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Management of papillary and follicular thyroid cancer

Papillary and follicular thyroid cancers are well differentiated and slow growing, and have unique characteristics. Adjuvant treatments are thyroid hormone suppression and radioiodine (^{131}I) therapy rather than chemotherapy and radiotherapy. Prognosis is generally excellent and is influenced by factors related to the patient, the disease and the therapy. Factors associated with a less favourable outcome are male sex, family history of papillary cancer, age >40 years, tumour diameter >4 cm, invasive or poorly differentiated tumour and lymph node or distant metastases[1,2]. 5-year survival rates in England and Scotland may be lower than in many European countries[3], and audits suggest that variation in therapeutic effects is due to deficiencies in management[4,5]. Evidence from large randomized controlled trials is lacking because of the rarity, slow progression and good prognosis of these tumours, but retrospective clinical studies do shed light on controversial areas[1,2]. National guidelines under the auspices of the British Thyroid Association[6] address these issues and recommend an aggressive, three-stage management approach for most patients, including total or near-total thyroidectomy, ^{131}I ablation and thyroid hormone suppression therapy.

The first management stage for those with tumour diameters >1 cm includes total thyroidectomy with central node dissection and postoperative ^{131}I ablation. (Most patients should have undergone fine-needle aspiration cytology for diagnosis and for planning of treatment.) The reason for additional ^{131}I ablation is that, after surgery, most patients have thyroid remnants detectable on radioiodine scan. The treatment destroys residual thyroid tissue, including occult carcinoma, and facilitates subsequent detection of recurrent disease. Radioiodine ablation may be given four weeks after surgery, thyroid hormone treatment having been withheld postoperatively. A post-ablation scan is performed and, if uptake is discovered outside the thyroid bed, suggesting metastases, further therapy may be needed. Patients require thyroid hormone replacement, and the greater the suppression of thyroid stimulating hormone (TSH) the better the outcome[7]. Thyroxine is started on discharge from hospital and the dose is adjusted until serum TSH is <0.1 mu/L. Lobectomy followed by TSH suppression is considered only in low-risk patients with a unifocal non-invasive tumour $\leqslant 1$ cm[8].

After total thyroidectomy and ^{131}I ablation the second management stage includes a diagnostic radioiodine scan and serum thyroglobulin estimation (after thyroxine withdrawal) at six months. (Thyroglobulin is produced by normal and neoplastic thyroid cells and its detection after total thyroid ablation suggests recurrent disease; monitoring is less sensitive when the patient is on thyroid hormone suppression because thyroglobulin production depends on TSH stimulation[9].) If there is significant uptake in the neck, further ^{131}I is administered and a post-treatment scan is performed. If there is no significant uptake in the neck, thyroxine is restarted and low-risk patients enter the third management stage.

The third stage involves long-term follow-up to detect recurrent disease. Mortality rate at 30 years is 8% but recurrence rate is 30%. Two-thirds of recurrences are in the first 10 years after treatment but one-third are later[1]. Follow-up methods include clinical examination, TSH monitoring to ensure adequate suppression, diagnostic scan and serum thyroglobulin measurement. If thyroglobulin becomes detectable in a patient taking thyroxine then thyroxine is withdrawn, a diagnostic scan is performed and the thyroglobulin measurement is repeated. In selected patients, recombinant human TSH administration avoids the need for thyroxine withdrawal[10]. Management of those with a negative scan but detectable thyroglobulin is controversial. The thyroglobulin level suggesting recurrent disease is not known and the particular value may be less important than the change in level with time and the risk category of the patient. If a false-positive thyroglobulin and a false-negative scan are ruled out, local recurrence is likely and initial investigation includes neck ultrasound (possibly with fine-needle aspiration cytology) and chest X-ray. If these investigations are negative, a non-contrast CT scan of the chest and bone scans are considered. Glucose is taken up by tumours, and fluoro-18-deoxyglucose positron emission tomography scanning may be useful. Over-enthusiastic investigation is clearly possible and observation may suffice if thyroglobulin levels do not rise progressively.

The most common causes of death are local recurrence and pulmonary metastases. Locally recurrent tumour is resected surgically with subsequent ^{131}I therapy. Recurrences outside the neck are most frequently in lung but are also seen in bone. Patients whose metastases take up ^{131}I are treated with radioiodine and the overall 10-year survival

rate in those with distant metastases can be as high as 40%[2].

Guidelines for the management of differentiated thyroid cancer in adults[6] are comprehensive and lay great stress on the importance of aggressive early treatment. The management of medullary cell cancer of the thyroid is also covered. About 1000 new cases of thyroid cancer are reported in England and Wales each year[11], so a district general hospital serving a population of 500 000 will assess only 10 per year. In view of the long-term risk of recurrent disease, many of these patients should be under scrupulous lifelong follow-up. The best results are likely to come from well coordinated specialist care by a multidisciplinary team.

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REFERENCES

1 Mazzaferri EL, Jhiang SM. Long term impact of initial surgical and medical therapy on papillary and follicular cancer. Am J Med 1994:97:418–28

2 Loh KC, Greenspan FS, Gee L, Miller TR, Yeo PPB. Pathological tumor-node-metastasis (pTNM) staging for papillary and follicular thyroid carcinomas, a retrospective analysis of 700 patients. J Clin Endocrinol Metab 1997;82:3553–62

3 Teppo L, Hakulinen T and the Eurocare Working Group. Variation of survival in adult patients with thyroid cancer in Europe. Eur J Cancer 1998;34:2248–52

4 Vanderpump MPJ, Alexander L, Scarpello JHB, Clayton RN. An audit of the management of thyroid cancer in a district general hospital. Clin Endocrinol 1998;48:419–24

5 Hardy KJ, Walker BR, Lindsay RS, Kennedy RL, Secki JR, Padfield PL. Thyroid cancer management. Clin Endocrinol 1995;42:651–5

6 British Thyroid Association. Guidelines for the Management of Thyroid Cancer in Adults. London: Royal College of Physicians, 2002

7 Pujol P, Daures J-P, Nsakala N, Baldet L, Bringer J, Jaffiol C. Degree of thyrotrophin suppression as a prognostic determinant in differentiated thyroid cancer. J Clin Endocrinol Metab 1996;81:4318–23

8 Mazzaferri EL. Thyroid carcinoma: papillary and follicular. In: Mazzaferri EL, Samaan N, eds. Endocrine Tumours. Oxford: Blackwell Scientific, 1993:278–333

9 Oszata M, Suzuki S, Miyamoto T, Liu RT, Fierro-Renoy F, DeGroot LJ. Serum thyroglobulin in the follow-up of patients with treated differentiated thyroid cancer. J Clin Endocrinol Metab 1994;79:98–105

10 Robbins RJ, Tuttle M, Sharaf RN, et al. Preparation by recombinant human thyrotropin or thyroid hormone withdrawal are comparable for the detection of residual differentiated thyroid carcinoma. J Clin Endocrinol Metab 2001;88:619–25

11 Coleman PM, Babb P, Damiecki PG, et al. Cancer Survival Trends in England and Wales 1971–1995: Deprivation and NHS Region (Series SMPS, no. 61). London: Stationery Office, 1999:471–8

Drug-facilitated sexual assault, 'ladettes' and alcohol

In the past year the media have given much attention to the issue of drug facilitated sexual assault (DFSA), more emotively referred to as 'date-rape'[1]. In DFSA the victims are subjected to non-consensual sexual acts while they are incapacitated or unconscious through the effects of alcohol or drugs; they are therefore prevented from resisting or unable to consent[2].

For a rapist, the ideal substance to facilitate a sexual assault is one that is readily available, is easy to administer, impairs consciousness and causes anterograde amnesia. Drugs that have been associated with sexual assaults include flunitrazepam, gamma hydroxybutyrate and ketamine[2,3]. To preserve any evidence of such drugs, practitioners involved in the forensic assessment of complainants of sexual assault are encouraged to request blood and urine samples at the earliest opportunity[4,5]. The perception that drugs are frequently being administered (to males as well as females) in order to facilitate a sexual assault has led to development of 'prevention' strategies—many of them originating from college and student campuses in the USA, where concerns first arose. The prevention strategies generally relate to ways of avoiding surreptitious addition of date-rape drugs to alcoholic drinks; so young people are advised 'do not leave drinks unattended; don't take beverages, including alcohol, from someone you do not know well; at a bar, accept drinks only from the bartender or server; at parties, do not accept open-container drinks from anyone; be alert to the behaviour of friends—anyone appearing intoxicated may be in danger' [www.gnesa.org/date_rape_drugs/drugs.html]. The development of dipsticks that test drinks for drugs is being explored.

Important though these strategies are, few address or emphasize the evident fact that the most available and widely used date-rape drug is alcohol. Hindmarch and colleagues[6] have reported the results of 3303 urine samples

from individuals who claimed to have been sexually assaulted and believed that drugs were involved. 2026 samples were positive and in 44% of these the drug was alcohol alone. Alcohol, by itself or together with another agent, was by far the commonest substance detected, followed by cannabis (present in 30% of positives). Flunitrazepam was detected in 11 cases (0.54%) and gamma hydroxybutyrate in 100 (4.9%); ketamine was not tested. Hindmarch and colleagues conclude that no single drug other than alcohol can be particularly identified as a date-rape drug, and that alleged sexual assaults take place against a background of licit or recreational alcohol or drug use, where alcohol and drugs are taken concurrently. Despite these findings, media-led coverage and local initiatives[7] still concentrate on the 'drug' aspect of DFSA.

In the past decade in the UK the ready availability of palatable high-alcohol-volume drinks, coupled with the so-called 'ladette' culture, seems to have generated greater public acceptance of heavy drinking in young people—a special cause for concern in young women[8]. There is reason to fear that alcohol manufacturers, by mixing alcohol with fruit juices, energy drinks and premixed alcopops and using advertising that focuses on youth, lifestyle, sex and fun, are trying to establish a habit of drinking alcohol at a very young age. The Chief Medical Officer has focused on the increasing incidence of cirrhosis, calling for a harm-reduction strategy in young people to prevent cumulative damage to the liver[9]. We suggest that an important part of any public awareness campaign on the hazards of heavy drinking is the increased likelihood of suffering a sexual assault.

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REFERENCES

1 Carrell S. Special investigation: date rape. A fact the Home Office won't face up to: drug-assisted date rapes are up 50 per cent. Independent on Sunday. 16 December 2001

2 LeBeau M, Mozayani A. Drug-Facilitated Sexual Assault. A Forensic Handbook. London: Academic Press, 2001

3 Stark MM, Wells D. Drug-mediated sexual assault. J Clin Forens Med 1999;6:53–5

4 Rogers D, Newton M. Sexual assault examination. In: Stark MM, ed. A Physician's Guide to Clinical Forensic Medicine. New Jersey: Humana Press, 2000

5 Sexual assault in adults. Drugs Therap Bull 2002;40:1–4

6 Hindmarch I, ElSohly M, Gambles J, Salamone S. Forensic urinalysis of drug use in cases of alleged sexual assault. J Clin Forens Med 2001;8: 197–205

7 Metropolitan Police Service. Who's watching what you're drinking: Awareness Campaign. London: MPS, 2001

8 Plant M, Plant M. Heavy drinking by young British women gives cause for concern. BMJ 2001;323:1183

9 Department of Health. Annual Report of the Chief Medical Officer of the Department of Health. London: DoH, 2001