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Incidental detection of synchronous primary tumours during staging workup for prostate cancer

Orhan Özsoy[a], *Gérald Fioretta*[b], *Carmen Ares*[a], *Raymond Miralbell*[a]

[a] Radiation Oncology Service, Geneva University Hospitals, Geneva, Switzerland
[b] Geneva Cancer Registry, Institute for Social and Preventive Medicine, University of Geneva, Geneva, Switzerland

Summary

Questions under study: To assess the prevalence of incidental synchronous primary cancers discovered by abdominal CT scan among prostate cancer patients.

Methods: Patients with prostate cancer in Geneva, Switzerland, were retrospectively analysed regarding incidental diagnosis of synchronous second primary malignancies, including a cohort of 398 patients treated from 1991 through 2001 with radical radiotherapy (RT) and a second cohort of 419 patients treated from 1991 through 2001 by radical prostatectomy (RP) in order to analyse the differences between RT and RP patients. Both cohorts were evaluated regarding incidence of synchronous second primary cancers, compared with that expected in the general population (Standardized Incidence Ratio, SIR). The influence of staging workup on the diagnosis of incidental primary malignancies was studied.

Results: Six synchronous cancers (4 renal, 1 pancreatic, 1 rectal) were observed on abdominopelvic CT-scan among 480 patients (398 RT patients and 82 RP patients) (1.2%), who had been subjected to staging workup. For renal-cell carcinomas (RCC) in 398 RT patients (RCC) SIR was 18.19 (CI [Confidence Interval] 4.96-46.57), (p <0.001). After exclusion of 12 patients from RP cohort (n:419) in whom the prostate cancer was an incidental finding during surgery for bladder cancer (SIR 33.50 [CI 17.83–57.28]), (p <0.001), 407 patients were observed. There was no synchronous RCC among 325 RP patients who had no CT-scan.

Conclusions: In patients with prostate cancer, abdominopelvic CT staging detects incidental second primary cancers (mostly commonly RCC) with a greater frequency than that expected.

Key words: prostate neoplasms; kidney neoplasms; incidental cancer; synchronous second primary cancer; X-ray computerised tomography

Introduction

In the last two decades prostate cancer diagnosis has usually been followed by a pretreatment staging workup for most patients considered for radical radiotherapy (RT). Staging recommendations usually include both radionuclide bone scans and CT scans of the abdomen and pelvis. Although the sensitivity of both investigations is low for detection of disease extension to the lymph nodes or bones, abdominal CT studies can incidentally reveal clinically silent findings such as cysts, vascular abnormalities or tumours [1, 2]. Discovery of an incidental primary malignancy in particular often changes patient management. For example, in many cases the second primary tumour may require treatment more urgently than the prostatic malignancy, for which therapy would then be deferred.

The purpose of this report was to document the power of abdominal CT scan to detect synchronous primary malignancies in prostate cancer patients undergoing a staging workup before curative RT, compared with the incidence of second malignancies in patients undergoing radical prostatectomy (RP), in whom staging workups were not routinely carried out.

As multiple primary cancers of the urinary tract are not infrequent [3–5], we hypothesised that most incidental cancers detected by CT would be confined to the same organ system. Although there are reports in the literature regarding incidental intra-abdominal tumours, usually of renal origin, detected during imaging for unrelated health problems [2, 3, 6, 7], to our knowledge there are no published data concerning this aspect of prostate cancer staging.

No conflict of interest in relation to this article.

Methods

Between 1991 and 2001 at Geneva University Hospital 398 patients (mean age 67 years) treated by curative RT for prostate cancer underwent a staging workup including abdominal CT. Clinical records and those of the Geneva Tumour Registry (GTR), were reviewed in order to identify all synchronous primary cancers, characterise their mode of discovery and document subsequent follow-up in these patients. The GTR identified a second cohort of 419 prostate cancer patients (mean age 64 years), treated in Geneva during the same period by RP, of whom 84 patients also underwent a staging workup including abdominal CT. All second primary malignancies diagnosed within 6 months of the diagnosis of prostate cancer were obtained from the GTR records.The role of the staging workup , and of the abdominal CT scan in particular, was evaluated in each patient in whom a synchronous tumour was diagnosed. Using the GTR database we calculated standardised incidence ratios (SIR) by dividing the observed incidence of a specific second malignancy among prostate cancer patients by the incidence expected for the same tumour in a population with the same age profile.

Results

Among 398 patients in the RT cohort, 6 incidental second malignancies were detected (1.5%): four renal-cell carcinomas (RCC), one pancreatic cancer and one rectal cancer. All 6 malignancies were detected in asymptomatic patients by CT scan (398 RT patients and 82 RP patients: 1.2% of 480 patients who had a scan). No further malignancies were discovered 6 months after treatment of prostate cancer. Table 1 summarises the pertinent clinical information for these 6 patients. All incidental tumours were treated by cu-rative surgery before starting radiotherapy for prostate cancer; 4 of 6 patients (66%) are alive and free from recurrence of the second primary malignancies. The rate of detection of RCC was significantly increased compared with that expected in the general population, with an SIR of 18.19 (CI 4.96–46.57) ($p < 0.001$).

However, detailed analysis of RP cohort patients revealed that among 419 patients coded as having undergone RP, 12 were in fact bladder cancer cases in whom prostate cancer was diagnosed incidentally during cystectomy with an SIR of 33.50 (CI 17.83–57.28), ($p < 0.001$). After exclusion of 12 patients in the RP cohort we observed 407 patients. No synchronous primary cancer was diagnosed among 82 patients (20% of 407 patients) submitted for preoperative CT scanning of the RP cohort.

On the other hand, in the analysis of 325 RP patients without preoperative staging workup, one primary cancer (bladder cancer) was identified via cystoscopy motivated by macroscopic persistent haematuria before RP. But only 20.6% (84 of 407 patients) of the RP cohort underwent cystoscopy. This finding was therefore considered a purely database finding not representative of the whole population.

Table 1

Clinical features and outcome for the six patients with incidental second cancers diagnosed after staging workup for prostate cancer.

Patient	Age	Prostate cancer	Second cancer	Follow-up (years)	Status prostate cancer at last follow-up	Status second cancer at last follow-up
1	67	cT1cN0M0; G2; PSA* 3.6	pT3bN0 Renal adenocarcinoma	16.17	NED**	NED
2	66	cT3aN0M0; Gleason 5; PSA 13	pT1N0 Ampulla of Vater carcinoma	14.58	NED	NED
3	69	cT3aN0M0; Gleason 6; PSA 29	pT2N0 Renal clear cell carcinoma	13.33	NED	NED
4	68	cT3aN0M0; Gleason 8; PSA 10	pT3N0 Rectum adenocarcinoma	1.08	NED	Dead liver metastases
5	66	cT3aN0M0; Gleason 8; PSA 23	pT3N0 Renal clear cell carcinoma	5.67	NED	Dead brain metastases
6	62	cT2bN0M0; Gleason 6; PSA 33	pT1N0 Renal clear cell carcinoma	6.83	NED	NED

* PSA: Prostate specific antigen; ** NED: No evidence of disease

Discussion

Incidental asymptomatic renal tumours diagnosed by imaging procedures (i.e. abdominal ultrasonography, CT and MRI) performed for unrelated health problems have been reported in the literature [2, 5, 6]. The increasing use of abdominal imaging may partly explain the rising incidence of primary RCC [7–9]. In fact the number of imaging studies almost doubled between 1986 and 1994 [10]. Thus the proportion of RCC discovered incidentally has also risen to 48–66% in recent years, most of them with localised tumours at presentation [11, 12]. This change in renal cancer presentation (i.e. lower stage and grade) has been associated with a better prognosis following surgical treatment [11, 13–15]. Harada et al. suggested that clinical symptoms have a significant impact on the prognosis of patients with organ-confined RCC, and that the appearance of clinical symptoms may reflect the increased invasive potentials [16]. Gudbjartsson et al. concluded that the increased frequency of incidental detection of RCC has improved the survival of the patients with RCC [14]. However, in another report Gimenez et al. found no drop in the mortality of RCC with the increase in the incidence of RCC [17]. Four incidental RCCs discovered among the cohort of prostate cancer patients undergoing abdominal CT staging in our series were localised and lymph node negative (N0) tumours. These tumours were all treated surgically with curative intent before addressing the problem of the prostate cancer. The statistical analysis result for 4 RCC cases in the RT cohort is clearly significant ($p < 0.001$) in view of the 4 RCC patients for 0.22 expected.

Koyama et al. reported that among multiple primary malignant neoplasms in urological patients, prostate cancer and RCC tend to be discovered incidentally and concomitantly, whereas the diagnosis of bladder cancer is a rare incidental finding [18]. Fenton and Weiss calculated a prevalence of subclinical RCC of 0.21% (range 0.11–0.76%) on five series including 16 174 middle-aged American patients undergoing CT screening for different benign and malignant (chiefly lung and colon cancer) diseases [6]. Four RCCs were incidentally discovered among a pooled subgroup of 945 patients screened for colon cancer (prevalence 0.42%). This was less than half the prevalence observed in our series of patients undergoing a CT staging workup for prostate cancer. One may speculate whether patients with prostate cancer are at increased risk of RCC compared to those presenting with other primary tumours such as lung or colon. Barocas et al. observed a higher incidence of RCC in men with prostate cancer (SIR 1.25, $p < 0.001$); they concluded that a common aetiological factor is possible, but also that the results may be explained by detection bias [19]. Age at screening may also influence the likelihood of discovering an incidental second malignancy, with a higher risk for older patients. Thus, in our cohort of prostate cancer patients treated by RT (prevalence of incidental RCC 1%), the mean age was 67 years, older than the above-mentioned CT-screened colon cancer patients (mean age 64 years), in whom a 0.42% prevalence of incidental RCC was observed. Similarly, in a cohort of 1520 lung-cancer patients undergoing CT staging (median age 59 years), the prevalence of subclinical RCC was correspondingly lower (0.26%) [6].

The low proportion of abdominal CT (20%) among the group of patients undergoing RP compared to patients treated with RT in our series probably reflects a more favourable stage and grade at diagnosis for patients undergoing surgery, for whom a complete staging workup may not have been recommended due to the low likelihood of metastases. Another factor may influence the difference of percentage of CT scan between RT and RP groups: in our study RT patients were all treated in the same radiation oncology unit with the same staging protocol, whereas RP patients were treated in different hospitals or private clinics in Geneva with probably different staging protocols or habits among urologists. Obviously the low percentage of CT scan in the RP group (20%) may not be representative of the general population. On the other hand, the lack of synchronous second primary renal cancer in RP patients without CT scan (325 prostate cancer patients [80% of the RP cohort] as "a spontaneous test group" compared with RT cohort) may be a finding to support the power of CT scan in detecting synchronous second cancers.

The observed association between bladder and prostate malignancies among the RP cohort did not appear to be indicative of a higher prevalence of incidental bladder cancer in prostate cancer patients; on the contrary, this reflected the incidental discovery of a certain number of asymptomatic prostate cancers at the time of cystectomy for bladder cancer in an older patient population, as has been reported by others [20–22]. Consequently, to avoid bias in our findings we excluded 12 bladder cancer patients from the RP cohort as they are not cancers detected at prostatectomy performed for prostate cancer. The presence of one incidental bladder cancer identified by cystoscopy motivated by macroscopic persistent haematuria before RP, among 325 patients without preoperative CT-scan or cystoscopy, was considered a purely database finding and not representative of the whole population.

RT and RP are usually concurrent and alternative modalities for the management of localised prostate cancer. Ultrasonography, CT scan, MRI (magnetic resonance imaging), radionuclide bone scan and positron emission tomography (PET) are radiological modalities used – even if not routinely – for staging of prostate cancer [23, 24]. Age, tumour stage, PSA level, Gleason score, risk group, choice of the physician and of the patient, resectability of the tumour, risk from anaesthesia, comorbidities or potential toxicities of treatment modalities may influence the decision for extension of staging workup and the choice of management [25, 26].

Staging workups with abdominal CT and bone scan are less often performed nowadays because of the increasing numbers of favourable patients (i.e. with prostatic specific antigen serum levels below 10 ng/ml and Gleason score below 7) considered for radical treatment. Although an abdominal CT cannot be recommended simply on the basis of the potential of screening for second incidental malignancies, in the near future PET with choline or acetate tracers labeled with F^{18} or C^{11}, whole body magnetic resonance imaging, or combined PET-CT imaging may become the usual diagnostic tools for prostate cancer workup. Osman et al. reported 3 indeterminate renal lesions and one solid renal mass among 250 patients undergoing PET/CT [27]. Improving the early detection of incidental and potentially severe second cancers, especially RCC, may be among the potential benefits of these new technologies [8, 28, 29].

Thus, the increased detection rate of incidental second malignancies (especially RCC) with abdominal CT in prostate cancer patients represents relevant data requiring more extensive documentation in subsequent investigations. The clinical relevance of the higher incidence of renal tumours with prostate cancer may be its influence on treatment strategy. Clinicians should take decisions for the management of both tumours. In a recent report Mattar et al. recommended, for incidentally diagnosed RCC, active surveillance for older patients and those with competing risks due to medical comorbidities, since their risk of early progression due to growth or metastases appears to be low. Otherwise, they suggested avoiding active surveillance for younger and healthier patients until prognostic factors are better defined [30].

Conclusions

Abdominopelvic CT as part of the metastatic staging workup before curative therapy for prostate cancer detects asymptomatic synchronous second RCCs with an incidence significantly increased compared with that expected in the general population. In daily practice clinicians should establish individualised management strategies when diagnosing synchronous prostate and renal cancers.

Correspondence:
Orhan Özsoy MD
Division de Radio-oncologie
Hôpitaux Universitaires de Genève
CH-1211 Genève 14
Switzerland
E-Mail: orhan.oezsoy@rsv-gnw.ch

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