SHORT REPORT

Incidental findings in pelvic lymph nodes at radical prostatectomy

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Aims: To assess the frequency and cause of incidental (non-metastatic) lymph node pathology discovered before or at radical prostatectomy.

Methods: Eight hundred and fifty four consecutive lymphadenectomies received between 1988 and 2001 were reviewed. All had been processed and stained routinely. Additional techniques, indicated by morphology, were then performed.

Results: Incidental pathology was found in 15 cases: florid sinus histiocytosis following prosthetic joint replacement (eight), non-caseating granulomas (three), small lymphocytic cell lymphoma (two), follicular lymphoma (one), and foreign body reaction (one). Incidental pathology was present in 1.8% of 854 patients who underwent pelvic lymphadenectomy during radical prostatectomy.

Conclusion: Awareness of possible non-metastatic lymph node pathology aids histological diagnosis and may be clinically relevant.

Radical prostatectomy is a potentially curative surgical procedure in patients with clinically gland confined carcinoma. Pelvic lymph nodes removed during radical prostatectomy may be presented for frozen section if there is a high clinical suspicion of metastatic disease. More commonly, they are received in the fixed state with the radical specimen, as a staging lymphadenectomy.

Because radical surgery for prostate cancer is increasing in the UK, a retrospective review of lymphadenectomy specimens has been completed to indicate the non-metastatic pathology that may be present.

"Radical prostatectomy is a potentially curative surgical procedure in patients with clinically gland confined carcinoma"

MATERIALS AND METHODS

All radical prostatectomy specimens received at University College and Middlesex Hospitals, London were identified using the Radical Prostatectomy Database. Between January 1988 and December 2001, 1001 prostatectomy specimens were received, including 854 with bilateral pelvic lymph nodes.

Intraoperative frozen sections of the lymphadenectomy specimens had been performed in 82 patients. Requests for frozen sections were based on the biopsy Gleason score, serum prostate specific antigen, and findings on intraoperative palpation of the lymph nodes. These criteria and the selection of patients for radical surgery have changed over time. Thus, 80% of the frozen sections were performed between January 1988 and December 1993.

The standard protocol for examining pelvic lymph nodes was to process the entire specimen in blocks of 3 mm thickness and to examine one haematoxylin and eosin (H&E)

stained section from each block. This approach is based on the typical form of the pelvic lymph nodes. They are usually palpable but hardly visible, being extensively replaced by adipose tissue. The lymph node component is often reduced to a rim, frequently ≤ 1 mm. Thus, these nodes are rarely amenable to counting, precise measurement, or dissection. Moreover, metastases have been reported in the surrounding adipose tissue in the absence of lymph node involvement (anecdotal reports).

The reports on the series of 854 cases were reviewed to identify those with incidental (non-metastatic), pathology. The H&E sections were reviewed by the authors (AW, AS, AD, and MCP), and the findings were used to dictate further histochemistry or immunohistochemistry:

- Ziehl Neelsen, Grocott, and periodic acid Schiff histochemistry to detect the presence of infective organisms.
- CD68 (Dako, Ely Cambridgeshire, UK) staining to identify histiocytic cells in the cases of sinus histiocytosis. These sections were examined in both normal and polarised light. Tissue from the first case of sinus histiocytosis associated with a joint prosthesis was embedded in resin and 1 μ m sections were cut and etched using a plasma asher. These sections were then examined using electron microscopy with backscatter illumination to identify wear particles. Analysis of 10 different wear particles was then carried out by dispersive x ray microanalysis (EDX).
- A panel of appropriate antibodies was used to elucidate possible lymphoproliferative disorders.^{1,2}

Results from staining procedures were correlated with relevant clinical information.

RESULTS

Table 1 summarises the findings. No intraoperative frozen sections had been requested in the 15 cases described.

In some instances, the urologists remarked on the enlargement or prominence of the lymph nodes but assumed that these features were a reaction to the multiple prostate biopsies or previously diagnosed haematological disease. In one patient, the size and nature of the assumed lymph node mass prompted a diagnosis of metastatic disease and surgery was abandoned after biopsy of the mass, but completed at a later date.

Eight patients undergoing radical prostatectomy were found to have pronounced sinus histiocytosis within their pelvic lymph nodes (fig 1). All of these patients had undergone lower limb joint prosthetic surgery up to a maximum of nine years before radical prostatectomy. CD68 positivity confirmed the cells to be histiocytes. The histiocytes contained spindle shaped particles, which were birefringent

Abbreviations: EDX, dispersive x ray microanalysis; H&E, haematoxylin and eosin

Table 1 Clinical and pathological features of incidental findings in pelvic lymph nodes retrieved at radical prostatectomy

Number of patients	Age range	Lymph node pathology	Clinical findings
8	57–75	Sinus histiocytosis: CD68 +ve	Previous lower limb joint prosthetic surgery
3	65–71	Well formed non-caseating granulomas: ZN, Grocott, and DPAS -ve	No evidence of systemic granulomatous diseases
1	56	Synthetic mesh and giant cell foreign body reaction associated with lymph nodes	Previous inguinal hernia surgery
2	71–72	Diffuse infiltrate of small lymphoid cells effacing the follicular architecture: CD20, CD5, and CD23 +ve confirming small lymphocytic lymphoma	In one patient small lymphocytic lymphoma was diagnosed before surgery
1	68	Lymph nodes partially replaced by small lymphoid cells: CD20, CD10, BCL2 +ve, κ light chain restricted, t(14:18) +ve, confirming follicular lymphoma	No peripheral lymph node enlargement. No bone marrow involvement

DPAS, diastase resistant periodic acid Schiff; ZN, Ziehl Neelsen.

on examination under polarised light. On electron microscopy, these particles were identified as metal fragments (fig 2). EDX investigation of the first case showed a high peak for titanium and a small peak for aluminium (fig 3). These EDX results were consistent with the particles being derived from a titanium 6/4 alloy, from which joint prostheses are commonly made.

Three lymph node specimens contained well formed, non-caseating granulomas. Histochemical stains for infective agents were negative in these cases, and no systemic cause for the granulomas was found.

Lymphomatous infiltrates were present in three of the pelvic lymph node specimens. Two of these infiltrates were shown to be small lymphocytic lymphomas. In one, the diagnosis was already established, and in the second case (in which one lymph node also contained a concomitant metastatic deposit from the prostatic carcinoma), the diagnosis was suggested on the morphology of the prostate biopsy. In the third case, a diagnosis of follicular lymphoma was based on the findings from the lymphadenectomy specimen. All three diagnoses were confirmed by immunohistochemistry.

Figure 2 Scanning electron microscopy on resin embedded sections showing metal particles about 1 μ m in length (arrow).

Figure 1 A low power view of a lymph node from a patient with lymphadenopathy and previous prostheses, showing pronounced sinus histiocytosis surrounding residual lymphoid follicles. On higher magnification (inset), the histiocytes are seen to contain multiple spindle shaped particles.

Figure 3 Dispersive x-ray microanalysis printout showing a short peak for aluminium (Al), and a tall peak for titanium (Ti), consistent with the particles being derived from titanium 6/4 alloy, from which joint prostheses are commonly made.

In addition, an unusual case of a foreign body giant cell reaction to synthetic mesh was found at the site of the pelvic lymph nodes.

DISCUSSION

Our results illustrate that processes other than metastatic prostate carcinoma may cause abnormalities in pelvic lymph nodes sampled at radical prostatectomy. Using the same prostatectomy database, Young *et al* found the incidence of metastatic prostate carcinoma at staging lymphadenectomy to be 4.6%.³ In our present study, 1.8% of lymphadenectomy specimens contained incidental lymph node pathology other than metastatic prostate carcinoma.

Histiocytic changes in lymph nodes that drain joint prostheses are well recognised in the orthopaedic literature.⁴ Case reports have highlighted the potential for these changes to mimic lymphadenopathy as a result of metastatic carcinoma from primary sites, including endometrium, skin, and prostate.⁴⁻⁷ Differential diagnoses of nodal infiltrates containing histiocytic cells include infections (mycobacterium—for example, *Mycobacterium leprae*—toxoplasma,⁴ and Whipple's disease⁸), Rosai-Dorfman disease, lymphangiographic changes, Langerhan's cell histiocytosis, monocytoïd B cell hyperplasia, virus associated haemophagocytic syndrome, metastatic melanoma,⁹ and malakoplakia.⁹ However, the presence of CD68 positive macrophages containing birefringent particles within their cytoplasm confirms the diagnosis of sinus histiocytosis related to previous joint prosthesis surgery.⁴

"As the prognosis in cases of Hodgkins lymphoma is often good, the associated lymphadenopathy should not necessarily prevent radical prostatectomy for gland confirmed adenocarcinoma "

Granulomatous inflammation of lymph nodes is also well recognised and may relate to several different disease processes. Infective agents are one well documented cause of this change. Other causes include secondary responses in nodes draining carcinoma or in association with Hodgkin's disease, other lymphomas, and foreign body reactions. Foreign body granulomas have been described in lymph nodes draining silicone implants

Take home messages

- Processes other than metastatic prostate carcinoma may cause abnormalities in pelvic lymph nodes sampled at radical prostatectomy
- Incidental pathology was present in 15 of 854 (1.8%) patients who underwent pelvic lymphadenectomy during radical prostatectomy and only one of these 15 patients had concomitant metastatic prostate carcinoma
- Awareness of possible non-metastatic lymph node pathology aids histological diagnosis and may be clinically relevant

of the metatarsal joints and from silicone genitourinary prostheses.^{10 11} In the cases described special stains and subsequent clinical investigation did not clarify the aetiology.

An incidental finding of non-Hodgkin's lymphoma is not uncommon, especially in an older male population, and has been reported previously in association with localised prostate carcinoma.¹² A history of haematological malignancy should be considered as a cause of pelvic lymphadenopathy, especially if nodal enlargement is bilateral. Because the prognosis in such cases is often good, the associated lymphadenopathy should not necessarily prevent radical prostatectomy for gland confined adenocarcinoma.^{13 14}

The remaining cause of unilateral incidental "pelvic lymphadenopathy" was a foreign body giant cell reaction to a synthetic mesh, which had migrated from a previous hernia repair. In this case, radical surgery was initially abandoned as metastatic prostatic carcinoma was assumed to be the cause. Surgery was completed by the perineal route, once the true nature of the histological changes associated with the lymph nodes had been identified.

Clearly, any of these incidental findings may occur in addition to metastatic prostate carcinoma. Only one of the 15 cases described here included concomitant metastatic prostate carcinoma. In our series, with one exception, the incidental pathology has not caused changes in surgical management, although the potential for misdiagnosis is noted in the literature.⁴⁻⁷ The postoperative diagnosis of the haematological malignancies has clinical implications.

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