



Case 10.1 Septic arthritis

A 37-year-old woman developed a symmetrical polyarthritis. A test for CCP antibodies was positive and erosive changes were seen on X-ray, confirming a clinical diagnosis of RA. The arthritis followed an aggressive course with poor response to a variety of disease-modifying antirheumatic drugs and she became increasingly disabled due to severe destructive changes in the knees, wrists and shoulders. A moderate dose of prednisolone was introduced at the age of 42, with some symptomatic improvement in her joints and she was referred to an orthopaedic surgeon with a view to knee replacements. However, 1 month before her orthopaedic appointment she presented to the emergency department with a painful swollen right knee. On examination she was unwell, febrile (38 °C) and had a hot, red right knee with a sizable effusion. Eighty millilitres of purulent synovial fluid was aspirated from the joint and microscopy of the fluid revealed numerous Gram-positive cocci. A diagnosis of septic arthritis was made on a background of severe RA and steroid therapy. She was treated with high-dose IV antibiotics and the joint was washed out via an arthroscope. Culture of blood and synovial fluid grew *Staphylococcus aureus*. She received 6 weeks' antibiotic treatment in total together with vigorous physiotherapy. Her knee, however, was significantly worsened by the infection and she could no longer straighten the leg or walk more than a few yards. Joint replacement was deferred for 6 months to reduce the risk of infection in the prosthesis.



Case 10.2 Rheumatoid arthritis – classic course

A 37-year-old woman gradually developed painful wrists over 3 months; she consulted her doctor only when the pain and early morning stiffness stopped her from gardening. On examination, both wrists and the metacarpophalangeal joints of both hands were swollen and tender but not deformed (Fig. 10.2). There were no nodules or vasculitic lesions. On investigation, she was found to have a raised C-reactive protein (CRP) level (27 mg/l) (NR <10) but a normal haemoglobin and white cell count. A latex test for rheumatoid factor was negative but autoantibodies to cyclic citrullinated peptides were detected.

The clinical diagnosis was early RA and she was treated with ibuprofen. Despite some initial symptomatic improvement, the pain, stiffness and swelling of the hands persisted and 1 month later both knees became similarly affected. She was referred to a rheumatologist.

She was seen 3 months after the initial presentation. By this time she was struggling to work, drive and carry heavy objects. A test for rheumatoid factor was now positive (titre 1/256) and anti-CCP antibodies were strongly positive. X-rays of the feet showed small but definite erosions in two metatarsal heads. She still had a raised CRP (43 mg/l) but normal serum complement (C3 and C4) levels.

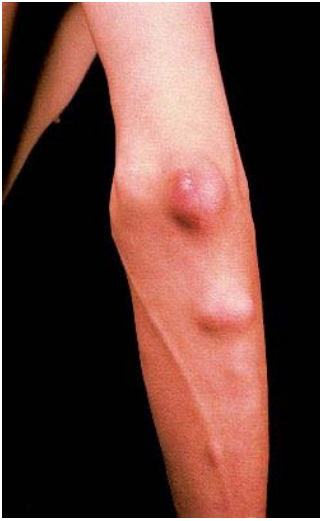
This woman had rheumatoid arthritis with some features suggesting a poor prognosis. Her treatment was changed to weekly low-dose methotrexate. This controlled the arthritis and no further erosions developed for several years. When the disease flared, she received anti-TNF therapy. In view of the poor prognosis, she would now be started on anti-TFN therapy by her rheumatologist when first seen in clinic.



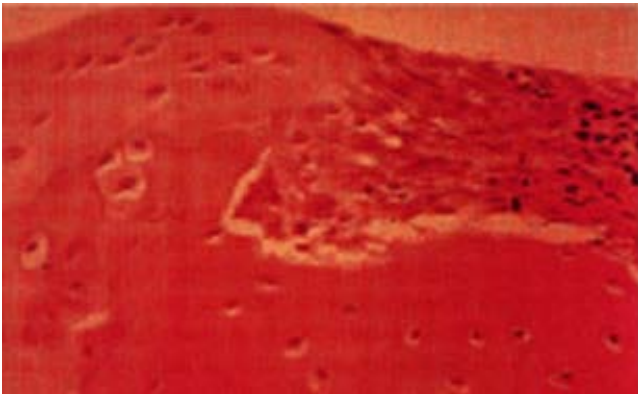
Fig. 10.2 Symmetrical synovitis in early rheumatoid arthritis. From *Medical Masterclass. Rheumatology and Clinical Immunology*, 1st Ed. Copyright © 2001 Royal College of Physicians. Reproduced with permission.



Case Figure 10.2a Hands from a patient with early rheumatoid arthritis, showing marked metacarpophalangeal joint swelling but no deformity of the overall structure of the hands. Slide courtesy of Martin Patrick.



Case Figure 10.2b Large rheumatoid nodules at the elbow. These typically form at sites of recurrent minor trauma.



Case Figure 10.2c Histology of pannus. Roitt and Rabson.

Early RA



Advanced RA



Case Figure 10.2d Deforming arthropathy in rheumatoid arthritis.



Case 10.3 Pulmonary fibrosis in rheumatoid arthritis

A 61-year-old man, with a 15-year history of seropositive RA, was admitted with increasing shortness of breath, myalgia and weight loss. He had previously smoked 40 cigarettes a day but had never been exposed to coal or silica dust. On examination, he was pale and thin, with generalized muscle tenderness. Widespread crepitations were heard over both lung fields. His joints were tender and he had subluxation of the metacarpophalangeal joints of both hands. There was bilateral cervical and axillary lymph node enlargement but no splenomegaly. Neurological and cardiac examinations were normal.

Investigations showed a raised CRP (81 mg/l) and a normochromic anaemia (Hb 95 g/l) but a normal white cell count. His serum IgG was raised at 44 g/l (NR 7.2–19.0), although IgA and IgM levels were normal. He had a strongly positive rheumatoid factor and anti-CCP antibodies titres. There were no detectable antibodies to DNA or to extractable nuclear antigens (ENA) (see Chapter 19) and the serum levels of muscle enzymes were normal. A chest X-ray suggested pulmonary fibrosis. High-resolution computed tomographic scanning of the chest confirmed severe pulmonary fibrosis, with no evidence of any ground glass shadowing (a feature that would suggest a good response to immunosuppression). Pulmonary function tests showed a severe restrictive defect, with a forced expiratory volume in 1 sec/forced expiratory vital capacity of 1.1/1.3. He was too unwell to undergo a lung biopsy.

This man's dyspnoea was rapidly progressive and he continued to deteriorate despite intravenous corticosteroids and cyclophosphamide. At autopsy, both lungs showed severe fibrosis, with the pattern of interstitial pneumonia (see section 13.4.3), which is a rare complication of RA with a poor prognosis. The onset of serious complications of RA so long after the initial diagnosis is not unusual.



Case Figure 10.3a Hands showing evidence of severe damage due to longstanding rheumatoid arthritis. Note ulnar deviation and subluxation of metacarpophalangeal joints.



Case Figure 10.3b Fibrosing alveolitis in RA – though patient has subluxation and this picture shows classical swan-neck deformities in deforming RA. Roitt & Rabson.



Case Figure 10.3c X-ray of hands severely affected by rheumatoid arthritis.



Case 10.4 Ankylosing spondylitis

A 21-year-old man presented to his local emergency department with acute pain and swelling of one knee. On examination, the joint was tender and restricted in movement. X-ray of the knee showed periarticular osteoporosis. On investigation, he had a raised erythrocyte sedimentation rate (ESR) of 102 mm/h, a mild anaemia (Hb 106 g/l) but no detectable serum rheumatoid factor. The knee effusion was aspirated; the fluid contained a polymorphonuclear leucocytosis but no organisms or rheumatoid factor. No diagnosis was made at this stage but he was treated empirically with diclofenac; his arthritis improved.

Fifteen months later he developed an iritis in his left eye. At this point, a history was also elicited of low back pain and prolonged early morning stiffness dating back to his late teenage years. His peripheral joints were normal but his lumbar spine was rigid and he had some pain and restriction of the neck. X-rays of his lumbar spine and pelvis showed the classic changes of ankylosing spondylitis and tissue typing revealed that he was HLA-B27-positive (Fig. 10.5). He continues to have widespread spinal discomfort, although daily exercises have reduced the stiffness in his neck. At his last clinic visit he asked whether he should receive an anti-TNF drug as he does fit the criteria.



Fig. 10.5 Bamboo lumbar spine in ankylosing spondylitis. From Medical Masterclass. *Rheumatology and Clinical Immunology*, 1st Ed. Copyright © 2001 Royal College of Physicians. Reproduced with permission.



Case Figure 10.4a Spinal fusion in ankylosing spondylitis.



Case Figure 10.4b X-ray of fused vertebrae in patient with ankylosing spondylitis – a late feature of the disease but one causing a great deal of disability. Slide courtesy of Martin Patrick.



Case 10.5 Reactive arthritis following infection (previously Reiter's disease)

A 19-year-old man presented with acute swelling of his right knee and left ankle and extremely painful heels. On questioning, he admitted to a penile discharge and dysuria for 4 days. On examination, he had bilateral Achilles tendonitis and his right knee and left ankle were red, hot and tender. He had aphthous-like mouth ulcers and ulcers around the glans penis. There were no skin lesions and, in particular, no evidence of keratoderma blenorrhagica or subungual pustules.

On investigation, he was found to have a raised ESR (60 mm/h) but a normal haemoglobin and white cell count. A latex test for rheumatoid factor was negative. X-rays of the joints were normal. Joint fluid aspirated from the right knee showed a polymorphonuclear leucocytosis but no organisms. Gonococci were not cultured from the urethral pus or from the joint fluid but chlamydial DNA was detected by the polymerase chain reaction. Tissue typing showed him to be HLA-B27 positive. A diagnosis of Reiter's disease was made. He was given diclofenac for symptomatic relief of the arthritis and tendonitis. The chlamydial urethritis was treated with doxycycline and his partner was screened for sexually transmitted infection. Four days later, he developed bilateral conjunctivitis and some photophobia. However, 6 weeks later he had fully recovered and did not relapse.



Case Figure 10.5a Patients with florid Reiter's syndrome can develop scaly and sometimes pustular changes on the hands and feet which resemble severe psoriasis. This is keratoderma blenorrhagica. Slide courtesy of Martin Patrick.



Case Figure 10.5b Conjunctivitis is the most common eye lesion in Reiter's syndrome, but uveitis also occurs. Slide courtesy of Martin Patrick.



Case 10.6 Behçet's syndrome

A 32-year-old man from a Turkish family presented with deteriorating vision and painful swollen knees. Further questioning revealed a 10-year history of relapsing and remitting mouth ulcers and a less severe history of genital ulceration. On examination he had reduced visual acuity associated with a florid retinal vasculitis. Two 1-cm mouth ulcers were found but no active genital ulceration. He had synovitis in both knees. Investigation revealed a raised ESR at 94 mm/h but a normal blood count and negative tests for rheumatoid factor, antinuclear antibodies, cytomegalovirus and HIV infection. A clinical diagnosis of Behçet's syndrome was made. He was treated with high-dose corticosteroids and azathioprine with good response, although his visual acuity remains permanently impaired. He might have benefited from therapy with adalimumab (a humanized antibody to TNF- α) but this was not available at the time.



Case Figure 10.6 Pathergy: pustular/acneiform lesions occurring along the line of the bra strap in a woman with Behçet's disease.



Case 10.7 Juvenile idiopathic arthritis

A 2-year-old girl was taken to her GP because she was unwilling to walk. Her GP found her right knee to be swollen and tender and referred her to an orthopaedic surgeon who was concerned that she may have septic arthritis, although she was systemically well. An X-ray was normal. Synovial fluid was aspirated under general anaesthetic, but was sterile on culture. The pain settled somewhat, although the knee was still swollen on examination. Two months later her left ankle also became swollen and painful. Blood tests showed a raised ESR at 40 mm/h, a negative test for rheumatoid factor and a low-titre (1/40) homogeneous ANA. DNA antibodies were not detected. Serum immunoglobulins were normal. A diagnosis of early-onset pauciarticular JIA was made and she was treated with ibuprofen with a good response. However, 1 month later the knee was still swollen and she was given an intra-articular steroid injection with complete resolution of the synovitis. Her vision seemed normal but ophthalmological screening revealed a severe chronic uveitis which was treated with topical steroids. At the age of 4 her joint disease was in complete remission, but her uveitis remained intermittently active, and she has developed a cataract in the right eye. She remains under long-term ophthalmological follow-up; *this emphasises the need for rapid ophthalmological screening as soon as a diagnosis of JIA is made.*



Case 10.8 Systemic lupus erythematosus

A 26-year-old woman presented with fatigue and painful, stiff knees of 4 weeks' duration. She had a 6-year history of Raynaud's phenomenon, frequent mouth ulcers and had had a blotchy rash and ill-health after a recent holiday in Spain. On examination, she had bilateral effusions in both knee joints, but all other joints were normal. She had no skin lesions, muscle tenderness, proteinuria or fever. A full blood count showed mild thrombocytopenia with a platelet count of 95 (normal 150–400 $\times 10^{12}/l$) and lymphopenia ($0.7 \times 10^9/l$, normal 1.5–4.0). The results of relevant immunological investigations are shown in Table 10.12. On the basis of these findings, a diagnosis of SLE was made and the patient treated with aspirin for her painful knees. She improved over 4 weeks and then remained symptom-free for 5 years. During this time, her antinuclear antibody remained positive at 1/1000, her anti-double-stranded (ds) DNA antibody level varied from 40 to 100 (normal <25) and her C3 and C4 levels were occasionally low. Later, she developed a bilateral, blotchy rash on her hands and thighs, consistent with active vasculitis. Her Raynaud's phenomenon concurrently became much worse. Following treatment with hydroxychloroquine, the skin manifestations gradually disappeared and the steroids were tailed off.

This patient presented with arthritis and Raynaud's phenomenon. She is unusual in that the arthritis of SLE usually involves small joints. It is important to note that she remained perfectly well without treatment for 5 years, despite persistently abnormal serology.

Table 10.12 Investigations in Case 10.8 (also see Table 19.6)

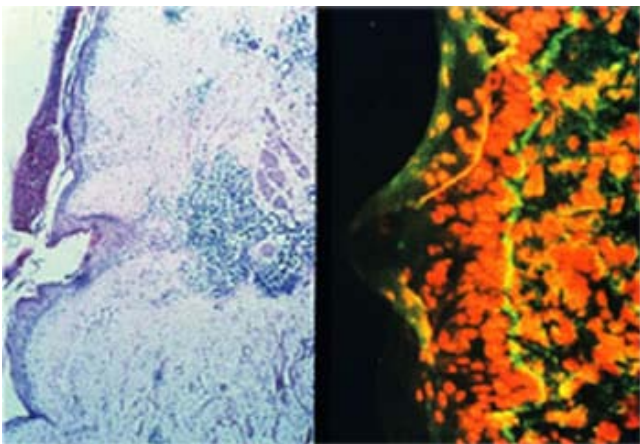
C-reactive protein	8 mg/l (normal)
Rheumatoid factor	Negative
Antinuclear antibody	Positive (titre 1/1000; IgG class, homogeneous pattern)
Anti dsDNA-antibodies	80 (<25)
Antibodies to extractable nuclear antigens	Negative
<i>Serum complement levels</i>	
C3	0.35 g/l (NR 0.65–1.30)
C4	0.05 g/l (NR 0.20–0.50)
<i>Serum immunoglobulins</i>	
IgG	22.0 g/l (NR 7.2–19.0)
IgA	3.8 g/l (NR 2.0–5.0)
IgM	1.2 g/l (NR 0.5–2.0)
Biopsy of normal, sun-exposed skin (lupus band test)	Granular deposits of IgG and complement at dermo-epidermal junction



Case Figure 10.8a Blotchy erythema on the dorsum of the hands in a patient with SLE. Not all patients with SLE have the classical photosensitive 'butterfly' rash. Slide courtesy of Martin Patrick.



Case Figure 10.8b Well-demarcated digital ischaemia due to Raynaud's phenomenon.



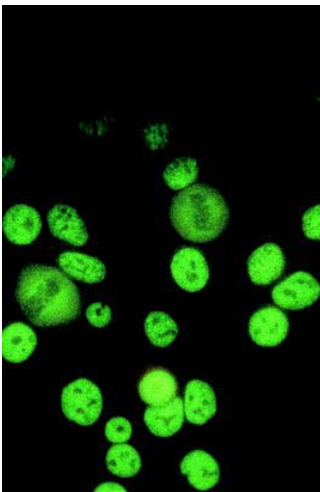
Case Figure 10.8c Lupus band test. Roitt & Rabson 2000.



Case 10.9 Mixed connective tissue disease

A 19-year-old typist presented with acute, bilateral arthralgia of her wrists and knees. The pain prevented her from sleeping or typing. On examination, there were no effusions or tenderness of any joints. No diagnosis was made but she was treated symptomatically. Two months later, she developed severe Raynaud's phenomenon, with arthralgia and pronounced sausage-like swelling of her fingers and some proximal muscle weakness. On investigation, she had a low haemoglobin (108 g/l) but a normal white cell count and differential. Her ESR was raised (63 mm/h), and her serum contained ANA (titre 1/160; speckled pattern) (see Chapter 19). dsDNA binding was normal but antibodies to ENA were detected and found to be largely directed against nuclear ribonucleoprotein (RNP); there were no antibodies to the Sm antigen (see Chapter 19). A latex test for rheumatoid factor was negative. Complement levels (C3 and C4) were normal but she had a raised serum IgG of 21.8 g/l (NR 7.2–19.0). X-rays of the hands and knees were normal. There was no proteinuria and her serum creatinine and blood urea were normal. Her creatine kinase was elevated at 2100 IU/ml (normal <100) and a muscle biopsy showed features of a low-grade myositis.

A diagnosis of mixed connective tissue disease (MCTD) was made and the patient started on prednisolone 40 mg daily. The muscle weakness and joint pain improved dramatically, but attempts to reduce and discontinue the steroids were unsuccessful; muscle weakness returned each time the drug was discontinued. Azathioprine was introduced as a steroid-sparing immunosuppressive. Her Raynaud's phenomenon has slowly worsened and is now associated with progressive sclerodactyly.



Case Figure 10.9a Cultured human cell line (Hep 2) shows fine speckled immunofluorescent staining of nuclei.



Case Figure 10.9b Well-demarcated digital ischaemia due to Raynaud's phenomenon.



Case Figure 10.9c Well established sclerodactyly in late stage systemic sclerosis or MCTD. Slide courtesy of Martin Patrick.



Case 10.10 Sjögren's syndrome

A 38-year-old woman was referred to an oral surgeon for investigation of a dry mouth. She had a sister with arthritis. Examination and investigations were unremarkable except for a raised ESR (42mm/h). Six months later, she developed a mild conjunctivitis and complained of sore eyes. On testing, rheumatoid factor was now positive (Rose–Waalder titre 1/64); total serum proteins were raised (98g/l); and immunoglobulin levels showed a raised IgG of 28g/l (NR 7.2–19.0), with a slightly raised IgM of 2.8g/l (NR 0.5–2.0) and a normal IgA. Schirmer's test was performed (see section 10.8.2). The test was markedly abnormal as only 3.5mm of the filter strip in the right eye and 1.5mm of that in the left eye became wet (Fig. 10.12).

She was treated with methylcellulose eye drops to prevent corneal ulceration. Over a period of many years, her rheumatoid factor titre steadily increased and ANA and antibodies to the extractable nuclear antigens Ro and La became detectable. Seven years after the development of the dry mouth and dry eyes (together known as the sicca complex), she developed a mild, bilateral non-erosive polyarthritis of her hands, wrists and knees. A diagnosis of secondary Sjögren's syndrome was made. The disease has remained mild. NSAIDs have been given for the arthritis but have had no effect on the sicca complex.



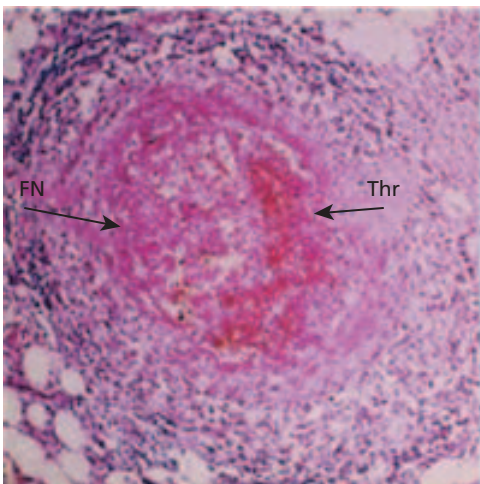
Fig. 10.12 Dry eyes in Sjögren's syndrome demonstrated by Schirmer's test. From *Medical Masterclass*. Rheumatology and Clinical Immunology, 2nd Ed. Copyright © 2008 Royal College of Physicians. Reproduced with permission.



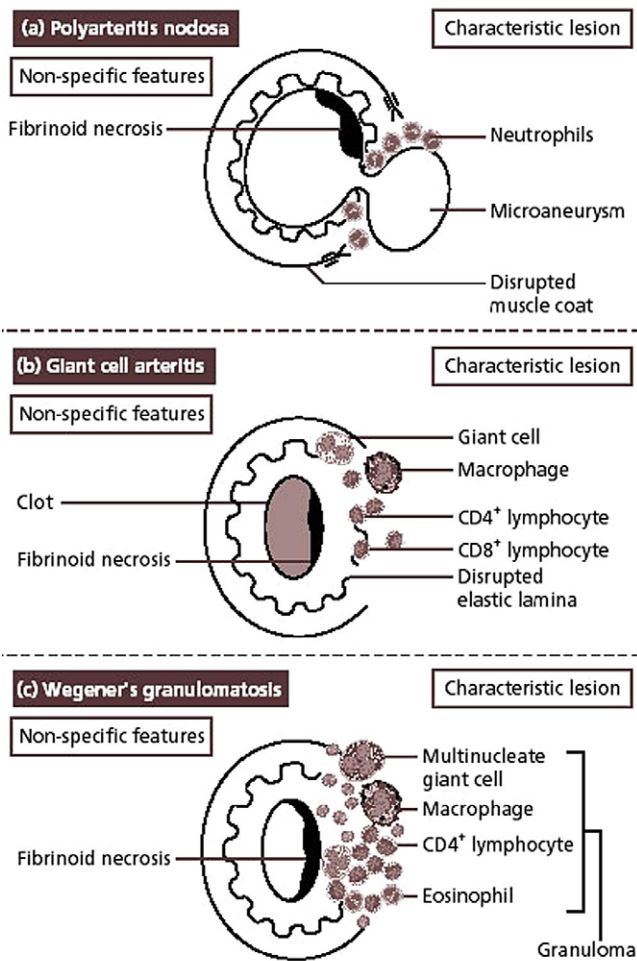
Case 10.11 Polyarteritis nodosa

A 64-year-old man developed diplopia due to a right sixth nerve palsy, lethargy, weight loss and skin lesions on the right leg which were thought to be erythema nodosum. Six weeks later, he presented with aches and pains in his shoulders, which his doctor thought were due to polymyalgia rheumatica. He improved dramatically on steroids, but unfortunately they had to be withdrawn because of hypertension. On investigation, he had an ESR of 104 mm/h, a polymorphonuclear leucocytosis and some proteinuria (1.5 g/24 h) with occasional granular casts. Biopsy of a skin lesion showed non-specific changes. A renal biopsy was normal. No diagnosis was possible.

Four weeks later, he developed profound malaise with fever, marked muscle weakness and anaemia. His haemoglobin was 77 g/l with a CRP of 70 mg/l, a negative direct Coombs' test and a reticulocyte count of 5.4%. Blood urea, serum creatinine and creatinine clearance were normal, as was serum creatine kinase level. ANA, dsDNA binding and antineutrophil cytoplasmic antibodies (ANCA) were negative, with normal C3 and C4 complement levels. Biopsy of an affected calf muscle showed a florid arteritis. All the medium-sized arteries showed reduction of their lumens or complete occlusion. On the basis of this muscle biopsy, a firm diagnosis of polyarteritis nodosa was made. The patient was started on 60 mg of prednisolone per day. Over the next few days his temperature fell and his symptoms improved.



Case Figure 10.11a Polyarteritis nodosa – histology of a biopsy of affected calf muscle shows occlusion of the vessel due to thrombus (Thr) and fibrinoid necrosis (FN) of the vessel wall resulting in the weakness associated with aneurysm formation (not shown). Roitt & Rabson.



Case Figure 10.11b Histology of three types of vasculitis in patients who may present with arthritis/arthralgia or myalgia.

Case 10.12 Polymyalgia rheumatica

A 73-year-old woman presented with sudden pain and stiffness of her shoulder muscles. She had become increasingly depressed over the preceding 3 months, with anorexia and loss of weight. On examination, there was limitation of movement of both shoulders with muscle tenderness; neurological examination was normal. The temporal arteries were extremely tender on palpation. On investigation, her haemoglobin was 101 g/l with a raised CRP of 68 mg/l. A diagnosis of polymyalgia rheumatica and temporal arteritis was made and a temporal artery biopsy taken. Treatment was started immediately with 60 mg of prednisolone daily and within 24 h the patient was markedly improved; she became more alert and her muscle stiffness lessened. The temporal artery biopsy showed a vasculitis with infiltration by lymphocytes, macrophages and giant cells (Fig. 10.15). Improvement continued over the next few days. Steroids were gradually withdrawn over 2 months but her polymyalgia relapsed a year later and she again improved on steroids.

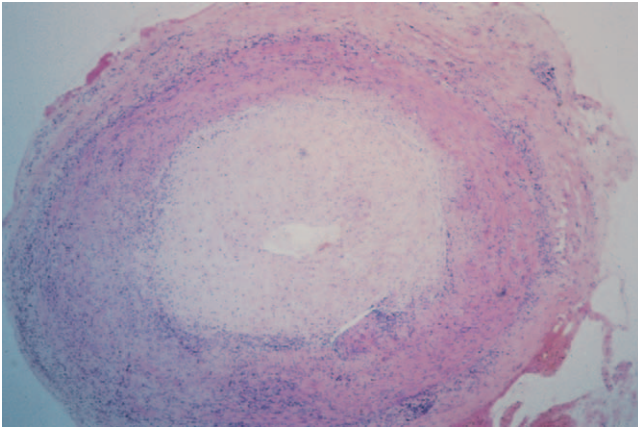


Fig. 10.15 Occluded, temporal artery in giant cell arteritis. The vessel wall is thickened and infiltrated with lymphocytes and macrophages. From Medical Masterclass. Rheumatology and Clinical Immunology, 2nd Ed. Copyright © 2008 Royal College of Physicians. Reproduced with permission.



Case 10.13 Polymyositis

A 32-year-old woman with a past history of ulcerative colitis (quiescent for the last 7 years) presented with a dry cough. The cough became productive of clear sputum and she was admitted 2 months later with increasing dyspnoea, myalgia and arthralgia. A clinical diagnosis of fibrosing alveolitis was made and confirmed by transbronchial biopsy. She was treated with prednisolone, which improved her arthralgia, and it became clear that she had a severe proximal myopathy. Serum creatine kinase was found to be very high and a muscle biopsy showed necrosis and a cellular infiltrate compatible with polymyositis. She had a circulating autoantibody to Jo 1 antigen (see Chapter 19).

She recovered eventually, after a stormy course which included treatment with pulsed methylprednisolone, oral azathioprine and three plasma exchanges of 2.5L. She has persistent myalgia and some arthralgia and remains on 20 mg prednisolone daily; the prognosis is poor.