Multi-Slice Computed Tomography 5-Minute Delayed Scan is Superior to Immediate Scan after Contrast Media Application in Characterization of Intracranial Tuberculosis

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

AB 1 **Dailun Hou**
BC 1 **Huifang Qu**
CD 1 **Xu Zhang**
AB 1 **Ning Li**
EF 1 **Cheng Liu**
AF 2 **Xiangxing Ma**

1 Division of Computed Tomography, Department of Radiology, Shandong University School of Medicine, Shandong Chest Hospital, Jinan, China
2 Department of Radiology, Qilu Hospital, Shandong University, Jinan, China

Corresponding Author: Xiangxing Ma, e-mail: maxiangxingdoc@126.com
Source of support: Departmental sources

Background: The aim of this study was to determine whether the diagnosis of intracranial tuberculosis (TB) can be improved when multi-slice computed tomography (MSCT) scans are taken with a 5-min delay after contrast media application.

Material/Methods: Pre- and post-contrast CT scans of the head were obtained from 30 patients using a 16-slice spiral CT. Dual-phase acquisition was performed immediately and 5 min after contrast agent injection. Diagnostic values of different images were compared using a scoring system applied by 2 experienced radiologists.

Results: We found 526 lesions in 30 patients, including 22 meningeal thickenings, 235 meningeal tuberculomas/tubercles, and 269 parenchymal tuberculomas/tubercles. Images obtained with 5-min delayed scan time were superior in terms of lesion size and meningeal thickening outlining in all disease types (P<0.01). The ability to distinguish between vascular sections from the cerebral sulcus and tubercle was also improved (P<0.01).

Conclusions: Image acquisition with 5-min delay after contrast agent injection should be performed as a standard scanning protocol to diagnose intracranial TB.

MeSH Keywords: Medicare Part C • Tomography, Spiral Computed • Tuberculosis, Central Nervous System

Full-text PDF: http://www.medscimonit.com/abstract/index/idArt/890719

📄 2256   🎞 2   📊 4   📚 35

Background

According to World Health Organization (WHO) data, there were 9 million new cases of tuberculosis (TB) globally in 2007, and China had the world's second-largest tuberculosis epidemic, with 1.3 million new cases in the same year, accounting for 14% of the overall global incidence [1]. Central nervous system (CNS) disease, which accounts for approximately 1% of all active tuberculosis (TB) cases, is one of the most devastating clinical manifestations of tuberculosis (TB) [2]. Recently, the incidence of intracranial tuberculosis has progressively increased. According to British Infection Society guidelines, the brain of every patient with TB should be imaged with contrast-enhanced CT. Early brain CT can help diagnose TB and provides important baseline information, particularly when considering surgical interventions for hydrocephalus [3].

Currently, much faster scanning speed is an advantage of multi-slice spiral computed tomography (MSCT). However, for intracranial lesions, especially the relatively small blood supply granulation tissues within TB lesions, it has been unclear which scan timing window is optimal for intracranial TB lesions – immediate scan or delayed scan. To solve this problem, dual-phase MSCT scanning was done in a group of patients with intracranial TB to discover the optimal scan timing window for displaying intracranial TB. We also hoped this finding could be used as supportive evidence for standardized procedures of intracranial TB CT scanning.

Material and Methods

General data

This study was approved by the Ethics Committee of Shandong Chest Hospital, and written informed consent was obtained from each patient before CT scanning. We enrolled 30 patients, including 19 males and 11 females, ages 10–58 years (mean age=29.3 years) who were clinically diagnosed with intracranial TB between January 2008 and November 2011.

All patients had the most common clinical manifestations such as headache, fever, vomiting, and nausea and all met the clinical diagnosis criteria for intracranial TB: i) clinical manifestations of fever and headache (more than 14 days), vomiting, perceptual transformation, and dissociated sensory loss [4,5]; ii), cerebrospinal fluid (CSF) examination showing increased CSF lymphocytes (higher than 20×10^6/L, lymphocytes >60%), elevated protein level (higher than 100 mg/dl), and lowered glucose (CSF glucose <60% of blood glucose level), negative results for both India ink stain test and microscopic test on cancerous cells [4,6]; iii), X-ray computed tomography findings showing exudates in both brain basal cistern and cistern

of lateral sulcus, infarcts in basal ganglia region, gyriform enhancement, and formation of tuberculoma; and iv) evidence of tuberculosis involvement of other organs, such as positive PPD test [7,8]. Cranial computerized tomography (CT) was performed in all 30 patients, including pre- and dual-phase post-contrast CT scans.

According to the location and the morphologies, the intracranial lesions were divided into 3 groups: 1) the meningeal thickening group (thickening involved in various meninges, such as basal cistern meninges, pia mater, and ependyma), 2) the meningeal tuberculoma group (including meningeal tubercle), and 3) the parenchymal tuberculoma group (including parenchymal tubercle). Tuberculous encephalitis, tuberculous vasculitis, and tuberculous brain abscess were excluded from the present study.

The inclusion criteria were: 1) the meningeal thickening type: cord-like or spindle-shaped abnormally enhanced lesions on basal cistern meninges, pia mater, and ependyma; 2) the meningeal tuberculoma type (including meningeal tubercle): oval or round enhanced nodular lesions on basal cistern meninges, pia mater, and ependyma, with unenhanced center/invisible enhanced center; in case of clustered distribution, the countable number of nodules was taken; and 3) the parenchymal tuberculoma type (including parenchymal tubercle): oval or round nodular lesions in parenchyma, may have unenhanced center.

Image acquisition

MSCT of the head was performed using a GE LightSpeed 16-Slice CT scanner (MSF Medical Equipment & Service LTD., Lightspeed). Unenhanced and contrast-enhanced MSCT images were obtained for all patients. Scan range was from the OM line to the parietal lobe of the brain, with a section thickness of 5 mm and a layer spacing of 5 mm. The contrast agent iohexol (350 mg/mL) was injected intravenously with a dose of 1.2 ml/kg (patient body weight) and a speed of 2.5 ml/sec. Dual-phase acquisition was performed immediately after and 5 min after contrast agent injection.

Image analysis

The marks of contrast phases on all images obtained were erased, then images were analyzed by 2 professional radiologists according to the following scoring method: for the size of isolated lesion, larger at the delayed phase (DP) than the immediate phase (IP): DP scored 2, and IP scored 0; larger at IP than DP: DP scored 0, and IP scored 2, equal on the both phase images: both phases scored 1; for the marginal definitions, more clearly at DP than IP: the DP scored 2, and IP scored 0; more clearly at IP than DP: the DP scored 0, and the IP scored 2; same on the 2 phase images: both phases scored

Table 1. Comparison on image qualities of various types of lesions between delayed phase and immediate phase scans.

Item		Meningeal thickening	Meningeal tuberculoma	Parenchymal tuberculoma
Scores on lesion size	Immediate phase	0.36±0.49	0.36±0.52	0.41±0.53
	Delayed phase	1.64±0.58	1.64±0.58	1.59±0.60
	P value	<0.01	<0.01	<0.01
Scores on marginal definition	Immediate phase	0*	0.27±0.45	0.12±0.32
	Delayed phase	2.00*	1.73±0.49	1.88±0.34
	P value	<0.01	<0.01	<0.01

* Indicates that all data of the group are 0 or 2.

1; and quantitative analysis of the ability to distinguish the isolated lesion from the vascular section: tightly associated or indistinguishable: scored 1, otherwise (easily distinguishable), scored 2.

The ability of the 2 enhanced phases in displaying the lesion were compared, including the size, the margins, CT value change of the substantial part, and ability to distinguish the lesion and peripheral vasculature. If there was disagreement, a consensus decision was reached through consultation. All data were reported as means±SD (standard deviation). Statistical analysis was performed using the SPSS 13.0 statistical package (SPSS, Chicago, IL, USA). The quantitative data acquired was conducted by the normality test method, and was approximately normally distributed (P>0.05), thus the t-test was used. A statistically significant difference was defined as P<0.05 in all tests.

Results

Classification of the lesions

In 30 patients with intracranial tuberculosis, a total of 526 lesions were eligible to be included. Of these lesions, 22 were meningeal thickening type, 235 were meningeal tuberculoma/ tubercle type, and 269 were parenchymal tuberculoma/tubercle type.

For tuberculous-meningitis-induced meningeal thickening, the images obtained from 5-min delayed scan were more superior to those obtained from the immediate phase in terms of both lesion size displaying and margin outlining, regardless of the location of involvement (basal cistern meninges, pia mater, or ependyma) (P<0.01). With respect to intracranial tuberculoma, regardless of location affected (basal cistern meninges, pia mater, or ependymal), the images obtained from 5-min delayed scan were superior to those obtained from the first phase in terms of both lesion size and margin displaying (P<0.01) (Table 1).

For distinguishing vascular sections from the cerebral sulcus and the tubercle, the images obtained from 5-min delayed scan had much better performance than these obtained from the immediate phase scan (P<0.01) (Table 2).

Discussion

Necessity of delayed enhanced scan in cranial multi-slice CT

One of the biggest advantages of multi-slice CT was the high temporal resolution, which contributed to sub-millimeter thickness acquisitions over large longitudinal coverage in a very short time. The technique was considered as a revolutionary advance in medical imaging, especially in high quality CT angiography [9]. However, regardless of whether the sequence or the spiral scanning technique was used, the cranial scan could be completed within 1–2 s, thus the high temporal resolution may be only useful in cerebral vascular imaging or some intracranial lesions with rapid arterial blood supply. In fact, not all intracranial lesions had rapid arterial blood supply (e.g., intracranial tuberculosis lesions). Based on our clinical experience, immediate MSCT scanning after contrast agent injection was unable to demonstrate the changes of intracranial TB lesions in morphology and density. In most case, it was even weaker than the earlier non-spiral CT in the ability to show lesions. In the earlier non-spiral CT scan practice, contrast agent injection was performed in the therapy room before the patient was ushered to the scanner table, thus there was no significant difference in delayed or immediate scan, while currently, there was usually only 30 s to 1 min elapsed from the contrast injection to MSCT scanning. Nonetheless, a study on the preference of delayed scan in MSCT scanning has never been reported. Aiming to solve this problem, a novel scan protocol was designed in the present study. All patients were received immediate and 5-min delayed head scanning after contrast agent injection. Subsequently, the lesion-revealing performance of both scans on various types of TB lesions was compared.

Table 2. The performances of distinguishing various types of lesions from vascular section by delayed phase and immediate phase scans.

Item		Meningeal thickening	Meningeal tuberculoma	Parenchymal tuberculoma
Number of lesions tightly associated with or indistinguishable from peripheral vasculature	Immediate phase	20	183	196
	Delayed phase	4	1	1
Number of lesions easily distinguished from the vasculature	Immediate phase	2	52	73
	Delayed phase	18	234	268
Scores	Immediate phase	1.09±0.68	1.22±0.74	1.27±0.75
	Delayed phase	1.82±0.39	2.00±0.06	2.00±0.06
	P value	<0.01	<0.01	<0.01
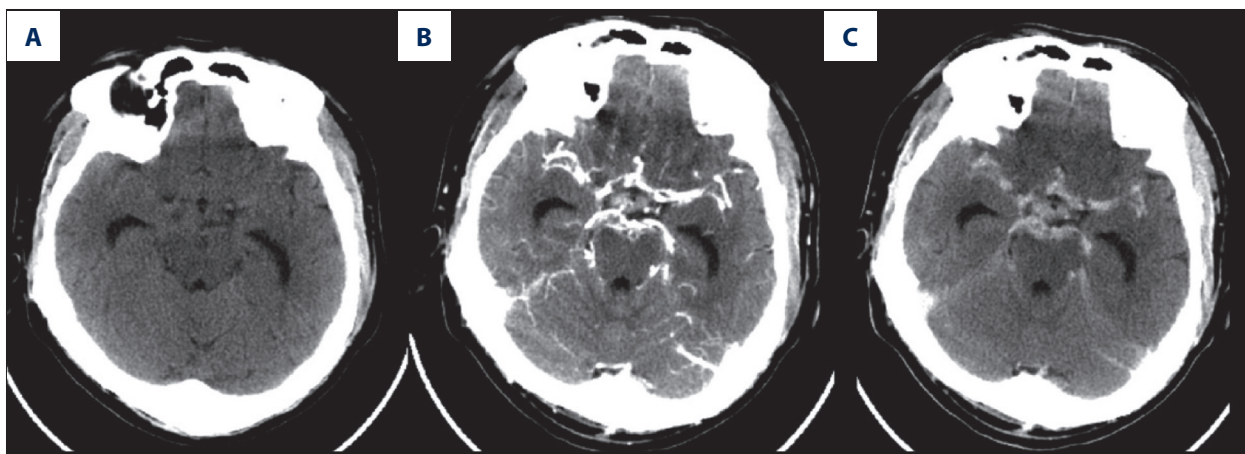
Figure 1. Meningeal thickening of the cisterna ambiens. At pre-contrast CT scan (**A**), partial obstruction of cisterna ambiens was revealed. Image of the immediate phase scan (**B**) showed detectable enhancement of the affected meninges, but was hardly distinguished from the peripheral vasculature due to poor display. At delayed phase scan (**C**), meningeal thickening of the cisterna ambiens showed casting-like enhancement, demonstrating clearer boundaries.

The key point was to find out whether the delayed scan was superior in displaying intracranial TB lesions.

### Role of delayed scan on displaying intracranial TB lesions

According to the generally-accepted classification criteria, intracranial tuberculosis is be classified into 5 types: tuberculous meningitis, tuberculous encephalitis, tuberculous vasculitis, intracranial tuberculomas, and tuberculous brain abscess [2]. In our study, only tuberculous meningitis and intracranial tuberculomas were studied, because enhanced CT scan was inappropriate for tuberculous encephalitis imaging [10], and displaying tuberculous vasculitis needs proper arterial phase scanning [11], and cases of tuberculous brain abscess are rarely seen. Therefore, these 3 types of TB lesions were excluded from the present study.

All lesions were divided into 3 groups according to the CT findings. The first group was the tuberculous meningitis type, which commonly presents with diffuse, thick meningeal enhancement, and mainly involves the basal cistern meninges, pia mater, and ependyma [12]. Intracranial tuberculoma and tubercle, which only differ in size, were the second group. The parenchymal tuberculoma was the third type of TB lesion. In the present study, all these were well displayed on the 5-min delayed scan images, and were superior to those obtained on the immediate phase.

In our practice, we also found that it was difficult to distinguish the vascular sections in the cerebral sulcus from the small tubercles on the pia mater, especially on the immediate phase. Thus, we also did a comparison between the immediate phase and the delayed phase scanning to find a better phase for displaying pia mater tubercles.
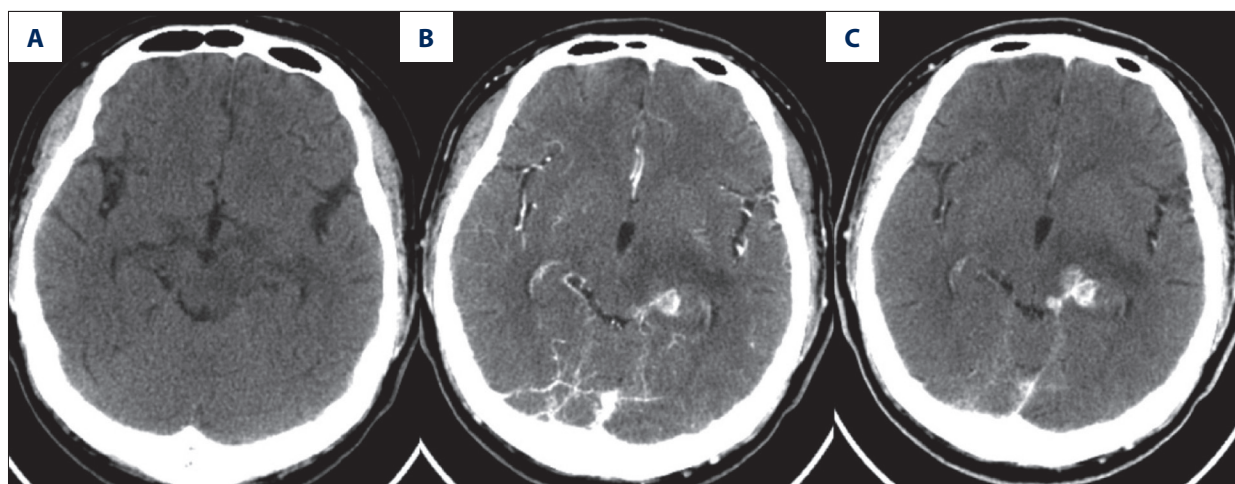
Figure 2. Meningeal thickening complicated by tuberculoma in left cisterna corpora quadrigemina was revealed. At pre-contrast CT scan (**A**), the lesions showed isodensity and mild edema was found in the peripheral regions. At immediate phase scan (**B**), the lesion showed slight enhancement, while the enhancement was further improved at delayed phase scan (**C**) because the range of lesion expanded and the boundary was more clearly outlined.
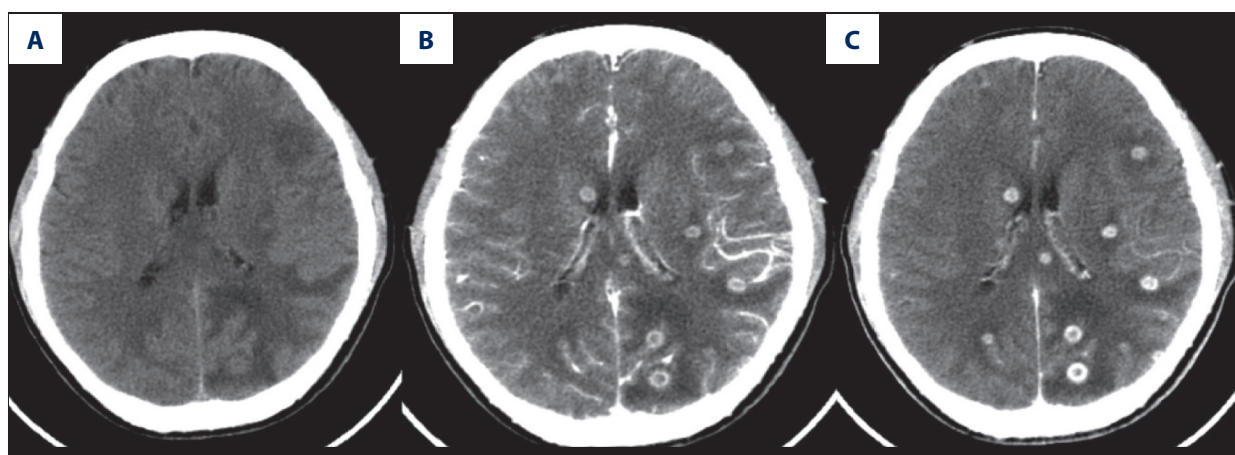

Figure 3. Multiple intracranial tuberculoma. At pre-contrast CT scan (**A**), the lesions showed isodensity or slightly higher density, and edemas at different extents were also revealed in the peripheral region. At immediate phase scan (**B**), the lesions showed mild and circular enhancement, while the enhancement was further improved at delayed phase scan (**C**) because the range of lesion expanded and the boundary was more clearly outlined.

Advantages of delayed scanning

Granulation tissue was the pathological basis of the meningitis-related meningeal thickening, regardless of which portion of meninges (basal cistern meninges, pia mater or ependymal) was affected. It was also components of the "wall" of tuberculoma and tubercle, usually with insufficient blood supply [2,13] and slow circulation speed, which both lead to reduced penetration of contrast agent, and thus result in deteriorated enhancement. Also, due to the slow circulation, the injected contrast agent tended to be accumulated in the granulation tissues, subsequently resulting in better enhancement at delayed time. However, there has been no report published to date on the best contrast time for intracranial lesions. As

a matter of experience, the 5-min delay is usually the proper scanning time. Thus, in the present study, a 5-min delay was selected to obtain sufficient enhancement, and thus achieving better display of the lesion size and margin outlines. Of course, it was confirmed in the present study that the images obtained at delayed scanning phase were superior in terms of both displaying lesion size and outlining meningeal thickening for all types (Figures 1–3). In a future study, an animal cerebral perfusion scan would be carried out, and the time to peak (TTP) of intracranial disease would be studied comprehensively and in detail.

In terms of sulcus vascular section and tubercle identification, the delayed scan has been shown to have prominent
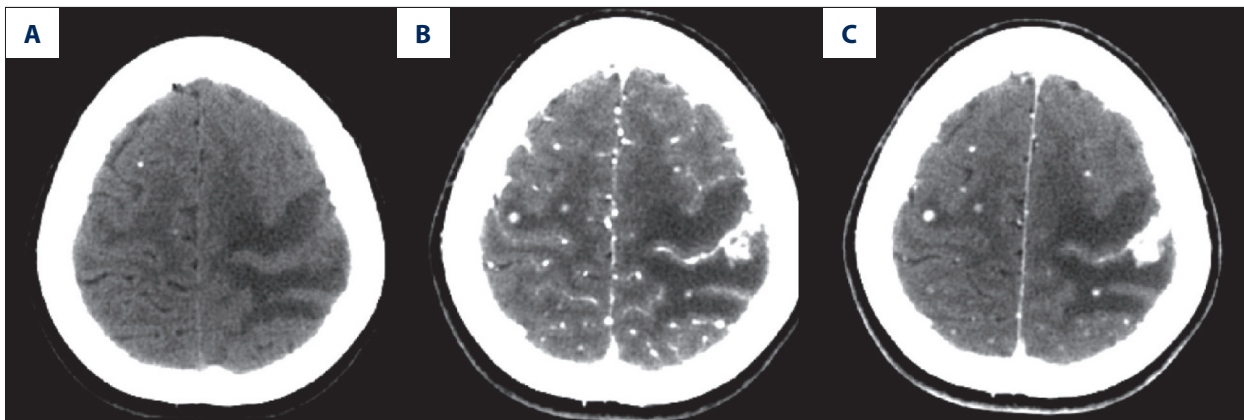
Figure 4. Miliary tubercle complicated by meningeal thickening in pia mater. At pre-contrast CT scan (**A**), some of the pia tubercle lesions showed a certain degree of calcification with density and swollen sulcus in left parietal lobe was also seen, with detectable finger-like edema zone. At immediate phase scan (**B**), thickening of left parietal lobe pia was seen, with significant enhancement. Multiple miliary enhanced nodules were diffusely distributed throughout the other pia maters, but indistinguishable from the normal vascular sections. At delayed phase scan (**C**), the enhancement of blood vessel receded and the lesions become more obvious.

advantages (Figure 4). After contrast enhancement, the vascular sulcus sections were highly enhanced at the immediate phase and were difficult to differentiate from the tubercle due to its smaller diameter. Moreover, it was unable to display the central caseous necrosis tubercle region by using current CT spatial resolution. Thus, although the tubercle lesions were enhanced, they were still difficult to differentiate from the vascular sections with similar diameter. Using 5-min delay after contrast ejection, density of the vascular sections was reduced and enhancement of the tubercle was further improved, resulting in significant differences in density, which makes the vascular sections and pia mater tubercle easily distinguishable.

Results of the present study show that the 5-min delayed scan has more advantages in obtaining better-quality images than the immediate phase scan, in terms of displaying meningeal thickening and intracranial tuberculoma, as well as distinguishing sulcus vascular section from tubercle. However, since blood vessels are another major tissue affected by intracranial tuberculosis, with presentation of wall thickening and luminal narrowing (stenosis), proper arterial phase maybe useful and should studied in further investigations.

Radiation dose may be the main weakness of this study. Because this was a prospective study, and our purpose was to determine the optimal scan timing window for displaying intracranial TB, 3 scans were applied, but the mean total radiation

of our study did not exceed the prescribed radiation dose. Of course, through our study, we found that image acquisition with 5-min delay after contrast agent injection was superior in displaying intracranial tuberculosis. If this scanning mode were used in our routine work, the radiation dose would be greatly reduced. Radiation protection was well-performed for all patients. Generally, MR imaging appears to be superior to CT in the detection and assessment of CNS tuberculosis, especially for bottom pool lesions, abnormal meningeal enhancing, and cerebral infarction display, but CT can detect abnormal intracranial calcification and there is no statistically significant difference in intracranial lesion detection rate between the 2 methods [14,15]. Currently, not all specialized TB hospitals have MR, and some patients are not suitable for MR examination, thus CT examination is still indispensable. We therefore believe that research for the appropriate CT scanning mode is necessary and has great value in clinical applications.

Conclusions

Because intracranial tuberculosis remains a condition with high mortality and morbidity, timely and proper imaging is still essential for diagnosis. Our study shows that delayed acquisition at 5-min after contrast agent injection can improve precision and accuracy for imaging evaluation and clinical diagnosis, and be the preferred scanning type.

References:

1. WHO, editor. Global tuberculosis control 2009: surveillance, planning, financing. Geneva: World Health Organization, 2009

2. Cherian A, Thomas SV: Central nervous system tuberculosis. Afr Health Sci, 2011; 11: 116–27

3. Thwaites G, Fisher M, Hemingway C et al: British Infection Society guidelines for the diagnosis and treatment of tuberculosis of the central nervous system in adults and children. J Infect, 2009; 59: 167–87

4. Ahuja GK, Mohan KK, Prasad K, Behari M: Diagnostic criteria for tuberculous meningitis and their validation. Tuber Lung Dis, 1994; 75: 149–52

5. Rock RB, Olin M, Baker CA et al: Central nervous system tuberculosis: pathogenesis and clinical aspects. Clin Microbiol Rev, 2008; 21: 243–61, table of contents

6. Youssef FG, Afifi SA, Azab AM et al: Differentiation of tuberculous meningitis from acute bacterial meningitis using simple clinical and laboratory parameters. Diagn Microbiol Infect Dis, 2006; 55: 275–78

7. Mahadevan B, Mahadevan S, Serane VT, Narasimhar R: Tuberculin reactivity in tuberculous meningitis. Indian J Pediatr, 2005; 72: 213–15

8. Kilpatrick ME, Girgis NI, Tribble D, Farid Z: The value of the tuberculin skin test in patients with tuberculous meningitis. J Egypt Public Health Assoc, 1996; 71: 1–8

9. Liu PS, Platt JF: CT angiography in the abdomen: a pictorial review and update. Abdom Imaging, 2014; 39: 196–214

10. Wasay M, Kheleani BA, Moolani MK et al: Brain CT and MRI findings in 100 consecutive patients with intracranial tuberculoma. J Neuroimaging, 2003; 13: 240–47

11. Lammie GA, Hewlett RH, Schoeman JF, Donald PR: Tuberculous cerebrovascular disease: a review. J Infect, 2009; 59: 156–66

12. Sutlas PN, Unal A, Forta H et al: Tuberculous meningitis in adults: review of 61 cases. Infection, 2003; 31: 387–91

13. Kim TK, Chang KH, Kim CJ et al: Intracranial tuberculoma: comparison of MR with pathologic findings. Am J Neuroradiol, 1995; 16: 1903–8

14. Bernaerts A, Vanhoenacker FM, Parizel PM et al: Tuberculosis of the central nervous system: overview of neuroradiological findings. Eur Radiol, 2003; 13: 1876–90

15. Unal A, Sutlas PN: Clinical and radiological features ofsymptomatic central nervous system tuberculomas.Euro Neurology, 2005; 10: 797–804