

## TRANSCRANIAL DOPPLER IN TUBERCULOUS MENINGITIS: A CASE STUDY

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**SUMMARY** – Tuberculous meningitis has a highly variable presentation. Difficulties in establishing the diagnosis of tuberculous meningitis have been well recognized. Unusual manifestations of tuberculous meningitis are nowadays quite frequently seen, with an increasing incidence of the disease in the general neurology practice. A 44-year-old woman presented with progressive loss of vision on the left eye in the past two days and two episodes of seizures (partial and secondary generalized). One week before that, she had transient diplopia, blurred right vision, and gait unsteadiness. There was no past history of systemic tuberculosis. Transcranial Doppler findings first suggested that it was a basal pathologic process with vascular involvement, which was not clear from clinical history and examination, computed tomography or angiography findings. Our opinion is therefore that every case of specific meningitis, infectious retrobulbar neuritis and opticochiasmatic arachnoiditis should be additionally examined with transcranial Doppler. Thus, more reliable information concerning complications due to specific arteritis could be obtained.

**Cljučne riječi:** *Central nervous system diseases – ultrasonography; Bacterial infections – ultrasonography; Tuberculosis, meningeal – ultrasonography; Blood flow velocity; Case report*

### Introduction

Unusual manifestations of tuberculous meningitis (TM) are nowadays quite frequently seen, with an increasing incidence of the disease in the general neurology practice<sup>1-3</sup>. The clinical picture may be nonspecific, presenting as chronic meningitis, and may be modified by various complications without the evidence of meningeal irritation<sup>4</sup>. Within the central nervous system (CNS), hydrocephalus, tuberculomas and tuberculous vasculitis are the most important complications<sup>1-4</sup>. Proliferative changes with localized exudate are frequently seen in inflamed vessels of the meninges, that lead to panarteritis. Terminal segment of internal carotid artery (ICA) and proximal portions of middle (MCA) and anterior (ACA) cerebral arteries are most frequently involved with inflammatory exudate<sup>2-5</sup>.

Currently, transcranial Doppler (TCD) is used for noninvasive detection of changes in blood flow velocities

(BFV) of basal cerebral arteries involved in bacterial meningitis<sup>6-8</sup>, cysticercotic arachnoiditis<sup>9</sup>, and TM<sup>10</sup>.

The purpose of the report is to discuss the role of early TCD in reaching definitive diagnosis, in addition to computed tomography (CT), cerebral angiography (CA), magnetic resonance imaging (MRI), and leptomeningeal biopsy.

### Case Report

A 44-year-old woman presented with progressive loss of vision on the left eye in the past two days and two episodes of seizures (partial and secondary generalized). One week before that, she had transient diplopia, blurred right vision, and gait unsteadiness. There was no past history of systemic tuberculosis (TBC). On admission, the patient had unremarkable general examination. Neck stiffness, Kernig and Brudzinski signs were not found. Bilateral anosmia and amaurosis on the left eye, slight horizontal nystagmus, and diminished left direct pupillary reaction were observed. Motor functions were intact. Tendon reflexes were normal and there were no sensory changes. Higher cortical functions, memory and judgment, were

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Received November 12, 2003, accepted in revised form April 21, 2004

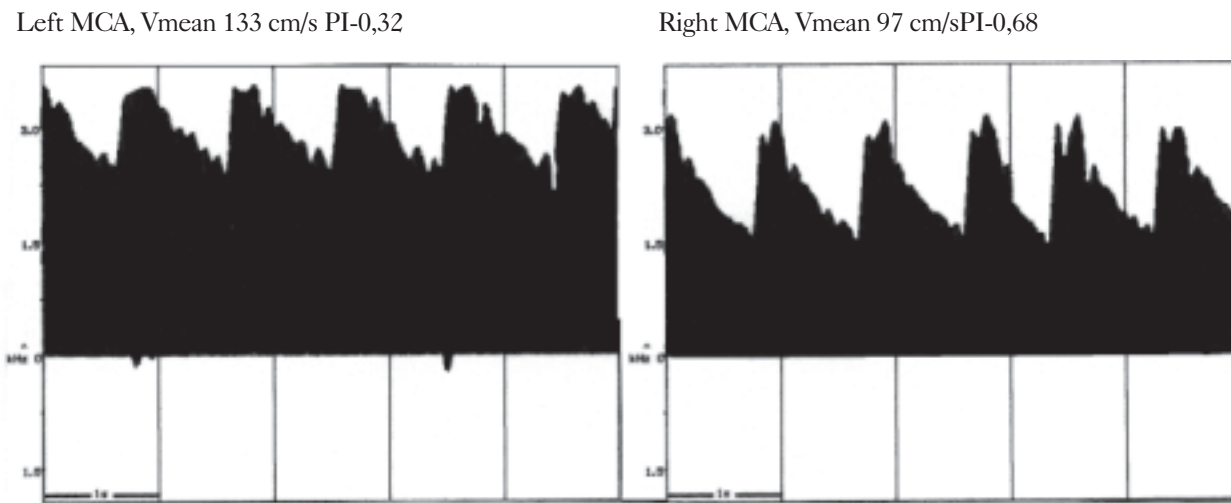


Fig. 1. a) TCD curve of middle cerebral arteries

preserved. All laboratory tests were normal. Cerebrospinal fluid (CSF) examination showed cell count  $120/\text{mm}^2$ , protein content 92 mg/dL, and glucose 34 mg/dL. CSF microbiology tests were negative for common bacteria as well as for toxoplasmosis, echinococcosis, cryptococcosis, aspergillus, candidiasis, VDRL and HIV. Mantoux reaction was negative.

Doppler ultrasound of extracranial ICAs showed asymmetry in BFVs (2.5 kHz on the left side *vs.* 1.2 kHz on the right side). TCD revealed local accelerated systolic, diastolic and mean BFV were recorded in the left MCA (mean 133 cm/s), along with a turbulent flow pattern *vs.* mean BFV of 97 cm/s in the right MCA (Fig. 1a). CT showed a small hypodense lesion in the right temporal region. On

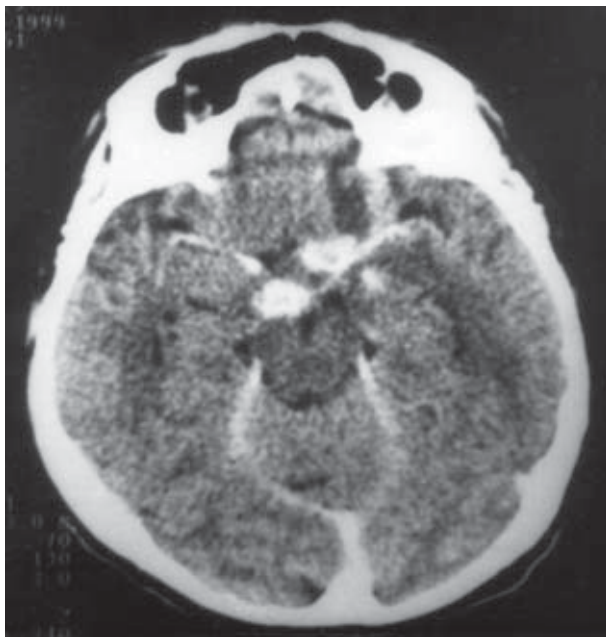


Fig. 1. b) contrast enhanced CT with 'pseudo-aneurysm' tuberculomas

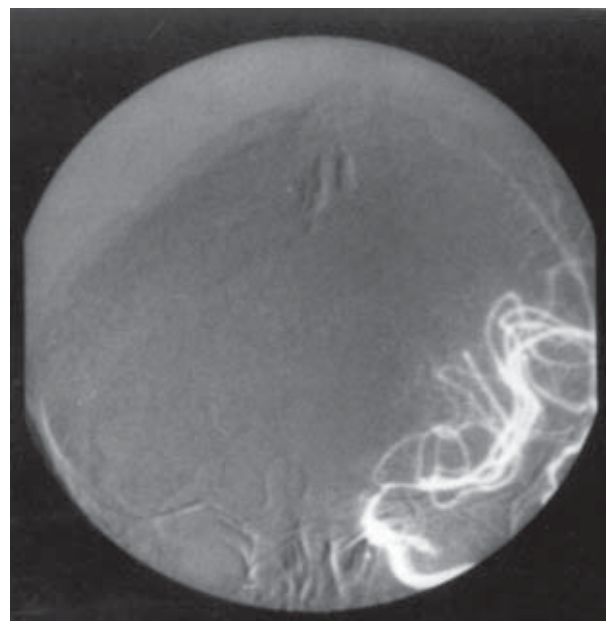
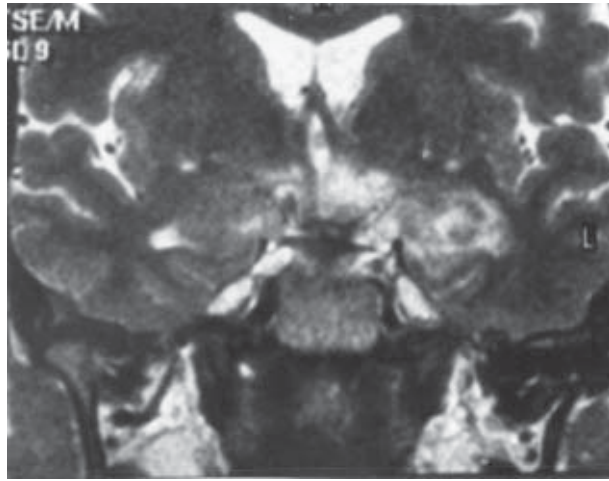


Fig. 1. c) left middle cerebral artery narrowing on angiography

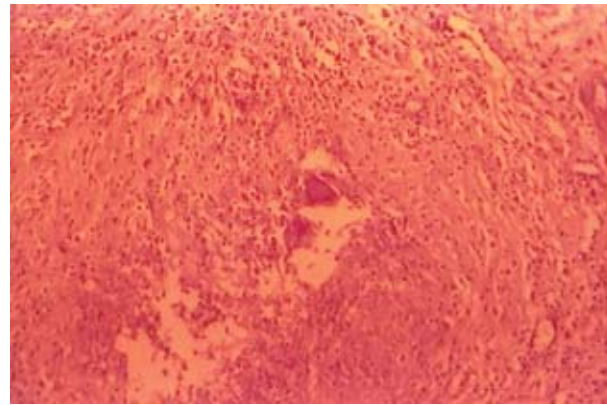


*Fig. 1. d) obliteration and compression of optic chiasm on MRI, with few hypertensity T2 lesions in the subcortical left frontobasal and temporal polar areas*

contrast enhancement, a few aneurysm-like formations located at the circle of Willis were seen, mainly on the right posterior communicating artery (Fig. 1b). Angiography demonstrated a narrowed and dislocated left initial part of the MCA (M1 segment) (Fig. 1c). MRI showed many subtentorial nodules in the chiasmatic cistern with propagation along the course of both MCAs and basilar artery (Fig. 1d). There was obliteration and compression of the optic chiasm. The left carotid siphon was relatively stenotic. There were a few hyperintensity T2 and hypointensity T1 lesions in the subcortical left frontal basal and temporal polar areas, due to brain edema.

The patient underwent surgical decompression of the opticochiasmatic space. A parachiasmatic abscess (tuberculoma) was evacuated. Macroscopically, the lesions were nodular, encapsulated and granulomatous. Leptomeningeal biopsy showed a histopathologic picture of TM: lymphocyte infiltrates around the blood vessels, connective tissue with formation of caseous granuloma – areas of caseous necrosis surrounded by epithelioid cells, lymphocytes and Langhans' type of giant cells. On fluorescent microscopy, there was no evidence of TBC bacteria. Biopsy result and positive polymerase chain reaction pointed to the diagnosis of TM.

Upon histologic verification, three tuberculostatic medications (isoniazid, ethambutol and rifampicin) and corticosteroids were started with remarkable clinical improvement. Vision impairment on the left eye regressed spontaneously (up to 20/100 with residual paracentral sc-



*Fig. 1. e) histopathologic picture of tuberculous meningitis: lymphocyte infiltrates, areas of caseous necrosis, epithelioid cells surrounded by lymphocytes, and Langhans' type of giant cells in the center*

otoma and nasal visual loss) within six months. On 9-month follow-up, the MCA BFVs were within the same range.

## Discussion

Tuberculous meningitis has a highly variable presentation. Difficulties in establishing the diagnosis of TM have been well recognized. The absence of predisposing factors, i.e. immunosuppression from a known disease or drug therapy, medical history or evidence for extrameningeal tuberculosis, was not suggestive of TM in our patient. The prodromal period of nonspecific symptoms, elevated temperature, malaise, headache, vomiting, mental and behavioral alterations were also absent. The lack of meningeal symptoms and focal neurologic deficits delayed the diagnosis at presentation. The only typical symptoms of TM were vision impairment and cranial neuropathy involving the first and third cranial nerves. CSF findings were suggestive of TM (lymphocyte predominance with raised protein and modestly lowered glucose level). The definitive diagnosis was based on the typical histology result and CSF positive PCR for TBC.

CT and MRI are rarely specifically diagnostic but are very suggestive of CNS tuberculosis, describing the evidence of hydrocephalus, basilar meningeal thickening, infarcts, edema and tuberculomas. These methods are useful in identifying complications and in follow-up<sup>1,4,11</sup>. In the present case, CT imaging did not reveal basal meningeal enhancement but erroneously indicated aneu-

rysms on contrast application, as previously reported<sup>12</sup>. The enhanced CT lesions in fact were small tuberculomas in the subarachnoid space, later confirmed on neurosurgery.

TCD findings first suggested that it was a basal pathologic process with vascular involvement. It was not clear from the clinical history and examination, CT or angiography. The TCD stenotic pattern of MCA and ICA as well as the MRI picture of chronic basal meningitis were the first noninvasive methods to suggest an inflammatory process.

The present case raises some important questions, such as whether it is necessary to examine every case of TM and meningoencephalitis with TCD. Also, whether TCD detection of cerebral arteritis in TM could be used in evaluating the effect of treatment.

Despite all methods conventionally used in the diagnosis and management of TM patients, our opinion is that every case of specific meningitis, infectious retrobulbar neuritis and opticochiasmatic arachnoiditis should be additionally examined with TCD. Thus, more reliable information concerning complications due to specific arteritis will be obtained.

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## Sažetak

## TRANSKRANIJSKI DOPPLER KOD TUBERKULOZNOG MENINGITISA: PRIKAZ SLUČAJA

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Tuberkulozni meningitis pokazuje velike razlike u manifestaciji. Dobro su poznate teškoće u postavljanju dijagnoze tuberkuloznog meningitisa. Danas se vrlo često bilježe neuobičajene manifestacije tuberkuloznog meningitisa, uza sve veću incidenciju ove bolesti u općoj neurološkoj praksi. Žena u dobi od 44 godine primljena je s progresivnim gubitkom vida na lijevom oku kroz prethodna dva dana i dvjema epizodama konvulzija (djelomične i sekundarne generalizirane). Tjedan dana prije toga imala je prolazne dvoslike, zamagljen vid i nesiguran hod. Nije imala anamnezu sistemske tuberkuloze. Nalaz transkranijuskog Dopplera je bio prvi koji je ukazao na to da se radi o bazalnom patološkom procesu sa zahvaćenim krvnim žilama, što nije bilo jasno iz kliničke anamneze i pregleda, kao ni iz nalaza kompjutorizirane tomografije i angiografije. Stoga je naše mišljenje da pregled transkranijuskim Dopplerom treba provesti u svakom slučaju specifičnog meningitisa, infektivnog retrobulbarnog neuritisa i optikohiazmatskog arahnoiditisa. Time bi se dobili pouzdaniji podaci o komplikacijama uzrokovanim specifičnim arteritisom.

*Ključne riječi: Bolesti središnjeg živčanog sustava – ultrasonografija; Bakterijske infekcije – ultrasonografija; Tuberkuloza, meningealna – ultrasonografija; Brzina protoka krvi; Prikaz slučaja*