Unsuspected pulmonary embolism on CT scans

Unsuspected pulmonary embolism on CT scanning: yet another headache for clinicians?

Sujal R Desai

Arguments for and against treatment of small unsuspected pulmonary emboli

Clinicians have long known that the symptoms and signs of pulmonary embolism are non-specific and that, unless the index of suspicion is reasonably high, the diagnosis is frequently overlooked. Against this background, clinically unsuspected pulmonary emboli are increasingly being spotted by radiologists on CT scans. Clinicians not only need to be aware of this, but also need to know how to deal with such serendipity. The quality of CT examinations has improved unimaginably; image acquisition, particularly with the new generations of multidetector CT (MDCT) machines, is now astonishingly fast and access to CT scanning has increased. The prevalence of incidental pulmonary emboli in consecutive inpatients undergoing MDCT scanning is now possible.12

The detection of unsuspected pulmonary emboli by CT scanning has been the subject of a number of previous reports.8-11 The prevalence of incidental emboli in these studies has varied from 0.6% to 5% and has depended to a large degree on the tests used for detection (single-slice CT vs MDCT vs echocardiography), the manner in which images were reviewed (hard copy vs workstation analysis) and the demographics of the study population (cancer vs non-cancer or inpatient vs outpatient).8-11 In the current issue of Thorax (see p. 536), another study documents the prevalence of incidental pulmonary emboli in consecutive inpatients undergoing MDCT scanning.10 Most patients were imaged on a 16-channel CT machine and, following the routine report, all studies were reviewed by an experienced thoracic radiologist unaware of the original findings. In nine out of 28 studies judged positive by the expert reviewer, filling defects were overlooked by the initial reporting radiologist but, in these patients, emboli were localised to the segmental (n = 6) and subsegmental (n = 3) vessels. Overall, emboli unsuspected at the time of referral were found in 28 of 487 (5.7%) scans. This figure is broadly comparable to the inpatient prevalence of unsuspected emboli in previous CT studies: in two reports comprising 634 inpatients the prevalence of unsuspected filling defects was 4.3%.7,8

An interesting aspect of the present study, implied but not stressed in earlier series, was the significant relationship between the likelihood of unsuspected pulmonary embolism and age. Unsuspected emboli were not detected in any of the patients aged below 50 years (n = 47), whereas incidental filling defects were present in almost 17% of those aged over 80 years (n = 66). The authors suggest that age may have been a surrogate for other relevant risk factors. However, an alternative explanation is that pulmonary emboli might simply be missed in the elderly because of the tendency to ascribe symptoms to age-related comorbidity.

The links between cancer and venous thromboembolism are widely acknowledged and one theme of earlier publications on incidental pulmonary emboli has been the emphasis on a background of malignancy. In the studies reported by Gosselin et al.10 and Storto et al.9 there was a history of malignant disease in 70% and 83% of patients, respectively. At first sight these results seem to imply that radiologists should be on the lookout for clinically unsuspected pulmonary emboli in patients with cancer. However, the published data warrant closer scrutiny, for there is an intrinsic bias: patients with cancer are just more likely than those without to have a CT examination because of the need for pretreatment staging, to say nothing of the further surveillance CT studies needed to monitor treatment response or detect relapse. It is therefore perhaps unsurprising that patients with malignancy account for a larger proportion of those with unsuspected pulmonary embolism on CT scans. It is noteworthy that clinically unsuspected emboli were seen in fewer than 10% of the 81 patients with cancer in the study by Gosselin et al.10 The experience at tertiary cancer centres is similar: the prevalence of non-suspected pulmonary embolism was only 4% (16/403 patients) in a recent study published from the M D Anderson hospital.11 Importantly, the results presented by Ritchie and colleagues show, for the first time, that there are no significant differences in the prevalence of incidental pulmonary embolism between patients with and without malignancy (18/343 (5.2%) vs 10/144 (6.9%). Thus, two points emerge: (1) despite the high prevalence of malignancy in patients with incidental pulmonary embolism, the converse scenario (that patients with cancer are more likely to have unsuspected pulmonary emboli) does not necessarily follow; and (2) the demonstration of incidental emboli
should not, in the absence of some clinical suspicion or other evidence, lead to a barrage of radiological tests in the forlorn hunt for an underlying neoplasm.

The above notwithstanding, there is perhaps a more pressing clinical issue. Indeed, most radiologists would readily admit that the task of detecting and reporting unexpected emboli is not particularly taxing. In contrast, once pulmonary embolism is reported, the clinician must make decisions on management and these are seldom easy. The pragmatist would argue that, unless there are contraindications, anticoagulation is warranted once a diagnosis of pulmonary embolism is made, incidental or otherwise. This certainly appears to be the case at the institution from which Ritchie and colleagues report their data and probably mirrors clinical practice elsewhere. The presumed logic is that, because the CT examination is a “snapshot”, the finding of an unsuspected filling defect (even when this is small or isolated to a segmental or subsegmental branch) might be the harbinger of trouble. Deviating from this mindset is unacceptable, for it may be construed as a failure to live with the facts and the evidence. The objection may be that it is not necessarily so serious a matter, that with the current state of CT scanning the obvious drawback of super-sensitive tests such as MDCT is that “abnormalities” which ultimately have no clinical impact may be identified. On a philosophical note, there are intriguing parallels outside the sphere of pulmonary embolic disease. For instance, as radiologists who regularly report thoracic CT scans will testify, small incidental pulmonary nodules are all too common on MDCT. Another area in which the detection of clinically questionable change arises is in connective tissue disorders where, because there is an expectation of lung disease, patients are often screened with CT. However, in this scenario, a problem that clinicians often face is what to do when—as occurs not infrequently—limited and physiologically “silent” disease is reported by the radiologist. Whatever the arguments for and against treatment of small unsuspected pulmonary emboli, it is hoped that data such as those presented by Ritchie et al will fuel pragmatic prospective studies. After all, it does seem remarkable now that a single paper published over 45 years ago (and questioned because of concerns about potential confounding factors) has essentially dictated the treatment of pulmonary thromboembolism. Although it seems unlikely that ethics committees would approve a placebo-controlled trial of treatment in symptomatic pulmonary embolism, the same reservations may not apply to patients with clinically unsuspected and haemodynamically insignificant pulmonary thromboembolism. The time to address these hitherto unanswered questions may be upon us!


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REFERENCES

Acute renal failure in CF

Acute renal failure in people with cystic fibrosis

Kevin W Southern

Time to reflect on antibiotic strategies for CF lung infection

The putative gene in cystic fibrosis (CF) encodes a protein, cystic fibrosis transmembrane conductance regulator (CFTR), which has an important role in transepithelial salt transport. The major organ affected in CF is the lung, with remorseless and intense chronic airway infection resulting from disabled clearance of dehydrated airway surface liquid. Airway inflammation leading to end stage lung damage is associated with respiratory morbidity and early death. The outlook for people with CF has improved considerably with a proactive approach to treatment of airway infection as one of the cornerstones of its management. Recent data from the US CF registry suggest a continuing improvement in median predicted survival to over 35 years (http://www.cff.org/research/2006NACFC/Plenary III). With an improving outlook, perspectives have changed and expectations of people with CF and their carers have broadened. A survey of acute renal failure (ARF) in patients with CF published in this issue of Thorax (see p 541) is particularly timely when reflecting on how best to achieve the goal of increased survival while balancing risks to patients.

ACUTE RENAL FAILURE AND CF
There are several reasons why people with CF are at risk of ARF. The salt transport defect makes people with CF prone to salt loss and consequently fluid imbalance and dehydration. The impact of CFTR dysfunction on pancreatic function and architecture results in significant hypinsulinaemia (CF-related diabetes) in a significant proportion of older patients with CF, again posing a challenge to fluid balance and the long-term possibility of diabetic kidney disease. Finally, as a cohort, these patients are exposed to industrial quantities of potentially nephrotoxic chemotherapeutic agents (in our CF centre some children have received a cumulative intravenous dose of over 300 g of the aminoglycoside tobramycin). Given cumulative exposure to potentially nephrotoxic drugs and the increased prevalence of CF-related diabetes in older people with CF, an increased incidence risk of ARF might be expected in the older age group; however, this was not the case in this survey where the majority of cases were children (only three over 18 years). This may represent better response rates from paediatric centres to this survey, and further studies are needed to examine this finding.

ROLE OF CFTR IN THE KIDNEY
Paradoxically for a condition in which salt transport is a primary abnormality, people with CF have apparently normal renal function. The CFTR gene is expressed abundantly in the kidney, particularly in the nephron, but CFTR appears to be functionally redundant at this site. Studies on a transgenic cftr knockout mouse model suggest that the absence of CFTR does not affect the ability of the kidney to manage fluid and salt imbalance, but that different salt and fluid transport processes are involved. Interestingly, CFTR does appear to have a role in the pathophysiology of autosomal recessive polycystic kidney disease, where fluid secretion into the cysts appears to be mediated through CFTR. The increased incidence of nephrocalcinosis in CF does not appear to relate to an intrinsic renal problem and is more likely related to hyperoxaluria.

Given the apparent pivotal role of CFTR in other organs, the lack of impact of CFTR dysfunction on the kidney is remarkable. It is even possible that absent CFTR function in the kidney may protect people with CF from renal insults, and certainly it has been recognised for many years that people with CF have increased renal clearance of many drugs including aminoglycoside antibiotics. More research is needed into the CF renal condition to understand the impact of CFTR dysfunction on renal physiology.

RELEVANCE OF ACUTE RENAL FAILURE IN CF
The incidence risk of ARF reported by Bertenshaw et al. is significantly higher than the non-CF population and is consistent with other recent reports. The authors suggest this may be an increasing phenomenon, quoting local figures, although there are no previous national data to assess this. Because of problems with recruitment and case verification, it is likely that the incidence risk quoted is an underestimate. It is important that CF teams reflect on these figures and, as a first line, adopt “common sense” procedures to prevent inadvertent renal damage. Patients should be monitored more closely during periods of hot weather and during fasts, particularly if using aminoglycoside antibiotics (for example, to improve a chest condition before a general anaesthesia). In addition, patients should avoid the concomitant use of potentially nephrotoxic agents such as ibuprofen, frusemide and aminoglycosides. If concomitant use is unavoidable, then careful monitoring is imperative.

Given the increased incidence of ARF in CF, there is a strong argument for more formal assessment of renal function on a regular basis in order to highlight at risk individuals. The glomerular filtration rate can be estimated by formulae that employ serum creatinine and other parameters such as height, weight and age. The Schwartz formula (40 × height (cm)/serum creatinine (μmol/l)) is commonly used; however, many formulae exist but none has been formally validated in CF. A concern is that these formulae
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