Unusual spinal tuberculosis after adequate chemotherapy for lymph node tuberculosis in an immunocompetent man

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Abstract
A 35 year old man developed paraplegia due to an epidural mass 15 months after completion of a full chemotherapy course for pulmonary and lymph node Mycobacterium bovis infection. His cellular immune function was normal after treatment. It is suggested that the lesion was a granulomatous healing response rather than bacteriological recurrence.

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Relapse of tuberculosis is rare after appropriate chemotherapy for sensitive organisms in a compliant, immunologically competent patient. We report the development of an exuberant granulomatous mass in the vertebral canal causing paraplegia 15 months after completion of chemotherapy for pulmonary and lymph node tuberculosis due to Mycobacterium bovis, which was fully sensitive to the drugs used.

Case report
A 35 year old Asian man was admitted to hospital with a two month history of fever, cough, and weight loss (13 kg). He smoked 10 cigarettes a day and drank up to one bottle of spirits a day. He had gross cervical lymphadenopathy. His chest radiograph showed extensive upper lobe shadowing. The Mantoux test (10 TU) reaction was negative. Sputum smears showed numerous acid fast bacilli. Standard chemotherapy was started (rifampicin, isoniazid, ethambutol, and pyrazinamide) plus prednisolone 40 mg daily.

Twice weekly Mantoux tests were performed and conversion to positive occurred on the 16th day of treatment, at which time the dose of prednisolone was reduced.1 Prednisolone was discontinued on the 36th day of treatment and the patient went home on day 44. Throughout this time his cervical lymphadenopathy was unchanged. His subsequent progress was complicated by relapse of the cervical lymphadenopathy, which settled with continued antituberculosis chemotherapy, aspiration, and a two month course of prednisolone. Ethambutol and pyrazinamide were given for four months and rifampicin and isoniazid for nine months.

Pretreatment sputum and urine samples showed acid fast bacilli. Culture yielded M bovis sensitive to isoniazid, rifampicin, ethambutol, and streptomycin. After four months' treatment the sputum, urine, and lymph node aspirates still showed acid fast bacilli, but all cultures were negative.

The cellular immune function was assessed in vitro on the basis of lymphocyte proliferation in response to mycobacterial antigens, purified protein derivative (PPD) and cytotoxic T cell activity.2 Initial assessment at the time of admission showed extremely poor proliferation and cytotoxic T cell activity. Four months later in vitro lymphocyte proliferation was high and cultured lymphocytes showed substantial cytolytic activity against both PPD presenting and antigen non-presenting autologous macrophages.

The patient returned 15 months after completing chemotherapy, unable to walk and with a two week history of back pain and leg weakness. There was pronounced quadriiceps wasting, absence of knee and ankle jerks, and patchy loss of sensation over the legs. Lumbar spine radiographs were normal. A myelogram showed a circumferential narrowing of the dural sac from the upper border of the second lumbar vertebra to the level of the sacral cul-de-sac, suggesting an extensive extradural obstructing lesion. Spinal computed tomodiography confirmed extradural block by a mass in the vertebral canal extending from the second to the fourth lumbar vertebra, with no evidence of bony erosion or widening of the vertebral canal (figure). Two core biopsy specimens from the second lumbar vertebra were normal. A diagnosis of an intraspinal tumour was made and lumbar laminectomy via a posterior approach was undertaken. The dura was covered by soft grey tissue. This was removed and placed in formol saline. Histological examination showed this to be granulomatous inflammation with focal caseating necrosis. No acid fast bacilli were demonstrated by auramine rhodamine stain. Culture of the tissue was not possible. In view
of the histology a further course of anti-
tuberculostis chemotherapy was commenced.
At that time cellular immunity, as measured
in vitro in terms of lymphocyte proliferation
in response to PPD, and cytolitic capacity
remained normal. The patient subsequently
recovered good neurological function and
remains well.

Discussion
Spinal tuberculouss lesions masquerading as a
tumour without disease of the bone have been
reported. Three were seen in a series of 190
cases of spinal tuberculosis reported by
Rahman and colleagues; all had had a
preoperative diagnosis of tumour and all had
responded to decompression. Babhulkar et al
reported 10 in a series of 220 cases with
extrasosseous, extradural tuberculous disease;
the lesion is described as a thick granulom-
atous membrane compressing the spinal
cord. None of these patients had been given
antituberculostis chemotherapy. In our patient
the primary lesion of _M. bovis_ infection may
have been in the intestine with lymphatic
spread throughout the abdomen and to the
spine.

Our patient had received an adequate
course of chemotherapy for a fully sensitive
organism. We believe him to have been fully
compliant, though we did not check this and
cannot completely exclude non-compliance as
a factor. Cytotoxic T cells, which lyse both
autologous mycobacteria infected macro-
phages and non-infected "bystander" macro-
phages, are known to play a part in the normal
immune response to mycobacterial infection,
and they may mediate delayed type hyper-
sensitivity reactions. Kumararatne and
colleagues have postulated that recurrence of
tuberculosis despite adequate chemotherapy
may sometimes be related to an inability to
generate cytolitic T cells capable of recognis-
ing mycobacterial antigens. Cytolitic activity
was low initially in our patient when he was
very ill and had a negative tuberculin test
response. Immune paresis is well recognised
in acute severe tuberculosis, occurring in up
to 20% of patients with active disease. The
paresis resolved once he had improved and
had recovered his tuberculin skin reactivity,
and his legs remained normal at the time of
his later presentation. His initial impairment
of cell mediated immunity to tuberculous
antigen presumably therefore reflects immune
suppression due to his severe infection and his
chronic alcohol abuse rather than any
constitutional immunoincompetence.

Although the spinal lesion could have been
due to bacteriological reactivation, we
consider this unlikely. Reinfection may cause
a second episode of tuberculosis after a full
course of chemotherapy, but this seems an
unlikely explanation for a granulomatous
lesion presenting 15 months after completion
of chemotherapy. We suggest that this clinical
recurrence was due to a granulomatous heal-
ing response, which, had it occurred else-
where (in the lung, for example), might have
been of little clinical importance.

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