CASE REPORT

Unusual case of cerebral demyelination and bilateral optic neuritis in an infant with suppurative BCG lymphadenitis

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SUMMARY

Cerebral demyelination and optic neuritis are often seen in children with acute disseminated encephalomyelitis following various infections and immunisations. An eight month old girl presented with a left axillary lymph node swelling and an erythematous lace-like rash over her cheeks and trunk. She then developed acute encephalopathy, bilateral nystagmus, right hemiparesis and left facial nerve palsy. Her electroencephalogram showed an encephalopathic process and visual evoked response study were grossly abnormal. Her MRI brain showed hyperintensities in the midbrain, pons and bilateral cerebellar peduncles. She was treated as postinfectious cerebral demyelination with intravenous antibiotics, methylprednisolone and immunoglobulin. Left axillary lymph node excision biopsy and GeneXpert test detected *Mycobacterium tuberculosis* complex that prompted initiation of antituberculous therapy. Her chest X-ray and cerebrospinal fluid examinations for tuberculosis were normal. She showed significant recovery after 2 weeks. This case illustrates a rare presentation of cerebral demyelination and bilateral optic neuritis following suppurative BCG lymphadenitis.

BACKGROUND

Acute disseminated encephalomyelitis (ADEM) is an acute and severe immune mediated, demyelinating disorder involving the white matter of the central nervous system (CNS). ADEM presents with multiple manifestations including encephalopathy coupled with evidence of multifocal lesions of demyelination on neuroimaging. ADEM in children has been reported following exanthematous viral infections, systemic infections or recent vaccinations and is postulated to be due to the immune system dysregulation.¹ Although ADEM can occur at all ages, it is most commonly reported in children and adolescents with an incidence rate of 8 per 1 000 000 people per year.² We report a rare case of ADEM following BCG lymphadenitis in an infant.

CASE PRESENTATION

An 8-month-old girl was referred to our centre with a history of increasing irritability, bilateral nystagmus and right facial nerve palsy. Six weeks prior to this presentation, she developed left axillary lymphadenopathy which was initially suspected to be BCG lymphadenitis. She was vaccinated at birth over the left deltoid with BCG. She

was promptly treated for lymphadenitis with intravenous cloxacillin. However, the swelling persisted and increased in size. Two weeks after the onset of lymphadenopathy, she developed low-grade fever and lace-like erythematous rash over her cheeks and limbs, sparing the trunk (figure 1A–C). The rash was non-pruritic in nature and it resolved spontaneously after 12 days. She was admitted to a local hospital as she developed low-grade fever, became more irritable and refused her feeds. Her initial MRI brain was reported as normal. She was treated as meningoencephalitis with intravenous ceftriaxone and aciclovir. However, she became more encephalopathic, floppy and developed nystagmus which prompted transfer of care to our hospital. She was born term to healthy, non-consanguineous parents and had achieved normal developmental milestones prior to the onset of her illness. They denied any pulmonary tuberculosis contact or consuming any unpasteurised milk.

On general examination, she was febrile with temperature of 38.4°C, pulse rate of 120 per minute and blood pressure 90/65 mm Hg. She was irritable, drowsy and had bilateral nystagmus. Her pupils were reactive and fundoscopic examination revealed blurred optic disc margins bilaterally. She was hypotonic with brisk deep tendon reflexes in all four limbs and had bilateral extensor plantar response. The left axillary lymph node measured 2 cm by 3 cm in diameter, firm in consistency with normal overlying skin (figure 1D). She had a 0.5 cm BCG scar blister over the left deltoid region. Her other systemic examination was normal.

In the ward, she developed two episodes of generalised seizures and became more obtunded. Subsequently, she was noticed to have a right lower motor neuron facial palsy.

INVESTIGATIONS

Total white cell count was $23.8 \times 10^9/L$, platelet count was $544 \times 10^9/L$, haemoglobin was 8.4 g/dL, erythrocyte sedimentation rate 105 mm/hour and C-reactive protein 16 mg/L. Renal function and liver function tests were within normal limits. Cerebrospinal fluid (CSF) study revealed glucose of 3.2 mmol/L, protein 670 mg/mL, cell count $0/mm^3$ with no organisms seen on Gram stain. Acid-fast bacilli were not detected on Ziehl-Neelsen staining. The CSF oligoclonal bands were positive. Serology tests for bartonella, borrelia, parvovirus,

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Figure 1 (A–C) Lace like, erythematous rash over both cheeks and the limbs. (D) Ipsilateral axillary lymphadenopathy on presentation. (E) Enlarged, tender and fluctuant axillary lymphadenopathy after methylprednisolone administration.

enterovirus 71 were all negative. Chest radiograph was normal and tuberculin test was negative.

Visual evoked potential study showed no reproducible waveform which was consistent with bilateral optic neuritis. Her electroencephalogram showed a diffusely slow background in keeping with an encephalopathic process.

The initial MRI brain was reviewed and showed hyperintense T2 signal over the right cerebellar white matter and the optic nerves appeared swollen (figure 2A,B). A repeat MRI brain (figure 3) revealed asymmetrical hyperintense T2 signals in the pons, midbrain and cerebellar peduncles. There was no hydrocephalus or basal meningeal enhancement seen.

TREATMENT AND PROGRESS

Based on the clinical presentation and the MRI scan findings, we treated her as ADEM with intravenous methylprednisolone (30 mg/kg/day for 5 days) and intravenous immunoglobulin (2 g/kg given over 2 days).

The nystagmus resolved but she still could not fixate or follow objects well initially. Over the next few weeks, she showed progressive improvement in her sucking, swallowing and muscle tone.

Figure 2 (A) Hyperintense T2 weighted signal intensities in the right cerebellar white matter at presentation and (B) swelling of both optic nerves in axial T2 weighted image.

Figure 3 Axial T2 weighted images showing increased signal in the pons and midbrain.

While her general condition was slowly improving, her BCG scar became blistered and ruptured. The left axillary lymph node was still increasing in size (figure 1E). Ultrasound of the left axilla showed multiple enlarged lymph nodes with oedema of the surrounding tissue. She subsequently underwent an excision biopsy of the lymph nodes. The histology (figure 4A, B) and GeneXpert test was positive for *Mycobacterium tuberculosis* complex. The drug sensitivity showed that the organism was sensitive to ethambutol, isoniazid, streptomycin and rifampicin but resistant to pyrazinamide. Specific DNA test for *Mycobacterium bovis* was not performed. She was put on antituberculous treatment with isoniazid, ethambutol, rifampicin and pyrazinamide for 2 months and then continuation of isoniazid and rifampicin for 10 months.

OUTCOME AND FOLLOW-UP

Her neurological deficits and developmental milestones gradually improved over the next 6 months. She was able to prop herself up on prone, roll over and grasp her toys well. Her vision took some time to improve and after 3 months, she was able to fix, follow and track across the room well. There was residual right facial nerve palsy.

DISCUSSION

ADEM is a monophasic, immune-mediated inflammatory demyelinating disorder of the CNS characterised by multifocal neurological symptoms. Though the exact mechanism of demyelination is unknown, it is postulated to occur due to a cross-reaction between the triggering infectious agents and the neural tissue.³ Our patient presented 1 month following the onset of axillary lymphadenitis with encephalopathy, motor deficits and optic neuritis.

Figure 4 (A) Foamy histiocytes forming granuloma and few microabscess foci (H&E ×600). (B) Numerous acid-fast pink bacilli of *Mycobacterium* within histiocytes (Ziehl-Neelsen stain, ×600).

In immunocompetent individuals, CNS tuberculosis usually takes the form of meningitis that causes an acute to subacute illness characterised by fever, headache, drowsiness, meningism and confusion.⁴ CNS tuberculosis in infancy often poses a diagnostic conundrum and classic signs and symptoms are often absent. The British Medical Research Council in 1948 identified three stages for tuberculous meningitis presentation.⁴ In the first stage, the patient is conscious with no co-existing neurological symptoms. Stage 2 is characterised by signs of meningeal irritation with mild alteration of mental status and in stage three, there is significant stupor, coma, convulsions and paresis.

However, the investigation results did not support the diagnosis of tuberculous meningitis. The CSF findings in ADEM is variable with lymphocytosis (lymphocyte counts of less than 100 cells) and mildly elevated protein levels (<70 mg/dL), whereas in tuberculous meningitis, there is pleocytosis with a lymphocyte count of >20 cells and >60% lymphocyte count. In our patient, the CSF cell count was nil and protein 0.67 mg/dL. Furthermore, CSF acid-fast bacilli on Ziehl-Neelsen staining and nucleic acid amplification of tuberculosis DNA by GeneXpert MTB/RIF test were also negative. Though the sensitivity of acid-fast bacilli microscopy is quite low (<10%), especially in CSF which contains a small number of organisms, the GeneXpert MTB/RIF test on extrapulmonary samples had an overall sensitivity of over 80% and specificity reaching 100%.⁵

ADEM on neuroimaging shows the involvement of deep and subcortical white matter lesions and grey matter lesions involving the thalami and basal ganglia on brain MRI. In contrast, tuberculous meningitis commonly present as hydrocephalus, basal meningeal enhancement and parenchymal abnormalities such as tuberculomas, abscesses and infarctions.³ Our patient's brain imaging was congruent with classical neuroimaging features of ADEM.

BCG vaccination is a live vaccine developed from *M. bovis*. Common mild complications due to the BCG vaccination encountered are regional lymphadenitis, cutaneous lupoid reaction and eczema vaccinatum.⁶ Disseminated BCG infection is a severe complication and occurs in two per million vaccinated children.⁶ Simple BCG lymphadenitis regresses spontaneously with no treatment. It is interesting to note that in our patient the BCG scar blistered and left axillary lymph nodes increased in size with steroid therapy. Animal model studies from the 1950s have shown that corticosteroid commenced in untreated or unrecognised tuberculosis can adversely suppress cell-mediated immunity leading to increased virulence of the *M. tuberculosis*, overwhelming disease and eventually death.⁷

To the best of our knowledge, this is the first reported case of ADEM following BCG lymphadenitis. *M. bovis* was the likely triggering infective agent as pyrazinamide resistance is an innate feature of *M. bovis* infection.⁸

Patient's perspective

'My baby was diagnosed to have acute disseminated encephalomyelitis (ADEM) at 8 months old. Her balance was off, legs weak, arms weak, vision lost and all mobility lost with the ADEM attack...'

'After 9 months, she has improved a lot. She's now able to walk with support, eat and drink by herself, starts talking and could focus better.' – quote from mum.

Learning points

- ▶ This case report highlights the unusual presentation of acute disseminated encephalomyelitis following BCG lymphadenitis.
- ▶ Corticosteroid therapy can worsen BCG lymphadenitis.
- ▶ Early diagnosis and prompt treatment of acute disseminated encephalomyelitis could improve neurodevelopmental outcomes.

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