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REVIEW ARTICLE

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The rare manifestations in tuberculous meningoencephalitis: a review of available literature

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ABSTRACT

Aim: Tuberculous meningitis is an infectious disease of the central nervous system caused by Mycobacterium tuberculosis (M. tuberculosis). It mainly involves the meninges and brain parenchyma, as well as the spinal cord and meninges; Disability and mortality rates are high. In recent years, due to the increase of drug-resistant tuberculosis patients, population mobility and the prevalence of acquired immune deficiency syndrome, the incidence rate of tuberculosis has increased significantly, and tuberculous meningitis has also increased.

Methods: At present, tuberculosis is still a worldwide infectious disease that seriously threatens human health, especially in underdeveloped and developing countries. China is the largest developing country in the world with a large population.

Results: The situation of tuberculosis prevention and control is grim. Its disability rate is the highest in tuberculosis infection. In addition to the common non-specific manifestations, tuberculous meningoencephalitis may also have rare manifestations of stroke, hearing loss and visual loss.

Conclusion: Understanding and timely improvement of corresponding examinations and targeted treatment will help improve the prognosis of patients.

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Introduction

German bacteriologist Robert Koch (1843–1910) has proved that Mycobacterium tuberculosis (MTB) is the pathogen of tuberculosis since 1882. With the emergence of BCG vaccine and anti-tuberculosis drugs, the once rampant tuberculosis has made great achievements in the prevention and treatment of the twentieth century. Tuberculous meningoencephalitis (TBM) is a non-suppurative inflammatory disease of the meninges and brain parenchyma caused by Mycobacterium tuberculosis. It is one of the most serious manifestations of tuberculosis infection, and also one of the manifestations with the highest disability rate. The most common manifestations of tuberculous meningoencephalitis are fever, headache, disturbance of consciousness, nausea with (or without) vomiting, epilepsy, changes in mental state and may be accompanied by common complications, such as brain oedema and hyponatraemia. The rare manifestations include stroke, including cerebral infarction, intracranial vein thrombosis, subarachnoid haemorrhage, hearing impairment and visual impairment, which seriously affect the prognosis of TBM patients. Tuberculous meningoencephalitis is rare due to atypical early symptoms and delayed laboratory examination. Early identification, diagnosis and treatment are still difficult. Therefore, this article reviews the rare manifestations of tuberculous meningoencephalitis.

Causes of cerebral nodule complications

Tuberculous meningitis can cause inflammatory changes in the pia mater, arachnoid, ventricular choroid plexus and ependyma, increase cerebrospinal fluid secretion, and lead to intracranial hypertension due to malabsorption, and often lead to high-pressure hydrocephalus.

Continuously increased brain pressure is prone to brain hernia, mainly tentorial hernia, axial hernia and foramen magnum hernia [1]. In the late stage of the brain nodule, when the arachnoid membrane of the skull base is widely adhered or the tuberculous inflammation directly invades the nerve, cranial nerve paralysis will occur. Tuberculous spinal meningitis and arachnoiditis, formation of intramedullary granuloma

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or tuberculous fibrous exudate around the spinal cord and nerve root, often lead to paraplegia, dysuria and nerve root pain. Tuberculous vasculitis throughout the course of the disease is prone to large vessel occlusion, leading to cerebral infarction, tuberculous granuloma and tuberculous abscess compressing brain parenchyma, as well as hemiplegia, such as simultaneous aphasia of dominant hemisphere.

Tuberculous granuloma with high intracranial pressure or cortex is prone to convulsions. Tuberculous inflammation invades diencephalon and presents corresponding symptoms of diencephalitis.

Cerebral infarction

Cerebral infarction refers to ischaemic necrosis or softening of local brain tissue caused by cerebral blood supply disorder, ischaemia and hypoxia. The incidence rate of tuberculous meningoencephalitis with cerebral infarction is about 15–57% [2,3].

Seventy-five percent of the infarctions occurred in the 'tuberculosis area' of the caudate nucleus, ventral thalamus and forelimb of the internal capsule and were supplied by the medial columnar artery and thalamic perforating artery; 11% of the infarcts occurred in the lateral basal ganglia, the 'ischaemic region' of the hind limb of the internal capsule, provided by the lateral columnar artery and thalamic artery [4].

According to the literature, autopsy found that most of the macro infarcts in the middle cerebral artery area were proliferative lesions, while in the very low artery area, there were small vascular necrotic lesions with small infarcts [5].

Its clinical manifestation is not fixed, but mainly depends on the location of the lesion. Most strokes can be asymptomatic, hemiplegic, aphasia, eye movement disorder, diplopia, an so on. Some researchers believe that cerebral infarction in tuberculous meningoencephalitis is due to vasculitis or intimal hyperplasia, and intra-arterial thrombosis may also play a role in the occurrence of stroke. Under the stimulation of secretion inflammation, arteritis and vasospasm may occur in arteries, which may lead to intima hyperplasia, and finally lead to stroke [3]. The diagnosis of tuberculous meningoencephalitis with cerebral infarction mainly depends on clinical symptoms and imaging manifestations. Routine examinations include MRI and CT [6].

DWI in head magnetic resonance imaging can show the scope of ischemic tissue early, which is more significant for early diagnosis. In addition to other diseases, hemiplegia, retesting and other clinical manifestations can be diagnosed by improving imaging examination and defining new responsibility focus [7].

Intracranial venous thrombosis

Intracranial venous thrombosis (CVT) is a kind of vascular disease that the cerebral venous return is blocked due to various reasons. Tuberculous meningitis with intracranial venous thrombosis has a low incidence rate, Its incidence rate is about 11%, mostly in the superior sagittal sinus, and its main clinical manifestations include headache, visual impairment, diplopia, hemiplegia, seizures, and so on [8]. Among them, intracranial deep vein thrombosis is relatively rare, with occasional case reports [9]. It is generally believed that this process mainly includes the following mechanisms: inflammation caused by vascular endothelial injury, platelet aggregation and increased release of procoagulant factors, leading to thrombosis.

Microglia release TNF-α And IL-1β and other cytokines play an important role in thrombosis. Leiden mutation of coagulation factor V is the most common cause of hereditary thrombosis. The decrease of anticoagulants and the increase of procoagulant factor (mainly factor V III) activity in patients with TBM lead to blood hypercoagulability and thrombosis [10]. In addition, TBM directly compresses the venous sinus by forming granulation tissue or abscess, and it can also lead to thrombosis by changing hemodynamics [11]. The clinical diagnosis of intracranial venous thrombosis depends on imaging examination [12]. Abnormal high density was found in the lesion area on CT, and related lesions could be seen on MRV. Vein imaging is limited. This disease can be diagnosed by imaging examination. The sensitivity of cranial MRV was about 84% [12]. Patients with tuberculous meningoencephalitis may suddenly have worsening headache, deepening consciousness and seizures during the course of the disease. The possibility of intracranial venous thrombosis should not be ignored [13].

Subarachnoid haemorrhage

Subarachnoid haemorrhage refers to the blood flowing into the subarachnoid space after the blood vessels at the bottom of the brain or on the surface of the brain break, leading to the corresponding clinical symptoms. Subarachnoid haemorrhage is rare in tuberculous meningoencephalitis. Only a few literatures have reported this phenomenon. The main clinical manifestation is sudden severe headache, with or

without nausea, vomiting and other symptoms [14]. At present, the aetiology of TBM with SAH is still unclear. At present, its pathogenesis is considered to be related to TBM vasculitis and late inflammatory reaction, which may lead to subarachnoid haemorrhage [15]. Pathological examination also showed that subarachnoid haemorrhage may be related to the rupture of inflammatory tuberculoma or fungal aneurysm [16]. The diagnosis of subarachnoid haemorrhage mainly depends on the clinical manifestations. Cranial CT is the first choice for imaging diagnosis, and the positive rate is about 85%. Head CT shows diffuse high-density images of basal cistern, ventricular system and convexity of brain. Intracranial arterial lesions can also be detected by digital subtraction DSA of the whole cranial artery and MRA of the intracranial artery magnetic resonance angiography. The main causes of subarachnoid haemorrhage are aneurysm rupture and haemorrhage [17]. The clinical manifestations of patients with nodular encephalopathy suddenly appear in the course of the disease, which can be diagnosed in combination with the corresponding changes of head CT.

Hearing loss

Hearing loss includes hearing sensitivity decrease, hearing threshold increase, hearing loss and even hearing loss caused by various reasons. The earliest literature report of tuberculous meningoencephalitis with hearing loss can be traced back to 1952 [18].

However, due to the acoustic neurotoxicity of streptomycin treatment, it was not considered as a rare manifestation of tuberculous meningoencephalitis until 2001. At that time, it was reported that a patient had hearing loss before diagnosis and anti-tuberculosis treatment [19].

The incidence rate of tuberculous meningoencephalitis with hearing loss is about 6.8%∼28% [20]. Most clinical manifestations are unilateral (rarely bilateral) progressive hearing loss with chronic progress.

Hearing loss of such patients can easily be masked by other symptoms of TBM, such as headache, nausea and vomiting. Most patients progress to severe hearing loss or even deafness [21].

Cochlear axis and cochlear aqueduct are the main routes of infection from the meninges to the inner ear. Tuberculous meningitis with hearing loss mainly involves the cochlea.

The development of hearing loss is similar to bacterial meningitis. They all have the characteristics of sensorineural hearing loss, especially high-frequency hearing loss [22].

The diagnostic method of hearing loss in tuberculous meningoencephalitis depends on hearing examination: that is, to evaluate the patient's hearing, hearing threshold and hearing function. Brain stem auditory evoked potential (BAEP) is more sensitive to early auditory nerve injury [23]. Cerebrospinal fluid examination and brain MRI enhanced examination are helpful for etiological diagnosis. The patients with tuberculous meningitis showed the above symptoms during the course of the disease. Hearing examination was improved to indicate hearing loss. Except for other diseases, they could be diagnosed.

Visual impairment

Visual impairment refers to partial or total impairment of visual organ results or functions due to various reasons. The incidence of visual impairment in tuberculous meningoencephalitis is 15%∼21.6% [24]. The main manifestations were decreased vision, decreased visual field and abnormal colour vision. Some patients may progress to partial or complete blindness. Arachnoiditis of optic nerve, tuberculoma of optic nerve and hydrocephalus are the most common causes of visual impairment [25].

Due to nervous system symptoms and the lack of vigilance of medical staff on visual dysfunction, this rare manifestation needs attention [26].

The visual impairment of tuberculous meningoencephalitis may be related to the drug toxicity of optic nerve involvement, optic arachnoiditis, optic chiasma compression, retinal vasculitis, hydrocephalus and ethambutol [27]. In the visual pathway, the optic nerve and optic chiasma are the most vulnerable. Tuberculous secretions can directly block and compress the optic nerve and optic chiasma, or block the cerebrospinal fluid pathway, resulting in hydrocephalus and optic nerve compression, resulting in visual impairment [28]. In addition, some studies have shown that patients with tuberculous meningoencephalitis combined with acquired immunodeficiency syndrome are more likely to suffer from optic nerve injury [29].

Visual loss mainly depends on ophthalmic examination to evaluate the patient's vision (or corrected vision), visual field, colour vision, eye movement and pupillary reflex. Maurya et al. showed that the positive rate of abnormal visual evoked potentials in patients with tuberculous meningoencephalitis was even higher [30].

If the above conditions occur during the course of the disease, the ophthalmic examination shows that the vision is decreased and the visual field is damaged. In addition to other diseases, the diagnosis can be made. In addition, skull MRI can also help diagnose the disease by directly showing the involvement of the optic nerve or visual pathway [31].

Brain abscess

Tuberculous brain abscess (pus collected in any part of the body) is still a rare manifestation of central nervous system tuberculosis, but it is reported that despite progress in treatment, the mortality rate is still high [32]. This manifestation is characterized by abscesses, which contain live tuberculosis bacteria, but there is no evidence of tuberculosis granuloma [33]. Management will use anti tuberculosis drugs for treatment. In addition, the treatment scheme may include simple puncture, continuous drainage, partial drainage, repeated drilling aspiration, stereotactic aspiration or total abscess resection.

Stroke

Stroke is a rapid tuberculosis infection of central nervous system drugs, Volume 11, Issue 4, 2011, Drug Chemistry, No. 325. The impairment of cerebral blood supply leads to the loss of brain function, which may be caused by ischemia caused by blockage or bleeding (blood leakage). The inability of affected areas of the brain to function is a medical emergency that can lead to permanent nerve damage, complications and death. Most tuberculous meningitis strokes may be asymptomatic, occurring in 15% to 57% of patients, especially in the advanced stage of severe disease. The use of corticosteroids and anti-tuberculosis treatment is considered to reduce mortality and incidence rate, but there is no evidence of their role in reducing stroke. Aspirin can also reduce mortality, but its role in reducing stroke, tuberculosis and meningitis needs further research.

Other

There other manifestations, such as the Syndrome of inappropriate antidiuretic hormone secretion (SIADH) [34,35], language alterations [36,37], and paradoxical reactions [38].

Conclusion

It is believed that more than two billion people worldwide are infected with tuberculosis, but about 10% of them will develop into clinical diseases. The incidence rate of central nervous system tuberculosis is related to the prevalence of community tuberculosis, but it is the most common type of chronic central nervous system infection in developing countries. In terms of the number of deaths and permanent sequelae, tuberculous meningitis is a serious disease that requires rapid diagnosis and treatment. Tuberculous meningitis can be divided into two stages. Mycobacterium tuberculosis enters the host through aerosol inhalation, and then the local infection of the lung is aggravated. Spread to regional lymph nodes.

The rare manifestation of tuberculous meningoencephalitis affects the prognosis of patients. Cerebral infarction, intracranial venous thrombosis, subarachnoid haemorrhage, hearing loss and visual loss. At present, there are no guidelines and expert consensus to guide the corresponding treatment. The literature reports focus on active anti tuberculosis treatment and symptomatic support treatment of tuberculous meningoencephalitis.

For stroke patients, studies have shown that steroids can be used to reduce mortality. Some studies have shown that aspirin can reduce the risk of stroke, but there is no consensus at present. For venous thrombosis, subcutaneous injection of low molecular weight heparin and oral anticoagulant is recommended for 3–6 months [39,40].

Surgical treatment of aneurysms is mentioned in the literature of subarachnoid haemorrhage. Due to the chronic development of hearing and visual impairment, early diagnosis and early treatment are proposed in the literature, which can effectively avoid the further impairment of its function. Therefore, in the process of diagnosis and treatment of TBM, be alert to rare manifestations, timely improve the corresponding examination, and targeted treatment will help to improve the prognosis of patients [41,42].

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Author's contribution

QuanhuiTan participated in the concept and design, data analysis and interpretation; The drafting of Rongli He's paper, Lan Wang's critical revision of the article, and Yun

Liu's acquisition of knowledge content and final approval of the version to be released; All authors agree to be responsible for all aspects of the work.

Author's statement

All authors meet the four author criteria.

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All authors declare that all data in this article can be used publicly.

References

[1] Bartzatt R. Tuberculosis infections of the central nervous system. Cent Nerv Syst Agents Med Chem. 2011; 11(4):321–327.

[2] Merkler AE, Reynolds AS, Gialdini G, et al. Neurological complications after tuberculous meningitis in a multi-state cohort in the United States. J Neurol Sci. 2017;375:460–463.

[3] Kalita J, Misra UK, Nair PP. Predictors of stroke and its significance in the outcome of tuberculous meningitis. J Stroke Cerebrovasc Dis. 2009;18(4):251–258.

[4] Pasticci MB, Paciaroni M, Floridi PA, et al. Stroke in patients with tuberculous meningitis in a low TB endemic country: an increasing medical emergency? New Microbiologica. 2013;36(2):193–198.

[5] Hsieh FY, Chia LG, Shen WC. Location of cerebral infarctions in tuberculosis meningitis. Neuroradiology. 1992;34(3):197–199.

[6] Chatterjee D, Radotra BD, Vasishta RK, et al. Vascular complications of tuberculous meningitis: anautopsy study. Neurol India. 2015;63(6):926–932.

[7] Tai MS, Viswanathan S, Rahmat K, et al. Cerebral infarction pattern in tuberculous meningitis. Sci Rep. 2016;6:38802.

[8] Pienaar M, Andronikou S, VAN TR. MRI to demonstrate diagnostic features and complications of TBM not seen with CT. Childs Nerv Syst. 2009;25(8):941–947.

[9] Bansod A, Garg RK, Rizvi I, et al. Magnetic resonance venographic findings in patients with tuberculous meningitis: predictors and outcome. Magn Reson Imaging. 2018;54:8–14.

[10] Tsimiklis CA, Gragnaniello C, Abou-Hamden A. Venous sinus thrombosis secondary to tuberculous meningitis: a novel cause of trigeminal neuralgia. BMJ Case Rep. 2014;2014:1–4.

[11] Ramdasi R, Mahore A, Kawale J, et al. Cerebral venous thrombosis associated with tuberculous meningitis: a rare complication of a common disease. Acta Neurochir. 2015;157(10):1679–1680.

[12] Guenifi W, Boukhrissa H, Gasmi A, et al. Thromboses veineuses cérébrales au cours de la méningo-encéphalite tuberculeuse. J Mal Vasc. 2016;41(3):210–214.

[13] Zuurbier SM, Coutinho JM. Cerebral venous thrombosis. Adv Exp Med Biol. 2017;906:183–193.

[14] Liu WEI, Li C-F, Liu X-M, et al. Case of subarachnoid hemorrhage caused by tuberculous aneurysm. World Neurosurg. 2018;110:73–78.

[15] Yeh ST, Lee WJ, Lin H-J, et al. Nonaneurysmal subarachnoid hemorrhage secondary to tuberculous meningitis: report of two cases. J Emerg Med. 2003; 25(3):265–270.

[16] Bale JF, Murph JR. Infections of the Central nervous system in the newborn. Clin Perinatol. 1997;24(4): 787–806.

[17] Huang PP, Choudhri HF, Jallo G, et al. Inflammatory aneurysm and neurocysticercosis: further evidence for a causal relationship? Case report. Neurosurgery. 2000;47(2):466–467.

[18] Edlow JA, Caplan LR. Primary care: avoiding pitfalls in the diagnosis of subarachnoid hemorrhage. N Engl J Med. 2000;342(1):29–36.

[19] Walker AS. Hearing of patients after tuberculous meningitis. Proc R Soc Med. 1952;45(11):781–782.

[20] Kotnis R, Simo R. Tuberculous meningitis presenting as sensorineural hearing loss. J Laryngol Otol. 2001; 115(6):491–492.

[21] Shah I, Meshram L. High dose versus low dose steroids in children with tuberculous meningitis. J Clin Neurosci. 2014;21(5):761–764.

[22] Akyol AG, Nazliel B, Oner Y, et al. Chronic bilateral hearing loss in an immunocompetent patient an atypical course of tuberculous meningitis. Neurosciences. 2014;19(4):322–325.

[23] Kuan CC, Kaga K, Tsuzuku T. Tuberculous meningitis-induced unilateral sensorineural hearing loss: a temporal bone study. Acta Otolaryngol. 2007;127(5): 553–557.

[24] Kalita J, Misra UK. Brainstem auditory evoked potentials in tubercular meningitis and their correlation with radiological findings. Neurol India. 2001;49(1):51–54.

[25] Garg RK, Malhotra HS, Kumar N, et al. Vision loss in tuberculous meningitis. J Neurol Sci. 2017;375:27–34.

[26] Amitava AK, Alarm S, Hussain R. Neuro-ophthalmic features in pediatric tubercular meningoencephalitis. J Pediatr Ophthalmol Strabismus. 2001;38(4):229–234.

[27] Malhotra HS, Garg RK, Gupta A, et al. An unusual cause of visual impairment in tuberculous meningitis. J Neurol Sci. 2012;318(1–2):174–177.

[28] Mehta S, Chauhan V, Hastak S, et al. Choroidal tubercles in neurotuberculosis: prevalence and significance. Ocul Immunol Inflamm. 2006;14(6):341–345.

[29] Moghekar AR. Neuro-ophthalmic manifestations in adult hydrocephalus. Int Ophthalmol Clin. 2014;54(1):115–121.

[30] Jaafar J, Wan Hitam WH, Noor RAM, et al. Bilateral atypical optic neuritis associated with tuberculosis in an immunocompromised patient. Asian Pac J Trop Biomed. 2012;2(7):586–588.

[31] Maurya PK, Singh AK, Sharma LA, et al. Visual pathway abnormalities in tuberculous meningitis. J Clin Neurosci. 2016;33:205–208.

[32] Umeda S, Fujikawa A, Tsuchiya K. [brain abscess]. no shinkei geka. No Shinkei Geka. 2021;49(2):368–374.
[33] Cano EJ, Campioli CC, Rodriguez AE, et al. New-onset seizures and a tangled up gram's stain: actinomyces brain abscess. IDCases. 2021;23:e01024.
[34] Mantia LL, Capsoni F. Psoriasis during interferon beta treatment for multiple sclerosis. Neurol Sci. 2010; 31(3):337–339.
[35] Benvenuti G, Lamers PP, Breuer G, et al. Microalgal tag production strategies: Why batch beats repeated-batch. Biotechnol Biofuels. 2016;9(1):64.
[36] Meng L, Saver JL, Alger JR, et al. Blood-brain barrier permeability derangements in posterior circulation ischemic stroke: frequency and relation to hemorrhagic transformation. J Neurolog Scie. 2012;313(1/2):142–146.
[37] Sreeramareddy CT, Qin ZZ, Satyanarayana S, et al. Delays in diagnosis and treatment of pulmonary tuberculosis in India: a systematic review. Int J Tuberc Lung Dis. 2014;18(3):255–266.
[38] Torres C, Riascos R, Figueroa R, et al. Central nervous system tuberculosis. Top Magn Reson Imaging. 2014; 23(3):173–189.
[39] Carod Artal FJ. Clinical management of infectious cerebral vasculitides. Expert Rev Neurother. 2016; 16(2):205–221.
[40] Thwaites GE, Nguyen DB, Nguyen HD, et al. Dexamethasone for the treatment of tuberculous meningitis in adolescents and adults. N Engl J Med. 2004;351(17):1741–1751.
[41] Kalantri A, Kalantri S. Can aspirin help? Elife. 2018;7: 35906
[42] Nataprawira HM, Ruslianti V, Solek R, et al. Outcome of tuberculous meningitis in children: the first comprehensive retrospective cohort study in Indonesia. Int J Tuberc Lung Dis. 2016;20(7):909–914.