CASE REPORT

Primary meningococcal arthritis as a presentation of nodal marginal zone lymphoma

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SUMMARY

A 68-year-old man presented with a 4-day history of worsening knee and arm pain. On examination, there was erythema and swelling of the left knee and both wrists. Joint aspiration grew *Neisseria meningitidis*. Blood tests showed an unusually high total protein level (100 g/L) and an IgM kappa paraprotein band of 45 g/L on protein electrophoresis. CT showed widespread lymphadenopathy, hepatosplenomegaly and multilevel thoracic vertebral collapse. A bone marrow biopsy revealed a lymphoplasmacytic infiltrate and a lymph node biopsy showed features of nodal marginal zone lymphoma with plasmacytic differentiation.

BACKGROUND

Arthritis occurs in 10%–12% of cases of meningococcal disease.¹ Primary septic arthritis (as defined as arthritis in the absence of meningitis and/or classical meningococcaemia signs) is a rare manifestation of meningococcal disease.² In fact, in one Australian case series, meningococcal arthritis accounted for only 0.4% of meningococcal cases.³ In this particular case, the diagnosis of meningococcal arthritis was straightforward but the abnormal serum total protein and the immunoglobulin results suggested a haematological disorder causing immunocompromise. Investigations led to a new diagnosis of a nodal marginal zone non-Hodgkin's lymphoma. In the literature, there is one case of meningococcal arthritis and meningitis leading to a diagnosis of Waldenström's macroglobulinaemia.⁴ This case is the first description of primary meningococcal arthritis as the presenting feature of nodal marginal zone lymphoma.

CASE PRESENTATION

A 68-year-old man presented with a 4-day history of worsening knee and arm pain. On the day of admission, the pain was in his limb joints and had increased in severity to the point where he was unable to stand and had been lying on his living room floor all evening. There was no headache, rash, cough or dyspnoea. There was also no history of weight loss, sweating or lethargy. He gave a medical history which was unremarkable and he was taking no regular medications. He drank 2 units of alcohol per week and he smoked 20 cigarettes per day. There was no significant family or travel history.

On examination, there was erythema, tenderness and swelling of the left knee and both wrists.

He was unable to bend his knees or weight bear. There was no palpable lymphadenopathy or hepatosplenomegaly.

INVESTIGATIONS

Initial blood tests showed haemoglobin 126 g/dL, white blood cell count $15.3 \times 10^9/L$, C reactive protein (CRP) 350 mg/L, creatine kinase 1374 u/L and total protein 116 g/L. Blood cultures were taken before administration of antibiotics, but these were negative. HIV antibody was negative. The left knee effusion was aspirated and *Neisseria meningitidis* group B, MLST type ST11105 was isolated. The result of *Neisseria meningitidis* growth from the knee aspiration took 54 hours after the aspiration was performed. The high serum total protein level and anaemia raised the possibility of an underlying haematological disorder. The serum immunoglobulins showed IgM 66.26 g/L (normal 0.5–3.0), IgG <1.5 (6–16) and IgA <0.3 (0.8–4.0). An IgM kappa paraprotein band of 45 g/L was present on protein electrophoresis and the urine was positive for Bence-Jones protein. A direct antiglobulin test was weakly positive (IgG coating). The serum lactate dehydrogenase was normal at 154 u/L (10–250).

A CT scan of abdomen and pelvis showed widespread lymphadenopathy, a pericardial effusion, hepatosplenomegaly and thoracic vertebral collapse at a number of levels. An echocardiogram confirmed a mild-moderate pericardial effusion with no evidence of tamponade.

A bone marrow biopsy showed evidence of a lymphocytic infiltrate, with lymphoplasmacytoid differentiation. A right level V cervical lymph node was excised and showed a diffuse infiltrate of intermediate-sized lymphoid cells, many of which exhibited plasmacytoid morphology. Immunohistochemistry showed positive staining with CD20, MUM-1 and BCL2, but no staining with CD10, Bcl6, CD23 or Cyclin D1. Ki67 staining was low to moderate. The histology best fitted a diagnosis of nodal marginal zone lymphoma with plasmacytic differentiation, with a diagnosis of lymphoplasmacytic lymphoma being less likely because of the presence of residual but disrupted follicles. The lymph node biopsy and bone marrow aspirate both agreed with a diagnosis of nodal marginal zone lymphoma. While MYD88 L265P mutation analysis was positive, it has been shown that nodal marginal zone lymphoma can be sometimes associated with this mutation.⁵

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DIFFERENTIAL DIAGNOSIS

The first issue was the differential diagnosis of polyarthropathy: infective, autoimmune, gout or pseudogout. The differential was quickly limited to an infective polyarthropathy after a positive gram stain from synovial fluid and associated raised inflammatory markers. The most common organism isolated in septic arthritis is *Staphylococcus aureus* (44%) and others include *streptococci*, *pneumococcus*, *Pseudomonas aeruginosa*, *Serratia* species and *Neisseria gonorrhoeae*.⁶ In this particular case, the initial gram stain of a gram-negative cocci pointed towards a more likely differential of *N. gonorrhoeae*, as this is a more common cause of septic arthritis than *Neisseria meningitidis*. However, the synovial fluid culture confirmed the diagnosis. In the case of primary meningococcal arthritis, the synovial fluid aspirate will be positive in 90% of cases, but blood cultures will only be positive in 40% of cases.⁶

The high total protein level and abnormal immunoglobulin profile raised the possibility of an underlying haematological condition such as myeloma, Waldenström's macroglobulinaemia, lymphoma and HIV infection. Having ruled out the others possibilities, non-Hodgkin's lymphoma was confirmed from a positive lymph node biopsy.

TREATMENT

On admission, piperacillin/tazobactam was initially given, which was then changed to flucloxacillin on the advice of microbiologist who initially thought this may be a *S. aureus* septic arthritis. This was further changed to ceftriaxone 1 g intravenous one time per day as per local hospital guidelines after the result of *N. meningitidis* and this was increased to 2 g after worsening joint symptoms. Treatment continued for 1 month until symptoms resolved. The second 2 weeks of treatment were given on an outpatient parenteral antimicrobial therapy basis.

He was treated with 6 cycles of rituximab and bendamustine for the lymphoma, with a complete remission on the end of induction CT scan and decrease of his paraprotein. Rituximab maintenance is planned to consolidate the response.

OUTCOME AND FOLLOW-UP

His joint symptoms began to resolve, the CRP became normal and he was discharged. He remains under follow-up at the haematology clinic.

DISCUSSION

This case highlights the important aspect that diagnosis of one condition can lead to diagnosis of another. In this patient's case, it was his weakened immune system from the nodal marginal zone lymphoma which led to his presenting symptoms of polyarthropathy as a result of primary meningococcal arthritis. In the literature, there is one case of a 74-year-old man presenting with meningococcal meningitis and arthritis and was found to

have an underlying Waldenström's disease.⁴ He had a recurrence of meningococcal arthritis 8 years later. There is also a case report of HIV being diagnosed after the patient presented with meningococcal arthritis.⁷ These cases highlight the importance of screening for an underlying impaired immune response in patients presenting with rare conditions such as meningococcal arthritis.

Learning points

- ▶ In a case of septic arthritis, early recognition and treatment is required in order to prevent joint destruction.
- ▶ Meningococcal infection may rarely present as septic arthritis in the case of invasive meningococemia, but primary meningococcal arthritis is rarer.
- ▶ Early recognition of primary meningococcal arthritis is important in order to prevent the risk of dissemination of the disease.
- ▶ Consider the possibility of an underlying health problem, for example, an immune defect, in those presenting with meningococcal arthritis.
- ▶ A high serum total protein should prompt investigation for HIV myeloma or lymphoma.

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Author note The 68-year-old man had been a patient of all three of us. He had been on AM ward with GAJH seeing as a junior doctor.

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