher values were revealed after 24 h of treatment with gefitinib in the PC3 and U285 cell lines. Kenacid-blue assays showed the highest IC_{50} values after 24 h of treatment in all considered cell lines. *Discussion and Conclusion:* Gefitinib showed inhibitory effects on cell proliferation of differentiated prostate cancer and non-malignant prostatic hyperplastic cells. Further investigations are in progress to evaluate the cytotoxic and differentiative effects of gefitinib on prostate cancer stem cells obtained with the prostasphere culture method from the considered cell lines (DU145, PC3, LNCaP and U285).

1 Mimenault *et al.*: Int J Cancer 118: 1022-1031, 2006.

2 Mimenault *et al.*: Mol Cancer Ther 9(3): 617-630, 2010.

96

CLINICAL IMPACT OF GENETICS ON RENAL CANCER: WHEN FOLLOW-UP NEEDS A MULTIDISCIPLINARY APPROACH

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Renal cancer occurs in hereditary and sporadic forms. The hereditary forms of the disease differ from the sporadic forms because they tend to be multifocal in the same kidney, bilateral and develop at young age. The true prevalence of hereditary

kidney cancer is not known as many cases are unrecognized. It is estimated that 3-5% of kidney cancer patients have inherited forms of the disease. Known hereditary kidney cancer syndromes include von Hippel-Lindau (VHL) disease, familial non-VHL clear-cell renal carcinoma (non-VHL CCRCC) with or without chromosome 3 translocation, hereditary papillary renal cancer, Birt-Hogg-Dube syndrome, hereditary leiomyomatosis and renal cell carcinoma syndrome, and tuberous sclerosis. Besides establishing the heredity of the tumors by family history, it is equally important to establish the associated clinical features, including the exact histology of the renal tumors in the family. Our experience considers a careful analysis of the patient's medical history and of the patient's family medical history as part of routine cancer follow-up. This approach may lead to support the cancer follow-up with the genetic counseling with a urinary assay of vanilmandelic acid, metanephrines, catecholamines and the constitutional karyotype analysis. The case study showed a CCRCC with a balanced translocation between chromosomes 3 and 4 (q12; p12), with a 50% risk of transmitting the same translocation to the offspring and a significantly increased risk of developing kidney cancer compared to the general population. The correct identification of familial adult renal neoplasia allows better management of the patient and their relatives, with early screening and careful follow-up, with the goals of minimizing disease-related morbidity and improving survival.

97

NOMOGRAM WITH PSA ACCELERATION PREDICTING HIGH-GRADE PROSTATE CANCER

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Background: Many patients diagnosed with low-grade prostate cancer have indolent disease and may not benefit from immediate therapy. Little is known about the relative utility of pre-diagnostic PSA kinetics to predict tumor aggressiveness. The aim of this study was to develop a model with PSA kinetics for high-grade prostate cancer risk and to determine its best range of values in terms of specificity and sensitivity. *Materials and Methods:* A prospective Institutional Review Board-approved database of 12-core prostate biopsies performed at the same Institution from January 2001 to June 2010 was searched for men with at least three consecutive PSA measurements for more than 730 days. The natural logarithm of PSA (log PSA) was used to create the best-fit line by least-squares' regression; the acceleration of PSA was the slope of this line (log PSA slope). A logistic