Management of metastatic squamous cell carcinoma cervical lymphadenopathy with "occult" primary – The role of surgery

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Introduction

* Cancer of unknown primary (CUP) is uncommon with 2/3 being metastatic SCC. (1-3% of all SCC head and neck cancers.)
* The dilemma:- *What kind of treatment would be appropriate* taking into account long-term disability?
* Ideally a multicentre RCT would give appropriate answers but numbers are so few that no such trial will be conducted for this group of patients.

References

* Clinical review. David W. Eisele. Members and invitees of the International Head and Neck scientific group.
* Part I. Review of diagnostic approaches. H&N July 2011.
* A review of therapeutic options. H&N July 2011.

Background

* Neider et al. before 2000 reviewed literature and showed that nodal recurrence and distant metastases were twice as common as the primary cancer appearance – *and even then there is the debate as to whether it is the index cancer or second primary*!
* Many questions remain unanswered.

Early stage neck disease.

* Without extracapsular extension (ECE), pN1 and early pN2 cases do equally well with surgery or DXT.
* Coster et al. reported 2/13 patients with recurrent neck disease after surgery – both had ECE.
* Miller 1/7 recurrence:- due to ECE.
* Simple excision of metastatic lymph node without ECE inadequate! (SMRND)
* Remember, the chances of primary tumour ever becoming evident is extremely low (<12%).
* Postoperative DXT does not improve locoregional or overall survival in this group of patients.
* Surgery **more cost effective** than DXT.

Advanced stage disease.

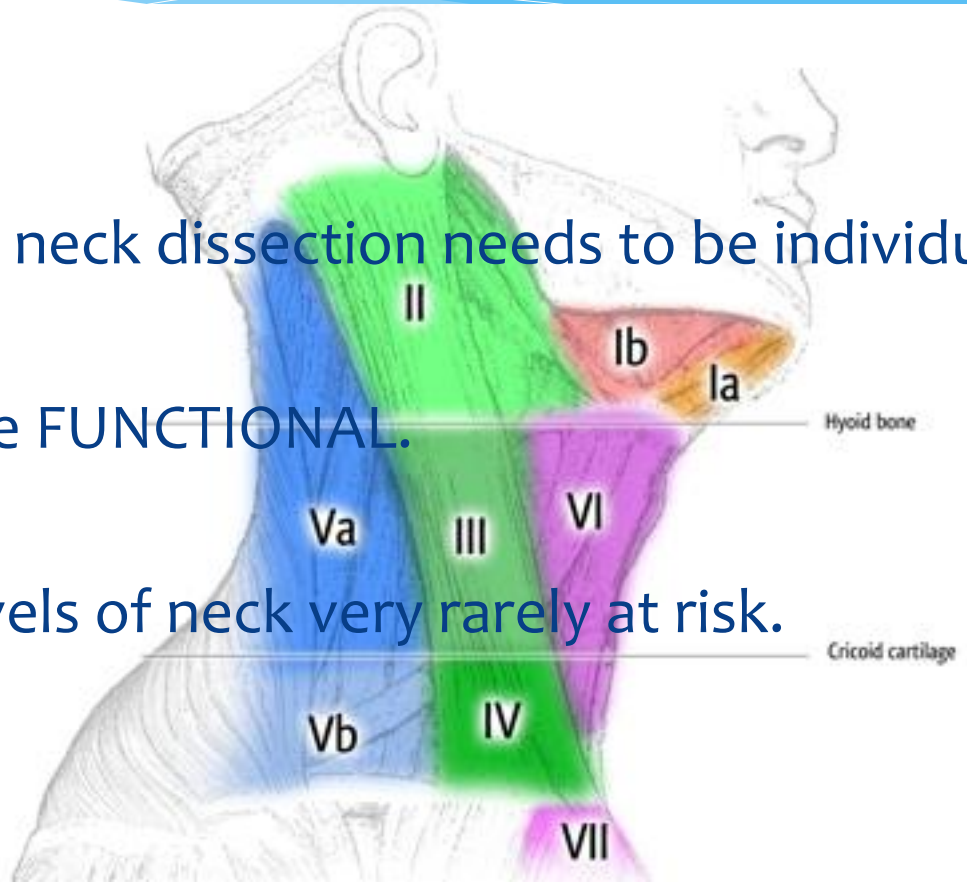
* Combined modality therapy more strongly indicated.
* Grau et al. reported 5-year neck control of **50%**; overall survival of **37%** and crude emergence of primary in 12% of 224 patients from 1975 to 1995.
* Recent small studies (better RT techniques and CT) with neck control rates **65.6% and 77.8%** and overall survival **68.5% and 77.8%**. Mucosal primary emergence 16.8% and 7.5%.
* Wallace et al. (and others) showed significantly better 5 year neck control with MRND: pre-RT ND 93%, post-RT ND 82%, no ND 73% (111 VS 70 patients).

Appearance of the primary tumour

* Up to 12% in various studies.
* BUT this is about the same incidence of metachronous second primary tumours.
* Most probably unrelated to the index cancer!
* Incidence **too small to justify morbidity** of elective "wide field" irradiation of potential primary sites.
* Survival rates not related to appearance of the "primary" anyway.
* Cost and disability of adjuvant DXT (*not justified*).

Neck Surgery

* Type of neck dissection needs to be individualised.
* Must be FUNCTIONAL.
* All 5 levels of neck very rarely at risk.



Systemic therapy

* Incidence of ***distant metastases*** ranges from 11 – 38% and strongly ***correlates with ECE, N2b and N3 disease***.
* *Probably only value of PET CT scan!*
* Rodel et al found in this group of patients combining platinum-based CT with RT decreased metastatic disease (36% vs 59%).
* Irresectable N2 and N3 disease also benefit from CRT.
* HPV positive tumours very responsive to primary RT =/- CT.

Conclusions

* Only in patients who have controlled neck disease would benefit from occult primary sterilisation (surgery/RT).
* Occult primary or second primary? More reason primary surgery!
* Latest technology very small risk of missing occult primary – treatment ("blind" CRT) weighed against morbidity.
* All 5 levels of neck rarely at risk – decrease surgical morbidity.
* Modern RT esp. IMRT have improved outcomes; *not without significant short and long-term toxic side effects though.*
* No real evidence that systemic therapy with RT (early disease) improves treatment efficacy in CUP.
* HPV tumours more sensitive to RT.

Conclusions

* Surgery or “involved field” RT alone is sufficient for pN1 or cN1 disease without macroscopic ECE.
* Advanced disease (N2 and N3 disease or N1 + ECE) – Combined approach.
* Probably unreasonable at this time to suggest a radical neck dissection should be performed in all patients with resectable N2 or N3 disease.