CASE REPORTS

Large B cell lymphoma of the subtalar and talonavicular joint synovium

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SUMMARY

We present the unique case of a 68-year-old man with a background of rheumatoid arthritis, who underwent left subtalar and talonavicular arthrodesis due to degenerative changes and chronic pain. Histology of the synovium demonstrated large B cell lymphoma. The patient subsequently underwent R-CHOP chemotherapy and radiotherapy to the affected area. This is the first described case of a primary large B cell lymphoma of the subtalar and talonavicular joints, without bony involvement.

BACKGROUND

We present the case of a 68-year-old man with a background of rheumatoid arthritis (RA) who underwent left subtalar and talonavicular arthrodesis secondary to degenerative changes and chronic pain. However, what at first appeared to be an uncomplicated case, resulted in an unusual diagnosis of diffuse large B cell lymphoma originating from the synovium of the subtalar and talonavicular joints. This case report focuses on the clinical presentation, medical intervention and outcome of a rare case of lymphoma.

CASE PRESENTATION

A 68-year-old man of Mediterranean origin underwent elective left subtalar and talonavicular arthrodesis, performed to alleviate the pain associated with his RA and secondary degenerative changes. He had had RA-associated symptoms for the preceding 6 years, and developed pain in his left foot approximately 18 months prior to the procedure. His other medical history included chronic obstructive pulmonary disease and partial pneumonectomy (following pneumonia as a child). There was no personal history of hepatitis or tuberculosis, and no family history of haematological malignancy.

The patient was an ex-smoker who drank minimal alcohol socially. His medications included sulfasalazine EN 1 g three times daily, hydroxychloroquine 200 mg once a day, and diclofenac as required.

Systemically he had no symptoms suggestive of systemic disease; he had no fever, no significant weight loss (he had gained weight with the immobility secondary to his painful foot), no history of long-standing night sweats, and ate a normal diet.

Preoperatively he complained of persistent pain around his ankle. Clinically the ankle, subtalar and talonavicular joints demonstrated significant mechanical problems and pain along the lateral aspect.

INVESTIGATIONS

Plain film radiographs demonstrated significant osteoarthritis of his talonavicular and subtalar joints (figure 1). An ultrasound of his ankle (undertaken during ultrasound guided injection of local anaesthetic and steroids) noted the ankle joint itself appeared normal with no evidence of synovitis or effusion. However, there was florid synovitis in the subtalar joint.

Furthermore, on clinical examination, no peripheral lymphadenopathy or organomegaly was present, and a left thoracotomy scar was noted. His blood count at preoperative assessment was unremarkable: Hb 14.5 g/dl, WBC $6.8 \times 10^9/l$, platelets 288, neutrophils $3.7 \times 10^9/l$ and lymphocytes $1.7 \times 10^9/l$.

TREATMENT

The patient underwent left subtalar and talonavicular fusion with bone grafting. Intraoperatively, the

Figure 1 Preoperative radiographs of the patient's left weight-bearing ankle.

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surgeon felt that the macroscopic consistency of the synovium was unusual (extremely hypertrophic and dark in colour), and therefore samples were sent for histology. Of note is the fact that no macroscopic bony destruction was observed, and the bony texture appeared normal in the subchondral layer and beyond.

Subtalar fusion was performed with 6.5 mm cannulated screws and talonavicular fusion with IO-fixation (figure 2), with no intraoperative complications. Postoperatively, the patient's recovery was unremarkable and he was discharged home non-weight bearing the following postoperative day.

Microscopically, the left subtalar and talonavicular joint specimens demonstrated similar features. Sections showed marked chronic synovial inflammation with variable-sized lymphoid follicles within a hyalinised stroma. Focally, there were a few areas with infiltration of atypical lymphoid cells. Cytomorphologically, the medium-sized to large lymphoid cells showed vesicular nuclei and prominent central nucleoli, indicative of neoplastic cells (figure 3).

Immunophenotypically, the neoplastic cells expressed CD20, BCL-6 and MUM-1 but were negative for CD10. MIB-1 showed a proliferation fraction of 50%. The findings led to a diagnosis of diffuse large B cell lymphoma, non-germinal centre type (figure 4).

OUTCOME AND FOLLOW-UP

The patient was reviewed 2 weeks postoperatively as regards his operation. His wound looked healthy and he was discharged in a below-knee cast to be seen again after 4 weeks for a check x-ray, and was to remain non-weight bearing.

Regarding the histological findings, the patient was discussed at the haematology multidisciplinary team meeting, and required urgent staging investigations. A bone marrow aspirate and trephine biopsy sample were consistent with normal lymphoid infiltrate. His PET scan was entirely negative other than for very mild uptake in the vicinity of the arthrodesis, indicative of postoperative inflammation rather than the lymphoma.

Figure 2 Postoperative radiographs of the patient's left weight-bearing ankle.

Figure 3 H&E staining of sample illustrating infiltration of medium to large lymphoid cells, showing vesicular nuclei and prominent nucleoli (magnification: A $\times 5$, B $\times 10$, C $\times 40$).

Screening blood tests included serum electrophoresis, which demonstrated a normal pattern, the blood film had an unremarkable morphology, and antibodies for hepatitis B, hepatitis C and HIV were all negative.

In light of these findings the patient was diagnosed with diffuse large B cell lymphoma (left subtalar joint) stage 1Ae, and was commenced on three courses of R-CHOP chemotherapy followed by radiotherapy to the affected area.

Figure 4 Immunohistochemistry demonstrating the cells to be positive for CD20, BCL-6, MUM-1 and MIB-1, and negative for CD10.

DISCUSSION

The patient was newly diagnosed with diffuse large B cell lymphoma (non-germinal centre type) identified on synovial biopsy from the left subtalar and talonavicular joints. Non-Hodgkin lymphoma is known to have skeletal involvement in up to 25% of cases,¹ and the involvement of the synovium is usually via direct extension from bone lesions.² This case, however, demonstrates a primary tumour to the synovium without bony involvement.

Several other case reports have identified involvement of the synovium in lymphoma without bony involvement, but not specific to the subtalar or talonavicular joint.^{3–6} Cases involving lymphoma and the ankle joint describe bony extension and obvious preoperative clinical features.^{7–10}

The association of RA and lymphoma has been well documented, often cited as doubling the risk of lymphoma.^{11 12} However, there remains uncertainty as to the causative factor of RA-associated lymphoma. Several case reports^{13 14} and cohort studies^{15 16} have identified elevated risks of lymphoma following treatment with disease-modifying antirheumatic drugs and intra-articular steroid use. Conversely, other studies associate this risk directly with the chronic inflammatory disease process.¹⁷

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

Learning points

- We present the first described case of a primary large B cell lymphoma of the subtalar and talonavicular joints, without bony involvement, lymphadenopathy or hepatosplenomegaly.
- The case exemplifies the importance of obtaining a histological diagnosis of specimens, even in routine operations, if there is a high index of suspicion of an irregularity to the tissue.
- The association between rheumatoid arthritis and lymphoma has been further highlighted by this case, however the pathophysiology between the two remains unknown.

REFERENCES

- 1 Dorfman HD, Siegel HL, Perry MC, *et al.* Non-Hodgkin's lymphoma of the synovium simulating rheumatoid arthritis. *Arthritis Rheum* 1987;30:155–61.
- 2 Ogoose A, Kawashima H, Hotta T, *et al.* Conditions suggesting lymphoma: CASE 3. Primary synovial lymphoma with osteoclast-like giant cells presenting as a tenosynovial giant-cell tumor. *JCO* 2005;23:3847–8.
- 3 Birlik M, Akar S, Onen F, *et al.* Articular, B-cell, non-Hodgkin's lymphoma mimicking rheumatoid arthritis: synovial involvement in a small hand joint. *Rheumatol Int* 2004;24:169–72.
- 4 Jamieson KA, Beggs I, Robb JE. Synovial presentation of non-Hodgkin's lymphoma. *Br J Radiol* 1998;71:980–2.
- 5 Jawa A, Lieberman AE, Alexieva CC, *et al.* Primary intra-articular non-Hodgkin's lymphoma of the elbow. A case report. *J Bone Joint Surg Am* 2006;88:2730–4.
- 6 Khan SY, Hutchinson DG. Primary synovial non-Hodgkin's lymphoma in association with ankylosing spondylitis. *Rheumatology* 2004;43:391.
- 7 Jun N, Akio M, Kazuo T, *et al.* Malignant lymphoma of talus with rapidly destructive changes. A case report. *Orthop Traumatol* 2000;49:294–9.
- 8 Mendezoon MJ, Wire KR. Diffuse large B-cell lymphoma of the ankle: a case study of surgical intervention and outcome. *J Am Podiatr Med Assoc* 2010;100:505–10.
- 9 Singh DP, Dhillon MS, Sur RK, *et al.* Primary lymphoma of the bones of the foot: management of two cases. *Foot Ankle* 1991;11:314–16.
- 10 White LM, Siegel S, Shin SS, *et al.* Primary lymphoma of the calcaneus. Case report. *Skeletal Radio* 1996;25:775–8.
- 11 Thomas E, Symmons DP, Brewster DH, *et al.* National study of cause-specific mortality in rheumatoid arthritis, juvenile chronic arthritis, and other rheumatic conditions: a 20 year follow-up study. *J Rheumatol* 2003;30:958–65.
- 12 Ekstrom K, Hjalgrim H, Brandt L, *et al.* Risk of malignant lymphomas in patients with rheumatoid arthritis and in their first-degree relatives. *Arthritis Rheum* 2003;48:963–70.
- 13 Bachman TR, Sawitzke AD, Perkins SL, *et al.* Methotrexate-associated lymphoma in patients with rheumatoid arthritis: report of two cases. *Arthritis Rheum* 1996;39:325–9.
- 14 Dawson TM, Starkebaum G, Wood BL, *et al.* Epstein-Barr virus, methotrexate, and lymphoma in patients with rheumatoid arthritis and primary Sjogren's syndrome: case series. *J Rheumatol* 2001;28:47–53.
- 15 Jones M, Symmons D, Finn J, *et al.* Does exposure to immunosuppressive therapy increase the 10 year malignancy and mortality risks in rheumatoid arthritis? A matched cohort study. *Br J Rheumatol* 1996;35:738–45.
- 16 Mariette X, Cazals-Hatem D, Warszawski J, *et al.* Lymphomas in rheumatoid arthritis patients treated with methotrexate: a 3-year prospective study in France. *Blood* 2002;99:3909–15.
- 17 Baeklund E, Iliadou A, Askling J. Association of chronic inflammation, not its treatment, with increased lymphoma risk in rheumatoid arthritis. *Arthritis Rheum* 2006;54:692–701.

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