



Letter to the Editor

Radiological data in microbiologically confirmed central nervous system tuberculosis

To the Editor,

Tuberculosis is the leading cause of death due to infection and remains a major global health problem. In 2016, there were an estimated 1 674 000 tuberculosis deaths in the world and the number of patients with tuberculosis was 10.3 million [1]. Central nervous system (CNS) tuberculosis is the most devastating form of tuberculosis [2], and is the second most common community-acquired CNS infection worldwide [3]. Early diagnosis of CNS tuberculosis is essential in reducing morbidity and mortality [4]. However, the clinical symptoms and signs of CNS tuberculosis are non-specific and the results of microbiological investigations are often too late for effective treatment [5]. Neuroimaging plays a key role in supporting diagnosis in CNS tuberculosis. In this analysis, we aimed to review the radiological findings in patients with microbiologically proven CNS tuberculosis.

This study uses multicentre Haydarpasa retrospective collection of data on patients with CNS tuberculosis, collected from 43 referral centres in 14 countries [5–8]. Microbiological confirmation necessitated positivity of at least one of the following tests performed on the cerebrospinal fluid: Ehrlich–Ziehl–Neelsen stain, *Mycobacterium tuberculosis* culture or *M. tuberculosis* PCR. Imaging findings were retrieved from the database. This study was approved by the institutional review board of the Fatih Sultan Mehmet Training and Research Hospital in Istanbul.

In order to simplify the data in the database, answers to specific questions related to radioimaging were grouped according to the following definitions. Parenchymal involvement comprised encephalitis, cerebritis, tuberculoma and abscess formation. Meningeal involvement included lesions of the meninges, no matter where they were located, with a subgroup indicating basilar meningitis. Vasculitis included vasculitis and infarction.

Out of 507 patients in the database, 444 had CNS imaging at diagnosis. In all, 392 (88.2%) had cranial computed tomography, 284 patients (63.9%) had cranial magnetic resonance imaging and 232 patients (52.2%) had undergone both. The 284 patients who underwent magnetic resonance imaging were included in this study. Among these individuals, cerebrospinal fluid was positive for Ehrlich–Ziehl–Neelsen stain in 72 (25.3%), culture in 210 (73.9%) and PCR in 68 (23.9%). Twenty-nine patients (10.2%) had positive results for both acid-fast bacillus (AFB) testing and culture, and both culture and PCR were positive in 34 (11.9%). The mean age of the patients was 37.66 ± 17.9 years. There were 144 women (50.7%).

Fifty-two patients (18.3%; mean age 36.9 ± 19.2 years) had normal magnetic resonance imaging examinations; of these, 23 were women. Fifteen patients (28.8%) showed other extracranial tuberculous foci. Ehrlich–Ziehl–Neelsen was positive in 16 (30.7%), culture was positive in 34 (65.3%) and PCR was positive in ten (19.2%).

Among the 284 patients with CNS tuberculosis, meningeal involvement was observed in 152 patients (53.5%) and basilar meningitis appeared in 78 (27.4%). Parenchymal involvement was diagnosed in 109 patients (38.3%); 92 patients had tuberculomas (32.3%), 15 patients presented with cerebritis (5.2%) and 15 patients had abscesses (5.2%). Complications of tuberculosis identified at radioimaging were hydrocephalus in 80 patients (28.1%), oedema in 57 patients (20%) and vasculitis in 55 patients (19.3%). Spinal tuberculosis was seen in only five individuals (1.7%). Localization of lesions was documented in 10 of the 15 patients with magnetic resonance imaging findings of an abscess, in 91 of 92 patients with tuberculoma and 52 of 55 patients with vasculitis (Table 1).

Table 1
Localization of lesions of tuberculous meningitis

Localization	n	%
Localization of abscesses (n = 10)		
Cerebellum	7	70
Cerebral hemispheres	6	60
Basal ganglia	2	20
Brainstem	1	10
Multiple sites	7	70
Localization of tuberculomas (n = 91)		
Cerebral hemispheres	49	53.8
Cerebellum	29	31.8
Basal ganglia	17	18.6
Brainstem	13	14.2
Deep white matter	5	5.4
Multiple sites	62	68.1
Localization of vasculitis (n = 52)		
Basal ganglia	14	26.9
Middle cerebral artery zone	10	19.2
Deep white matter	2	3.8
Cerebellum	1	1.9
Posterior cerebral artery zone	1	1.9
Brainstem	1	1.9
Anterior cerebral artery zone	1	1.9
Venous infarctions	3	5.7
Lacunae	4	7.6
Multiple vasculitic lesions	17	32.6

The major limitations of our study are its retrospective nature and the image interpretation by a single radiologist.

Although CNS tuberculosis is reported to present with meningeal involvement in up to 90% of cases [2], the present study performed in individuals with microbiologically proven CNS tuberculosis shows that meningeal involvement was seen in only about half of patients (53.5%) and parenchymal involvement comprised 38.3% of the cases. Both tuberculomas and vasculitic lesions were generally observed as multiple lesions at multiple sites. Cerebral hemispheres and basal ganglia were the most common localizations for tuberculoma and vasculitis, respectively.

Transparency declaration

We have no competing interests to declare.

Funding

No financial support was received for this study.

Acknowledgements

The ID-IRI study group consists of (in alphabetical order): Ahmad Khalifa, Ahmet Karakas, Akram Al-Mahdawi, Alexandru Crisan, Alper Sener, Arjan Harxhi, Asuman Inan, Ayhan Akbulut, Ayse Seza Inal, Aysegul Ulu-Kilic, Bahar Kandemir, Bojana Beovic, Botond Lakatos, Branislava Savic, Canan Agalar, Catalina Luca, Ebru Kursun, Emel Yilmaz, Emine Parlak, Filiz Pehlivanoglu, Ghaydaa Shehata, Gonul Sengoz, Gorana Ćosić, Gulden Yilmaz, Hanefi Cem Gul, Isabelle Masse-Chabredier, Isik Somuncu Johansen, Kadriye Yasar, Katell Andre, Mehmet Bitirgen, Mehmet Parlak, Melanie Catroux, Mihai Nechifor, Mucahit Yemisen, Muge Ozguler, Mustafa Nami-duru, Mustafa Sunbul, Nazif Elaldi, Nurgul Ceran, Oguz Karabay, Oguz Resat Sipahi, Olga Dulovic, Oral Oncul, Ozcan Devenci, Recep Tekin, Rok Civljak, Saim Dayan, Selma Alabay, Serda Gulsun, Serkan Oncu, Soline Simeon, Stephane Chadapaud, Sukran Kose, Umit Savasci, Uner Kayabas, Yves Hansmann.

References

- [1] World Health Organization. Tuberculosis: global tuberculosis report 2017. Geneva: World Health Organization; 2017.
- [2] Sanei Taheri M, Karimi MA, Haghighatkah H, Pourghorban R, Samadian M, Delavar Kasmaei H. Central nervous system tuberculosis: an imaging-focused review of a reemerging disease. *Radiol Res Pract* 2015;2015:202806.
- [3] Erdem H, Inan A, Guven E, Hargreaves S, Larsen L, Shehata G, et al. The burden and epidemiology of community-acquired central nervous system infections: a multinational study. *Eur J Clin Microbiol Infect Dis* 2017;36:1595–611.
- [4] Tai MS, Viswanathan S, Rahmat K, Nor HM, Kadir KA, Goh KJ, et al. Cerebral infarction pattern in tuberculous meningitis. *Sci Rep* 2016;6:38802.
- [5] Erdem H, Ozturk-Engin D, Elaldi N, Gulsun S, Sengoz G, Crisan A, et al. The microbiological diagnosis of tuberculous meningitis: results of Haydarpasa-1 study. *Clin Microbiol Infect* 2014;20:0600–8.
- [6] Erdem H, Ozturk-Engin D, Tireli H, Kilicoglu G, Defres S, Gulsun S, et al. Hamsi scoring in the prediction of unfavorable outcomes from tuberculous meningitis: results of Haydarpasa-II study. *J Neurol* 2015;262:890–8.
- [7] Senbayrak S, Ozkutuk N, Erdem H, Johansen IS, Civljak R, Inal AS, et al. Antituberculosis drug resistance patterns in adults with tuberculous meningitis: results of Haydarpasa-IV study. *Ann Clin Microbiol Antimicrob* 2015;14:47.
- [8] Cag Y, Ozturk-Engin D, Gencer S, Hasbun R, Sengoz G, Crisan A, et al. Hydrocephalus and vasculitis delay therapeutic responses in tuberculous meningitis: results of Haydarpasa-III study. *Neurol India* 2016;64:896–905.

G. Kilicoglu

Department of Radiology, Haydarpasa Numune Training and Research Hospital, Istanbul, Turkey

D. Ozturk-Engin*

Department of Infectious Diseases and Clinical Microbiology, Fatih Sultan Mehmet Training and Research Hospital, Istanbul, Turkey

H. Tireli

Department of Neurology, Haydarpasa Numune Training and Research Hospital, Istanbul, Turkey

Y. Cağ

Department of Infectious Diseases and Clinical Microbiology, Goztepe Training and Research Hospital, Medeniyet University, Istanbul, Turkey

G. Sengöz

Department of Infectious Diseases and Clinical Microbiology, Haseki Training and Research Hospital, Istanbul, Turkey

S. Senbayrak

Department of Infectious Diseases and Clinical Microbiology, Haydarpasa Numune Training and Research Hospital, Istanbul, Turkey

H. Erdem

Department of Infectious Diseases and Clinical Microbiology, Gulhane Training and Research Hospital, Ankara, Turkey

and ID-IRI study group

* Corresponding author. D. Ozturk-Engin.

E-mail address: dr.deryaengin@gmail.com (D. Ozturk-Engin).

25 January 2018

Available online 12 June 2018

Editor: S.J. Cutler