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BRAINSTEM TUBERCULOMA AS A MANIFESTATION OF PARADOXICAL REACTION IN A PATIENT WITH TUBERCULOUS MENINGITIS.

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ABSTRACT

Tuberculosis commonly involves the CNS, During drug treatment of CNS tuberculosis paradoxical response (PR) may occasionally occur. The term "paradoxicalresponse"refers to the development of previously nonexistent tuberculosis lesions or worsening of preexisting lesions during antituberculosis treatment(ATT). Etiology is still not clear but delayed type hypersensitivity and alteration in immune system is thought to be a cause. Continued treatment improves PR without severe sequelae. We report a 41 year-old female patient with tuberculous meningitis(TBM) who developed brainstem tuberculomaduring the course of ATT, after about 9 months of treatment as a paradoxical response to ATT. Early identification, continuation of ATT with steroids and ventriculoperitoneal shunting to relieve raised intracranial pressure resulted in complete recovery of our patient. Clinicians should be aware of this phenomenon as it can lead to clinical worsening as late as 9 months. The objective of this case report is to increase knowledge of clinicians about this phenomenon and also to report its such late occurrence.

Key words: paradoxical reaction. tuberculoma , tuberculosis

INTRODUCTION

Paradoxical reaction to ATT is a common phenomenon andmay affect up to 25% of patients1.It is defined as a transient worsening of disease, at a pre-existing site, or the development of new tuberculous lesions in a patient who initially improved on anti-tubercular therapy2. This phenomenon is more commonly associated with extrapulmonary tuberculosis2. Possible mechanisms include a strengthening of the host's delayed hypersensitivity response, and an increased exposure to mycobacterial antigens released as bacilli are killed by effective chemotherapy3. The paradoxical response can occur as an intracranial tuberculoma, pleurisy, pericarditis, lymphedenopathy, contralateral new parenchymal lesions,or the progression of the preexisting lesions4. Its early identification is important and it should not compel the clinicians to modify or discontinue theATT. We report such a case of paradoxical reaction in a 41year old female patient who during the course of treatment of tuberculous meningitis developed a life threatening mid brain tuberculoma after about 9 months of treatment with ATT.demonstrated atfundoscopy. On admission, laboratory investigations showed hemoglobin 8 g/dl, white blood

CASE REPORT

A 41 year old lady was admitted to us with history of headache,low grade fever for past 15 days and drowsiness for past 3 days.On examination, she had a GCS of 13/15, bilateral sixth nerve palsy,bilateralpapilloedema on fundoscopy and nuchal rigidity. She was diagnosed as havingtuberculous meningitis based on cerebrospinal fluid examination findings which showed Pleocytosis,570white blood cells, out of which 88% were lymphocytes,raised(121 mg/dl)proteins and low glucose(25mg/dl).Her initial CT scan brain was normal.She was started onATT. Patient showed a favourable response to ATT in the form of clinical improvement.Fever settled and she was discharged. However, during the course of treatment,after about 9 months of therapy, she developed recrudescence of fever and developed an acute onset headache followed by drowsiness,though she was fully compliant with treatment and there was nothing to suggest drug resistance as she showed dramatic initial improvement with ATT. Her CT scan was done which showed acute hydrocephlous and a ring enhancing lesion mid brain. MRI brain with contrast showed two ring enhancing foci in the mid

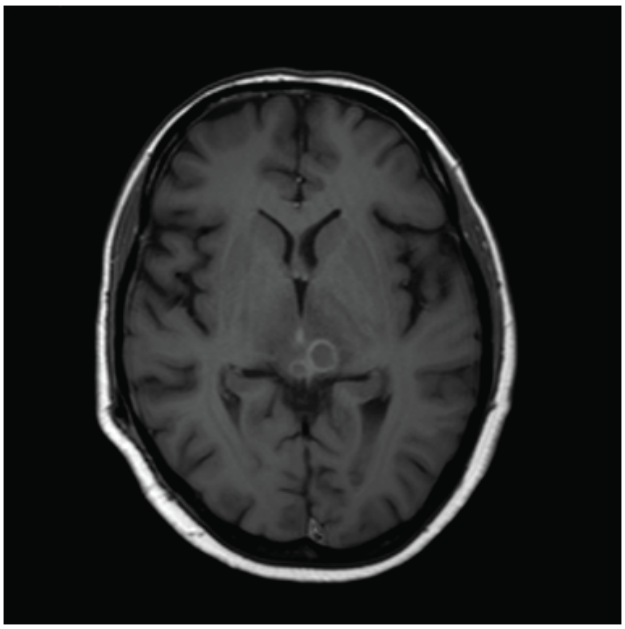

Fig 1. MRI T1 weighted axial section post contrast showing well defined contrast enhancing lesions in the region of mid brain

brain as shown in Figure 1. On MRI spectroscopy the lesion showed high lipid peaks further suggesting possible etiology being tuberculoma brainstem as shown in figure 2. She was continued on ATTandhigh dose steroids were added.Ventriculoperitoneal Shunting was also performed as the condition was life threatening and she had an acute hydrocephalous with signs of raised intacranialpressure.Again the patient showed marked clinical recovery.She was continuously followed up inoutpatientdepartment. Her CT scan repeated 2 months later showed marked regression in the size and almost complete resolution in the enhancement pattern and perilesional edema. ATT was given for complete 18 months.The further course of treatment being uneventful and ended with complete recovery from the illness.

Fig 2. MRSpectroscopy showing lipid peak suggesting it to be tuberculoma.

DISCUSSION

In many cases tuberculosis can worsen despite aggressive ATT,a condition commonly seen in countries like ours and if other causes like poor compliance to treatment and drug resistance are ruled out, this can be attributed to a phenomenon called paradoxical reaction which is as clinical or radiological worsening of preexisting tuberculous lesions or the development of new lesions following the initiation of active ATT. It can include the development of intracranial tuberculomas, as in our patient, worsening of existing lesions or development of new lesions in the lymph nodes, and various other manifestations4. Its time of occurrence is variable.It may occur as early as within 3 to12 weeks after the initiation of ATTor may be delayed up to18 months4as in our patient where it occurred after 9 months. It is important for clinicians to recognize paradoxical tuberculous reactions as inflammatory responses to treatment, and to understand that they do not necessarily indicate drug resistance or an inadequate response to therapy5.It was not the case of drug resistance as our patient has excellent clinical recovery after starting ATT and later on as well, she recovered completely with the same first line ATT. It should be noted that PR is a diagnosis of exclusion and it poses a particular problem in country like ours where it is difficult to differentiate from conditions such as drug resistance, poor compliance to drug therapy, concomitant diseases, poor drug absorption, where disease is common and drug susceptibility testing is not available. It is also believed that onset of PR may depend on the host immune response, virulence of tubercle bacilli, antigen load, site of infection, and effects of chemotherapy5 The mechanism of PR has not clearly been defined to date, although it is believed that, the immune response against mycobacterial proteins may be enhanced and cause a local hypersensitive reaction when active ATT is initiated and immunosuppression declines6. Its identification should not be delayed as it may manifest as a life threatening condition as in our patient.Themainstay of the treatment is the continuation of ATT and clinicians should be aware of this phenomenon and its such late occurrence and itshould not compel them to modify or discontinue ATT5. Some reports suggest the use of systemic steroids as an adjuvant treatment modality for PR6.The benefit of corticosteroid therapy for PR is apparent in intracranial tuberculomashoweveruseof steroids is somewhat controversial in other situations such as lymph node tuberculosis6. Previously it was thought to be an entity seen more commonly in HIV coinfected tuberculous patients who are simultaneously treated with antiretroviral therapy but it has been seen to occur in both HIV non infected and coinfected patients.7 Occurrence however is rare in nonimmunocompromisedpatients.In a study it has also been reported to occur in up to 11.1% of HIV-negative patients during treatment for TB2. In cases of intracranial lesions, surgical treatment in form of craniotomy or shunt operations can be performed to decompress the increased intracranial pressure, provided the development is acute and it has been identified early.The mortality of tuberculosis associated immune reconstitution syndrome has been estimated to be 3.2% within a recent meta-analysis8.

CONCLUSION

In summary, PR is not uncommon during treatment of TBM in nonimmunocompromised patients and can occur as late as after 9 months of ATT. Its prompt identification and management is crucial and its knowledge and awareness among neurologists is of utmost importance.

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FarheenNiazi; Study concept and design, protocol writing, data collection, data analysis, manuscript writing, manuscript review
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