Child's Nervous System (2019) 35:1273–1275
https://doi.org/10.1007/s00381-019-04270-5

LETTER TO THE EDITOR

Pediatric miliary tuberculosis presenting with stroke: contribution to the paper "Tuberculosis of the central nervous system in children"

María Isabel Sánchez-Códez[1] · Manuel Lubián-Gutiérrez[1] · Carmen Fernández-Bravo[1] · Myriam Ley-Martos[2]

Received: 19 May 2019 / Accepted: 19 June 2019 / Published online: 29 June 2019

Dear Editor:

We wish to thank Dr. Muzumbar and his coauthors for their recent article and his valued comments about neurological involvement of tuberculosis. Reading with interest his manuscript, we would like to report a case of disseminated tuberculosis disease presenting with extended stroke [1]. We believe that it represents a critical issue because tuberculous meningitis (TBM) is a destructive entity with high mortality [2, 3]. Neurological sequelae occur up to 80% in resource-poor setting and 60% in developed countries [2, 4]. Hydrocephalus, cerebrovascular complications, and tuberculoma are some indicators of poor outcome [1]. In order to update this article, providing a more comprehensive overview of the diagnosis and treatment of stroke in tuberculosis, we suggest that additional references are considered.

As such, we report a Moroccan infant without relevant family background and uneventful pregnancy. She presented repeated respiratory tract infections since 7 months. Progressive macrocephaly and ventriculomegaly since 2 months of age (cranial computed tomography (CT) was done at 7 months) and mother revealed failure to thrive beginning at 8 months. Close contacts were not sick. Immunizations were up to date not including BCG. At 10 months, she was referred to our hospital with a first episode consisting of generalized tonic seizures controlled with levetiracetam. Her parents reported fever to 102.2 °F, night sweats, and cough over the last week. On physical examination, her modified Glasgow coma scale (GCS) score was 15/15. She had a bulging fontanelle, left hemiparesis without other neurological deficits. She presented tachypnea, subcostal retraction, and hypoventilation with hypoxemia. She had inguinal lymphadenopathies without splenomegaly or hepatomegaly. Cranial CT (Fig. 1) showed a new right large fronto-parietal area of subacute hypointensity, suggesting ischemic injury. Focal ischemic infarct was observed in the right temporal territory and caudate nucleus. MRI showed a right stroke involving frontal and parietal lobes, coincident with severe leptomeningitis in medial cranial fossa that occludes the flow of medial cerebral artery. Nodular enhancement images in posterior fossa identified as tuberculomas were demonstrated, as well as ventriculomegaly previously reported (Fig. 1). According to the Modified Medical Research Council (MMRC) score, her clinical stage was II. CSF documented normal protein and glucose with lymphocytic pleocytosis (25 cells/μl). Chest X-ray showed miliary mottling tuberculosis and right middle lobe consolidation (Fig. 2). Purified protein derivative test was 0 mm at 72 h. Interferon gamma release assay was positive. *Mycobacterium tuberculosis* polymerase chain reaction (GeneXpert MTB) from CFS and gastric aspirates was positive. HIV was negative. Her isolates were pansusceptible to the first line anti-TB drugs. According to the World Health Organization, she received standard 4-drug regimen for 2 months followed by rifampicin and isoniazid during 10 months. She was also treated with aspirin and dexamethasone (0.6 mg/kg/day) IV during 48 h and subsequently prednisone orally (2 mg/kg/day) for 6 weeks tapered gradually. Ventricular drainage was unnecessary. A source case was not identified. She recovered well on pulmonary tuberculosis after treatment. Seizures did not present recurrence. At 22 months, she started to perform unsteady gait. However, we identified signs of cerebral palsy with severe left hemiparesis and marked spasticity. She did not present other deficits.

TBM includes a broad spectrum of central nervous system (CNS) complications. Hydrocephalus appears in about 80% of TBM cases [1, 3, 4]. Springer et al. reviewed a rate of cerebral infarction as a complication in up to 13 to 53% of patients [5]. Predominant basal exudate, close to the circle of

✉ María Isabel Sánchez-Códez
mscodez1990@gmail.com

[1] Department of Pediatrics, University Hospital Puerta del Mar, Avda/Ana de Viya, 21, 11009 Cadiz, Spain

[2] Department of Neurology Pediatrics, University Hospital Puerta del Mar, Avda/Ana de Viya, 21, 11009 Cadiz, Spain

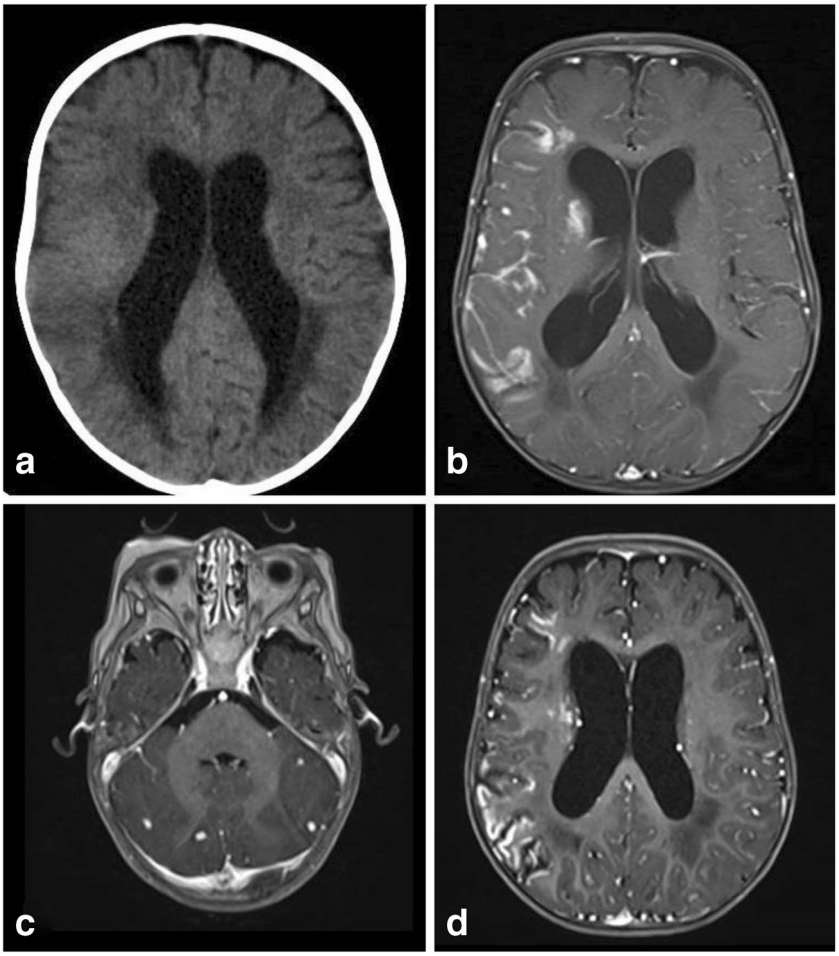

Fig. 1 Central nervous system radiological images. Cranial CT (**a**) and MRI (**b**–**d**). **a** Ventriculomegaly and loss of gray-white matter differentiation in the right middle cerebral artery territory. **b**, **d** Right stroke involving frontal and parietal lobes, coincident with severe leptomeningitis in medial cranial fossa that occludes the flow of medial cerebral artery. **c** Nodular enhancement images in posterior fossa identified as tuberculomas

Willis, plays an important role in the pathogenesis of TBM-related large cerebral infarction [5]. Distal internal carotid and middle cerebral arteries are the most affected [3]. Bilateral and large infarcts are associated with poor outcomes [2, 4].

Fig. 2 Chest radiography at admission. Miliary mottling consisting of little nodules uniformly sized and distributed. Right middle lobe consolidation

MMRC score is used to classify the severity of TBM at presentation [2]. Sumeet R. Dhawan and colleagues emphasized that stage III MMRC score (GCS of ≤ 10 with or without focal neurologic deficit) is the main factor related to poor outcome [4]. Nevertheless, a stage II MMRC score (GCS of 11–14 or 15 with any focal neurologic deficit) was associated with poor prognosis in other small cohorts [2]. Other risk factors are delayed detection and treatment of TBM [1, 3]. Initial clinical symptoms could be unspecific but more persistent than other respiratory infections [3]. Different studies have reported severe forms of disease in infants in contrast to older children [2, 4]. Duque Silva and colleagues analyzed 92 TBM pediatric patients and identified higher mortality rates in those less than 4 years, particularly 0–18 months. This subgroup presented more severe neurological sequelae than older subjects. Infarcts are also more common among young children (less than 4 years) [2]. Unfortunately, TBM is more prevalent in this group [3]. Prophylaxis and treatment of latent tuberculosis infection could prevent the development of disease in 90% of the cases [3]. However, some contact investigations are uneventful [4].

In conclusion, CNS affectation in tuberculosis is more frequent in pediatric patients and an earlier diagnosis and treatment could avoid bad prognosis. A high index of suspicion is needed, especially in meningitis/meningoencephalitis and focal CNS symptoms. TBM should be considered in infants with unexplained stroke. More studies about treatment and long-term prognosis of TBM infarcts in pediatrics are needed.

Compliance with ethical standards

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

References

1. Muzumdar D, Vedantam R, Chandrashekhar D (2018) Tuberculosis of the central nervous system in children. Childs Nerv Syst 34:1925–1935
2. Duque-Silva A, Hampole V, Cheng YN, Flood J, Barry PM (2018) Outcomes of pediatric central nervous system tuberculosis in California, 1993–2011. J Pediatric Infect Dis Soc XX(XX):1–11
3. Thwaites GE, van Toorn R, Schoeman J (2013) Tuberculous meningitis: more questions, still too few answers. Lancet Neurol 12:999–1010
4. Dhawan SR, Gupta A, Singhi P, Sankhyan N, Malhi P, Khandelwal N (2016) Predictors of neurological outcome of tuberculous meningitis in childhood: a prospective cohort study from a developing country. J Child Neurol 31:1622–1627
5. Springer P, Swanevelder S, van Toorn R, van Rensburg AJ, Schoeman J (2009) Cerebral infarction and neurodevelopmental outcome in childhood tuberculous meningitis. Eur J Paediatr Neurol 13:343–349