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Expression and clinical relevance of the lung resistance protein in germ cell testicular tumours

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Background: LRP was first described in a non-P-glycoprotein-mediated multidrug resistance lung cancer cell line. A prognostic role of LRP was suggested in ovarian cancer, and diffuse large B-cell lyphomas, but not in breast cancer. LRP expression and its clinical relevance in germ cell tumours (GCTs) are unknown.

Material and methods: LRP mRNA was determined by RT-PCR. LRP protein was detected by immunohistochemistry (IH) and Western blotting methods (WB). Seventy primary testicular tumours were evaluated. Tumour response to treatment and patient's clinical parameters were recorded. Ficher's exact test was used for statistical evaluation.

Results: LRP immunostaining was detected in 29 (41%) out of 70 primary testicular cancers; in 6 (40%) of the 15 seminomatous and 23 (42%) of 55 nonseminomatous (NS) cases. In the NS group 8 pure teratomas, 2 embryonal carcinomas, and 13 teratoma components of mixed tumour showed LRP expression. Among the mixed type of tumours 3 seminomas, 4 embryonal carcinoma components were also positive against LRP antibody. Pure teratoma and teratoma component of mixed tumour expressed significantly higher LRP compared with other subtypes of tumour (p=0.02). 22 out of 34 tumour expressed LRP protein and mRNA examined by WB and RT-PCR. In 18 of 22 tumour expressing LRP protein and mRNA were also positive by IH. The sensitivity and specificity of IH compared to RT-PCR and WB was 82% and 100% respectively. No correlation between LRP immunostaining and clinical staging was demonstrated (p=0,22). Sixteen patients (8 pure teratomas, 5 mixed tumour 4 with teratoma components and 3 others) with advanced stage disease received primary chemotherapy. Six patients died (5 pure teratomas and 1 mixed tumour with teratoma component) due to chemoresistance, however no significant association between LRP expression and chemoresistance was established (P=0,2),

Conclusion: LRP expression occurs in GCT and IH is a reliable method to evaluate LRP expression in testis cancers. We did not find correlation between LRP expression, and clinical drug resistance. However the high association of LRP immunostaining and teratomas suggests that LRP may contribute in chemoresistance, in this tumour type, which should be further evaluated.

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Long-term results following one course of adjuvant chemotherapy for high-risk stage I non-seminomatous germ cell tumors: the Spanish germ cell cancer group experience

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Purpose: Patients (pts) with clinical stage I non-seminomatous germ cell tumor (NSGCT) with pathologic high-risk features have a recurrence risk on observation of approximately 40%. This study evaluates the long-term efficacy of the administration of one course of adjuvant chemotherapy in a series of pts treated in a multi-institutional setting.

Material and Methods: From October 1994 to May 1999, 21 pts with clinical stage I NSGCT with vascular invasion (15 pts); or invasion beyond the albuginea, into the epididymis or the spermatic cord (6 pts), were treated in 9 hospitals with one course of cisplatin 100 mg/m2, etoposide 400-500 mg/m2 and weekly bleomycin 30 mg (BEP), after orchidectomy.

Results: Median time of follow-up was 61 months, with all pts followed-up for at least 3 years. All the pts have remained alive and free of disease to date. The actuarial event-free survival at 5 years was 100%. No grade 3 and 4 hematological toxicity was observed. Non-hematological toxicity was mild, and consisted mainly of nausea, vomiting and alopecia. No significant long-term sequelae were found.

Conclusion: After long-term follow-up, the administration of one course of BEP appears to be an effective therapeutic alternative for clinical stage I pts with high-risk of relapse. Comparison with adjuvant treatment with two cycles of BEP would be of interest.

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Does prostate cancer dedifferentiate over time?

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Background: It remains uncertain whether prostate cancer dedifferentiates over time. To illuminate further insight into this unanswered question, we have examined whether there is any histological upgrading from radical prostatectomy (RP) to local recurrence in patients with clinically isolated, biopsy proven, local recurrence following RP.

Method: Retrospective, single institution study. A total of 43 patients with clinically isolated, biopsy proven, local recurrence following RP were retrospectively analyzed to assess the change in Gleason score (GS) from RP to local recurrence. Central pathology review was undertaken for both RP and local recurrence biopsy specimens. The changes in primary and secondary Gleason grade (GG), and any potential correlation between the extent of GS change and other variables were also examined.

Results: Median age at the time of local recurrence was 67 years (range: 55-78). RP was performed between 1983 and 1998. Pathological stage was PT2 in 13, PT3a in 24, and PT3b in 6. 28 patients had positive surgical resection margins, while 15 did not. 8 had a short course (< 3 months) of hormone therapy prior to RP. Initial GS at the time of RP was 5, 6, 7, 8, and 9 in 1, 3, 29, 1, and 9 patients, respectively. Median interval between RP and local recurrence was 3.6 years (range: 0.3-17.7; mean: 4.2 years). Clinical evidence of relapse was confined to the prostate bed, as all had normal bone scan and CT scan of abdomen and pelvis. At the time of local recurrence, GS was upgraded in 13, unchanged in 23, and downgraded in 7. Excluding 8 receiving hormone prior to RP, GS was upgraded in 11, unchanged in 20, and downgraded in 4. Primary GG was upgraded in 10, unchanged in 28, and downgraded in 5. The extent of GS change was correlated with the interval between RP and local recurrence (p=0.08), but not pathological T stage or age.

Conclusion: There was a trend, though not statistically significant (p=0.36), toward a higher GS at the time of local recurrence. This trend was more pronounced when restricted to the 35 patients who did not have hormone prior to RP (p=0.08). The extent of GS change was associated positively with the elapsed time to local recurrence. The above findings are suggestive of cellular dedifferentiation over time. The main drawbacks of the study are selection bias and a small sample size.

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Concordance/Discordance of pathological evaluation of radical prostatectomy (RP) specimen between a community hospital and a tertiary teaching hospital

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Purpose: 1. To examine concordance or discordance between a community hospital (CH) and a tertiary teaching hospital (TTH) with respect to the grade, margin status, and tumor extent in RP specimens.

2. To assess and compare the completeness of a pathology report with respect to the aforementioned factors.

Materials and Methods: A phase II study, evaluating the combination of post-operative radiotherapy plus 2-year androgen ablation as either adjuvant or salvage therapy, accrued a total of 154 post-RP patients. All underwent retropubic RP for prostate adenocarcinoma as primary therapy. 113/154 RP cases were performed at a community hospital and the basis of this study. Their RP specimens were centrally reviewed by the Sunnybrook and Women's College Health Science Centre (a TTH) as a part of patient screening for study eligibility. The original CH pathology reports were compared with the central TTH consultative review with regards to concordance and completeness.

Results: Gleason score (GS): GS ranged from 4 to 9 in CH pathology reports. In TTH review, GS ranged from 6 to 9. 29% had GS 6 or less in CH reports, while only 17% did in TTH review. The highest concordance rate was for GS 7 at 87%. The lowest concordance rates were for GS 6 and 8. 62% of GS 6 were upgraded to GS 7 in TTH review. 11.5% of CH reports did not give GS, while 0.88% (due to marked anti-androgen treatment effect) did not in TTH review.

Resection margins and Tumor extent are shown in the table.