

Case report

Primary late-onset hypogammaglobulinaemia associated with inflammatory polyarthritis and septic arthritis due to *Mycoplasma pneumoniae*

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SUMMARY A case is reported of primary late-onset hypogammaglobulinaemia associated with a chronic seronegative, nonerosive arthritis, which was complicated by an episode of septic arthritis due to *Mycoplasma pneumoniae*. The patient had subcutaneous nodules which have not been regarded previously as a feature of the chronic arthritis associated with hypogammaglobulinaemia. The diagnosis of septic arthritis was delayed for 2 months until synovial fluid was specifically cultured for mycoplasmas. This delay resulted in considerable joint destruction. The importance of searching for mycoplasmas in similar cases is emphasised.

Late-onset primary hypogammaglobulinaemia is associated with an increased incidence of chronic inflammatory polyarthritis which usually remits on gammaglobulin replacement.¹ This type of arthritis is nearly always nonerosive, and subcutaneous nodules have not been regarded as a feature. Patients with hypogammaglobulinaemia are also susceptible to mycoplasma infections.² This case highlights the importance of considering mycoplasmas as a cause of acute arthritis in these patients.

Case report

A 40-year-old man presented in July 1980 with a 2-week history of painful swollen joints. For the previous 6 months he had complained of a cough productive of green sputum and had been maintained on regular antibiotic therapy.

He gave a 15-year history of chronic sinusitis, recurrent lower respiratory tract infections, and episodic steatorrhoea. He had suffered from a chronic arthritis for 10 years, beginning as a predominant tenosynovitis involving the hands and wrists. For the past year he had synovitis and effusions in the

knees, elbows and ankles, together with subcutaneous nodules on the ulnar borders of both forearms. His erythrocyte sedimentation rate (ESR) was normal, rheumatoid factor (serum and joint fluid) was not detected, and the synovial fluid contained few cells and was sterile on routine culture. He was treated as having rheumatoid arthritis with non-steroidal anti-inflammatory drugs and intra-articular steroids.

On admission to hospital he had a florid arthritis involving the left knee, right ankle, and first proximal interphalangeal joint of the left hand. He was pyrexial, with clinical and radiological signs of left lower lobe consolidation. Joint aspiration revealed a purulent fluid which was sterile on routine culture. Blood cultures were negative, but *Haemophilus influenzae* was isolated from the sputum. His pneumonia responded to ampicillin and flucloxacillin. However, his arthritis persisted despite additional courses of gentamicin and metronidazole. Synovial biopsy of the left knee showed nonspecific inflammation, with preservation of the underlying cartilage.

By September 1980 the patient's general condition had deteriorated with a considerable degree of weight loss. His left knee was warm and tender, with a large effusion. Tender swellings of both ankles and the first and third left proximal interphalangeal joints were also present.

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Investigations revealed Hb 9.3 g/dl (normochromic, normocytic), leucocytes $7 \times 10^9/l$ (predominantly polymorphs), ESR (Westergren) 104 mm/h. Rheumatoid factor was not found in either the serum or synovial fluid. Antinuclear antibody was absent. The serum and synovial C4 and CH50 were normal. He was HLA B27 antigen positive. Serum immunoglobulins were: IgG <50 mg/100 ml, IgA <5 mg/100 ml, IgM <5 mg/100 ml (SI: $g/l = mg/100 ml \times 0.01$). Radiologically there was joint destruction suggestive of previous infection in the right wrist and right ankle. X-rays of the hands and sacroiliac joints were normal. Repeat aspiration of the left knee revealed turbid synovial fluid (leucocytes $26.5 \times 10^9/l$) from which *Mycoplasma pneumoniae* was isolated.

The patient was treated with intravenous tetracycline and erythromycin and weekly intramuscular gammaglobulin replacement. Antibiotic therapy was changed to an oral regimen after 2 weeks and was continued for 6 months. On this regimen his acute joint symptoms subsided, he gained weight, and his nodules disappeared. He has since had no further episodes of polyarthritis. However, the infection had severely damaged his left hip, and arthroplasty is being considered.

Discussion

Respiratory infections with *Mycoplasma pneumoniae* in immunocompetent patients may be associated with arthralgia and arthritis, usually involving medium sized joints.³ Synovial effusions may occur; they usually have a low cell count and are sterile even when cultured specifically for mycoplasmas.⁴ The joint and respiratory symptoms may persist for up to one year.⁵

The clinical picture presented by our patient with hypogammaglobulinaemia was of *Haemophilus influenzae* pneumonia and septic arthritis due to *Mycoplasma pneumoniae*. His pneumonia resolved on ampicillin therapy so that there was no evidence to suggest that he had suffered an 'atypical' mycoplasmal pneumonia. Nevertheless, the mycoplasma must have gained access to the joints from the respiratory tract.

Mycoplasma pneumoniae have been isolated from the synovial fluid in another patient with acute arthritis, apparently supervening on the chronic polyarthritis characteristic of late-onset hypogammaglobulinaemia.⁶ The same organism has been reported as causing osteomyelitis in a case of congenital hypogammaglobulinaemia.⁷ *Ureaplasma urealyticum* organisms, which were called previously T-strain mycoplasmas, have also caused septic

arthritis in 2 cases of congenital hypogammaglobulinaemia.^{8,9} These reports suggest that patients with hypogammaglobulinaemia are particularly susceptible to mycoplasmal septic arthritis and that synovial fluid from all suspected cases should be cultured in appropriate media.

The features of this patient's chronic arthritis were similar to those described in patients with hypogammaglobulinaemia by Webster *et al.*¹ In their series the main differences from rheumatoid arthritis were the prominent tenosynovitis, sparing of the small joints of the hand, the absence of true erosions, and the rapid response to gammaglobulin replacement. Subcutaneous nodules did not occur. However, similar nodules have been reported in association with arthritis in a patient with congenital hypogammaglobulinaemia, the joint symptoms and nodules both regressing on gammaglobulin replacement.¹⁰ Unfortunately we were unable to obtain permission to biopsy a nodule in our case and so histology is not available.

The aetiology of the chronic polyarthritis of hypogammaglobulinaemia is unclear. It bears certain similarities to the arthritis that may follow intestinal bypass surgery. This is thought to be a reactive arthritis associated with an overgrowth of the bowel flora. Patients with hypogammaglobulinaemia do have an increase in their bowel flora, and infestation with *Campylobacter* sp. and *Giardia lamblia*¹¹ are common. Our patient also had episodic steatorrhoea, which has regressed on gammaglobulin. He is also HLA B27 positive. Thus there may be a link between intestinal infestation and the chronic arthritis. However, mycoplasmas (possibly *Myco. hominis*) have been isolated recently from the knee joints of 2 patients with hypogammaglobulinaemia and chronic arthritis (A. D. B. Webster, P. Furr, and D. Taylor-Robinson, personal communication), suggesting that all the joint disease associated with this condition may be infective in origin.

The case presented here highlights the importance of considering the diagnosis of hypogammaglobulinaemia in any case of unexplained chronic polyarthritis with a history of recurrent upper and/or lower respiratory tract infections. Joint fluid should always be aspirated and cultured for infectious agents. Mycoplasmas should be sought specifically, it being borne in mind that the individual species require different culture conditions. If the joint fluid is purulent and organisms are not detected by Gram staining, empirical treatment with intravenous tetracycline and erythromycin should be started immediately while awaiting the results of the culture. Mycoplasmas may take many weeks to grow, and, if the patient is not treated, irreversible joint destruction may occur within this period.

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