A past history of radiation therapy with portals which covered a joint is seldom mentioned as a risk factor for septic arthritis. However, local changes with other origins, as seen in rheumatoid arthritis [1], prosthetic surgery [2], crystal-induced arthritides [3], osteonecrosis [2, 4–8], sickle cell disease [2, 4–12] and haemarthrosis [10] are known to increase the susceptibility to infection. Chemotherapy is acknowledged as a systemic risk factor for septic arthritis, along with immunosuppressive drugs, diabetes mellitus, ageing and various immunodeficiencies [2, 13]. Only isolated observations [6, 9] and a short series [14] of septic arthritis have been reported as having a possible relation to radiation therapy. In all documented cases treatment was for breast carcinoma, hence septic arthritis was of the shoulder. Over the past 20 yr we have encountered six such cases, three others involving the sternoclavicular joint and one similar involvement after brachytherapy for carcinoma of the cervix. In the present work we describe and analyse our data, correlating them with the literature. We also compared our patients with a group of septic arthritis patients without radiation therapy.

Conclusions. In our study, a past history of radiation therapy was observed in 6/50 infections of the shoulder, 3/5 infections of the sternoclavicular joint, 6/23 cases of septic arthritis of the shoulder and all cases of septic arthritis of the sternoclavicular joint for females. Radiation therapy seems to be a risk factor for septic arthritis. Diagnosis would be aided by a greater awareness of the clinical and radiological features of this septic arthritis.

Key words: Radiotherapy, Septic arthritis, Breast carcinoma.

Method

A retrospective study was made of the files of all patients admitted to the rheumatology department for septic arthritis between January 1979 and December 1998 inclusive. The majority of cases of septic arthritis from the region are seen in this rheumatology department, even those from cancer centres and emergency and orthopaedic departments. Diagnosis was made on the basis of positive joint fluid culture and/or positive blood culture. Infections caused by mycobacteria or gonococci were not included, nor were those restricted to the sacroiliac joints or to the spine. A past history of radiation therapy was considered as relevant to the septic arthritis if treatment portals had covered the affected joints. A group of patients with septic arthritis who had not undergone radiation therapy was used as a control group. In six out of nine cases of septic arthritis related to breast cancer radiation therapy, the glenohumeral joint was involved. The control group was thus limited to this location. Patients with infections complicating joint injection and/or rheumatoid arthritis were not included in the control group because signs, symptoms and evolution may have been modified by these factors. For the same reason, our personal case post-injection was not included in the comparison with the control group. The two groups were compared for age, gender, risk factors, time from first sign to diagnosis, fever, white blood cell (WBC) count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), bacteriological data, radiographic abnormalities, treatment and evolution.

Results

Over the 20 yr period, 282 patients had been admitted to the rheumatology department with bacteriologically documented, non-gonococcal, non-mycobacterial septic arthritis of a peripheral joint. Ten patients, all female, had received radiation therapy that...
covered the infected joint. All but one had had mammectomy and axillary node dissection for breast cancer. The irradiated volume included the scapulohumeral joint in six patients and the sternoclavicular joint in three patients. The last patient had had brachytherapy and external radiation therapy for carcinoma of the cervix and presented with septic arthritis of the hip.

Of the 50 cases of septic arthritis of the glenohumeral joint seen in the department, 23 involved women. Hence, radiation therapy was a putative risk factor in one-tenth of cases in this location and one-quarter for females. Only five cases of septic arthritis of the sternoclavicular joint were observed, three of which were in female patients, and they had all received radiation therapy that covered the joint. In septic arthritis of the hip joint, a past history of radiation therapy was noted only once (1/33 overall).

The main features of our ‘post-radiotherapy’ cases are recapitulated in Table 1. The mean patient age was 69 yr. The median time elapsed since radiation therapy was 16 yr. All nine patients with breast cancer had had arm oedema since treatment. No patient had classical risk factors at the time of septic arthritis, nor tumour relapse or metastasis. Accordingly, chemotherapy, when initiated, had been discontinued 2 to 30 yr before admission. The mean time to diagnosis was 55 days. On admission, five patients had fever but in only one above 39°C. Mean WBC count was 7500/mm³. Only four patients had more than 10 000/mm³. ESR was markedly elevated (mean 101 mm/h), as was CRP (mean 120 mg/l). Staphylococcus aureus was the predominant species (seven cases), with streptococci accounting for the other three cases. The source was identified in three instances: infected skin burn (case 3), sinus from X-ray induced calcifications (case 4) and abscess of the toe (case 8). On admission, radiographs were normal in 5/10 patients. Three had narrowing of the glenohumeral joint space, associated in two with osteolysis of the humeral and glenar aspects. One patient had epiphysial osteoporosis and one other osteonecrosis of the medial part of the clavicle. A computed tomography (CT) scan was performed when plain radiographs were not explicit. It showed in every instance pus collection either in the joint space or in adjacent bursa. All patients were treated by a combination of two antibiotics, given first intravenously for 2 to 3 weeks, then by mouth for 7 months (range 3 to 18 months). A good to fair result was achieved in four patients. A poor result was observed in the six remaining patients owing to extensive and progressive joint destruction and to relapse in two patients (once in one patient, and five in the other). Destruction was predominantly at the epiphysial aspects, which contrasted with moderate joint space narrowing. Destruction continued to worsen even though clinical and laboratory findings suggested infection was under control (Fig. 1).

Comparison with control cases

The five cases of septic arthritis of the glenohumeral joint related to radiation therapy were pooled with the six published cases [6, 14] and compared with our control group of 23 patients with septic arthritis of the glenohumeral joint who had been admitted to the department during the same period but without radiation therapy. As stated above, all patients were female and all had received radiation therapy for carcinoma of the ipsilateral breast. In controls, only one-third of patients were female. Classical risk factors were absent in our patients but present in half of the controls: alcoholism (three cases), diabetes mellitus (two cases), steroid therapy (one case), splenectomy (one case) and malignancies without radiotherapy (myeloma, chronic lymphoid leukaemia, lung cancer, prostate cancer, kidney cancer, one case each). Time to diagnosis was much longer in radiation-related septic arthritis than in other forms [7]. In cases related to radiation therapy the initial signs were confounded by prior local changes and mitigated by a lower incidence of fever (absent in 6/11 patients versus 3/23 controls) and increased WBC (absent in 7/9 patients versus 7/23 controls) and increased WBC (absent in 7/9 patients versus 7/23 controls).
controls). By contrast, ESR was markedly elevated (ESR >100 mm/1h in 7/11 patients versus 7/23 controls). S. aureus predominated in all groups. In irradiated patients, antibiotics were administered for a longer period (10.8 months compared with 2.8 months in controls). Evolution was worse in radiation therapy-related cases. One patient achieved complete recovery, compared with 13/17 in controls. The incidence of relapse was 2/5 in patients and 2/17 in controls. As one patient had had five relapses, the number of relapses was three times higher than in controls. An extensive but surreptitious destruction of articular bone, without comparable destruction of joint cartilage was observed in 6/11 patients but only in 1/17 controls.

Discussion

In female patients admitted to our department with septic arthritis of the shoulder, one in four had previously undergone radiation therapy. All three women who had septic arthritis of the sternoclavicular joint, a rare location, had also had past radiation therapy. Septic arthritis developing in a joint submitted to radiation therapy for a nearby cancer possesses specific features. The complication was more likely to occur 10 to 30 yr after irradiation than in the first months. After so long an interval, all malignant lesions were cured and no metastasis could be found. Prior local changes of the now infected joint impeded the recognition of septic arthritis. In some patients, pain, limitation of motion and inflammatory skin changes had been present for years. Their worsening, due to joint infection, was at times improperly attributed to tendinitis, osteonecrosis or capsulitis [14]. Elevated ESR and CRP levels should raise strong suspicion of septic arthritis, even in the absence of fever and of X-ray abnormalities. Echography and CT scan or MRI should be considered essential. Echography is especially helpful because it makes the procedure of joint aspiration easier. Any fluid collection should be aspirated for bacterial isolation. Owing to skin changes, surgical procedures are to be avoided. Antiinfection therapy never shorter than 3 months in order to prevent relapse was not sufficient in all cases. Treatment of the sternoclavicular joint can be expected to have a favourable outcome. In other locations, destruction is likely. Bone tissue, but not cartilage and other articular soft tissues, had probably lost much of its resistance against induced inflammation. Even more disturbing were the very late relapses, 10 to 24 yr after the end of antibiotherapy.

The only other work on this topic drew no conclusion on the respective roles of chemotherapy, surgery and radiation therapy. Prior chemotherapy is unlikely to have contributed to infection 3 to 30 yr later, but if it did, additional local factors should be postulated. Extensive breast surgery should also be discussed as a risk factor. The long time course suggests that its effects, if any, are mediated by lymphoedema, a source of infection through abnormal lymph circulation and/or distal skin lesions. None of our patients had distal skin lesions due to lymphoedema, but two had other cutaneous portal entry. If lymphoedema is common in the lower limbs, it is rarely responsible for septic arthritis of the hip joint in the absence of a local risk factor. Furthermore, in the involved arm of cancer patients no infection of the elbow or wrist joints was observed. These joints were always included in the lymphoedema but had been excluded from the radiation therapy portals. In all our cases the right shoulder was involved and yet mammary carcinoma is predominantly of the left breast (57%).

The right side susceptibility could be explained by trauma in everyday activities or by the organization of the right, subclavicular lymph collector. Prior radiation therapy probably produces long-lasting joint changes [5]. If the weakening of local immune defence was caused by irradiation therapy dating back 3–20 yr, some cause should be found to explain why the bone sustained irreversible, radiation-induced, local damage whereas the adjacent soft tissue recovered. Known complications of radiation therapy are osteopenia and osteonecrosis [5, 7]. Mature cartilage is radioresistant [11]. Osteopenia develops slowly, beginning 1 or 1 yr post-radiation [5]. A characteristic but rarefied coarse trabeculation with focally increased bone density is documented by CT scan [15]. Two or 3 yr after radiation therapy, Howland et al. [5] observed a coarsening of the trabecular pattern with fewer trabeculae and cortical thickening. They suggest that bone remodelling units may be decreased in number more than in function and remain so for decades. The sudden influx of large numbers of cytokine-producing inflammatory cells due to infection may promote bone resorption beyond residual bone formation capabilities. Radiation therapy can thus induce irreversible bone changes. Our cases suggest that they persist even after three decades.

Conclusion

A past history of radiation therapy covering a joint is seldom mentioned as a risk factor for septic arthritis. Published reports and our experience suggest that this type of septic arthritis is not uncommon and that it has distinctive features. Subacute onset with limited radiological changes and pre-existing joint impairment due to sequelae of the initial treatment for ipsilateral cancer render it difficult to recognize this late complication and hence to treat it effectively. Slowly developing bone damage may coexist with rapidly progressing damage, a paradox which, if elucidated, may shed some light on the pathophysiology of septic arthritis in general, and on the mechanism of its main bone and joint complications.

The authors have declared no conflicts of interest.

References