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Proposed CT classification of lung injury in lymphobronchial TB

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Proposed CT classification of lung injury in lymphobronchial TB

Lymphobronchial tuberculosis (LBTB) is tuberculous lymphadenopathy affecting the airways, which is particularly common in children with primary TB. Airway compression by lymphadenopathy causes downstream parenchymal pathology, which may ultimately result in irreversible lung destruction, if not treated timeously. There are no current classifications that grade the severity of parenchymal changes on diagnostic imaging, nor any longitudinal studies, to demonstrate the natural progression of these changes. In an effort to influence timely bronchoscopic or surgical intervention, this paper proposes a classification of severity of parenchymal injury, as seen on cross-sectional imaging, resulting from bronchial compression by TB lymphadenopathy, and attempts to describe a presumptive evolutionary sequence of events from when the lung parenchymal injury is reversible to when there is irreversible lung destruction.

Background to the Problem:

TB is an infection caused by the bacillus *Mycobacterium tuberculosis*. The commonest manifestation of this infection is pulmonary. Twenty-four percent of the world's TB cases are in Africa, which also has the highest case rates and **deaths per capita** [1]. South Africa ranks eighth in the world with regard to the incidence of TB and in the top 20 for multi-drug resistant (MDR) TB [2]. TB is still the leading cause of death in South Africa [3]. The burden of the disease is further compounded by the fact that approximately 5.3 million people are living with HIV in South Africa [4]. As a result, although the incidence of TB is decreasing worldwide, South Africa remains the only country that still shows an increase in the incidence of TB [2].

Pathology of TB

Primary TB results from the inhalation of droplets containing the causative organism, *Mycobacterium tuberculosis*. Because of their immature immune system and poor cell-mediated immunity, infants and younger children (< 5-years old) are more likely to develop TB when infected [5]. These infected droplets cause a localised pneumonic process, called the Ghon focus. From here, the bacilli spread to the regional lymph nodes via the lymphatics. This local infective focus with associated lymphangitis and lymphadenopathy is known as the primary complex or Ghon complex [6,7]. It is this regional lymphadenopathy that is considered the hallmark of the radiological diagnosis of TB in children [6].

LBTB definition and pathogenesis

When TB nodes involve the airways, it is called lymphobronchial TB (LBTB) [8]. The airways can be involved by compression, erosion or infiltration [9]. LBTB is a complication of TB seen almost exclusively in children who are more at risk because of the small calibre and compressibility of their airways. Although regional lymphadenopathy is the radiological hallmark for the diagnosis of TB in children, compression of the airways by these enlarged nodes (i.e. LBTB) is seen in only 38% of patients on CT [10]. Newborns and children up to 3 years old are more likely to have lymphadenopathy and are consequently more likely to develop LBTB [11].

The clinical and associated radiological picture depends on the degree of luminal obstruction and on whether the node has eroded into the lumen of the airway. Initially, a child with LBTB will show symptoms of incomplete airway obstruction e.g. unremitting coughing, stridor and wheezing [12]. As the degree of obstruction increases, a “ball-valve” type of obstruction may develop: The lumen is only partly occluded during inspiration allowing airflow past the obstruction, but during expiration

the soft paediatric airway narrows and the obstruction becomes complete [Figure 1]. This leads to **air trapping** in the affected segment, lobe or lung. When the luminal obstruction is complete, the affected segment or lobe will show **collapse** as air is removed from the segment by resorption [13].

If a tuberculous lymph node ulcerates through the bronchial wall into the airway, the caseous contents of the node can be aspirated into the lung segment or the lobe supplied by that bronchus. The initial reaction to the tuberculous material is of a hypersensitive nature but as the airway obstruction becomes complete the reaction changes to an immune reaction. This leads to **expansile pneumonia, caseation** and **liquefaction** of the lung parenchyma [12,14]. Imaging of these pathological changes has not been adequately classified with regards to the severity of each, the progression from one stage to another or the associated risk factors relating to the location or degree of airway compromise and as an indicator for intervention before irreversible destruction has occurred. Figure 2 outlines a sequential pathogenetic mechanism and the available treatment options at each pathologic stage.

Imaging of LBTB

CT is considered the "gold standard" for **detecting mediastinal lymph nodes** in children with TB [15]. The commonest site for tuberculous lymphadenopathy is the subcarinal group, but multiple sites are usually involved [15,16]. These lymph nodes show characteristic "ghost-like" or rim enhancement and may infrequently show calcification [15]. In particular, some combinations of lymphadenopathy cause specific air-way compressions e.g. the combination of large subcarinal and large right hilar lymphadenopathy causes compression of the bronchus intermedius [16]. CT is also the best way of **imaging the airways** of children with LBTB [5].

The CT findings of patients with TB are well documented but there is a relative paucity of literature regarding CT findings of **LBTB**. This is despite the fact that was described by Seal and Thomas in 1965 [17]. The ability with CT to perform multiplanar reconstruction, 3-dimensional reconstruction [5] and 3-dimensional volume rendering [10] make it an extremely useful tool in this respect.

Where mentioned, the CT findings of LBTB include enlarged lymph nodes, hyperinflation, consolidation, drowned lung, necrosis, bulging fissures and cavitation [12,18]. These descriptive papers do not present a classification system of severity that distinguishes between reversible lung changes and irreversible parenchymal destruction to guide management decisions. There is also no study or opinion of whether these stages follow-on from each other and whether they represent a sequence of events. Griffith-Richards et al. described 3 different categories of **cavitation** in children with TB: "adult type" post-primary TB, progressive primary TB, and lymphobronchial TB [11] but this was a small series of only 10 children. The CT findings of the parenchymal **complications and associations** of LBTB on CT were described by Lucas et al. [16], but no severity classification was provided to aid management decisions. Lucas et al described the **parenchymal complications** of LBTB on CT scanning as varying from air trapping, through consolidation and collapse to expansile pneumonia, drowned lung, necrosis and cavitation [16]. Other complications and associations that can also be seen on CT, that are not related to the airway occlusion and include pericardial effusions, axillary adenopathy [19] and musculoskeletal involvement [20]. Goussard et al described the clinical, radiological and bronchoscopy findings of **expansile pneumonia** in 24 children with TB. They showed that patients with obstruction of >75% on fibreoptic bronchoscopy (FB) there was liquefaction on CT, while there was no liquefaction was present in obstructions <75%. They also described three patterns on CT images: (a) a dense homogeneous opacification with no evidence of liquefaction of the affected lobe and patent airways and visible air bronchograms (17%); (2) homogeneous opacification with areas of necrotic liquefaction in the

opacified lobe, together with glandular obstruction of the airways and absence of air bronchograms (67%) and (3) a combination of a homogeneously opacified lobe and areas of necrotic liquefaction and lobes with homogeneous opacification, with patent airways and visible air bronchograms (17%). Hilar lymphadenopathy with ring enhancement was also visible in all cases. [14].

MRI is not routinely used for the diagnosis of TB or LBTB, because of the need for sedation or anaesthesia in children under 6 years of age, but lymphadenopathy or parenchymal pathology can be detected when an MRI is performed for other purposes, e.g. investigation of TB spondylitis [19]. Only one small published series compares CT and MRI for the parenchymal changes in patients with LBTB. This study is informative in that it shows the parenchyma distal to airway stenosis resulting from TB lymphadenopathy to have a signal in keeping with caseating necrosis i.e. low signal intensity on T2. This is in contrast to airspace consolidation without caseation, that is of high signal intensity on T2 [21].

It is important to compare the parenchymal complications of LBTB with the parenchymal changes seen in airway obstruction due to other causes as there are no longitudinal studies to inform the sequence of events in LBTB. Intraluminal foreign bodies are well known to cause **air trapping** by a ball-valve mechanism [22]. Extraluminal or endoluminal tumours also obstruct airways giving rise to a spectrum of parenchymal changes ranging from **consolidation, atelectasis [13] and drowned lung [23] to multiple fluid-filled cavities [24], necrosis and cavity formation [25]**.

Even though there are no longitudinal follow-up studies to prove progression of one complication to another, the pathogenetic mechanisms known from other causes of obstruction and the underlying severity of the parenchymal changes, suggest a progressive evolution in severity towards lung destruction. Severity as a progression has only been alluded to in previous work. No

classification of parenchymal changes reflecting severity for LBTB or any other post obstructive pathology has been developed. There is also no longitudinal material to prove that there is a sequential and stepwise progression of parenchymal changes in LBTB. This material is unlikely to emerge because of radiation concerns using multiple CT scans in children and secondly because centres with TB predominance usually rely on CXR because of the cost implications of CT. More importantly, however, when creating a severity grading, it is not the ability to predict progression from one stage to the next that is important but rather the inevitable progression to non-salvageable destruction when there is no treatment.

Identifying the parenchymal complications of LBTB and recognising their severity has clinical relevance. Encountering a patient at risk of irreversible damage to their lungs should prompt urgent intervention. The study by Goussard has presented airway size predicting the likelihood of lung destruction [26]. Even though CT would also be able to provide an airway size as well as bronchoscopy [10] and detect endobronchial material. CT is also able to directly inform on whether the lung parenchyma distal to the obstructed airway is salvageable or not. Surgical intervention can take the form of enucleation of the obstructing node which decompresses the bronchus, allowing a return to normal when the lung is still viable. Alternatively, removal of intraluminal material is possible via bronchoscopy [27-29]. Recovering patency of the airway and allowing resolution of the parenchymal disease associated with the obstruction can thus be achieved. In these cases, the CT scan also serves as a road map for the surgical approach [30].

Proposed severity classification of lung parenchymal involvement in LBTB

Our proposed classification assumes the role of imaging beyond diagnosis, identification of airway compression and implicating the lymphadenopathy group causing it, and is intended to inform

management by identifying reversible change (**salvageable** lung) and differentiating it from irreversible change (**non-salvageable** lung).

The figure below [Figure 3] is our Stage 0 – V CT classification for the severity of lung parenchymal involvement in LBTB. Images collected for this pictorial classification were obtained from children younger than 13-years of age with proven TB (either by the demonstration of acid-fast bacilli or by the culture of bronchial or gastric aspirates) who were referred to a paediatric pulmonologist at a large teaching hospital in the Western Cape Region of South Africa, with signs and symptoms of large airway compression. The symptoms and signs included wheezing and persistent coughing as well as pneumonia not responding to treatment, clinical or radiological features of unilateral hyperinflation, lobar collapse or expansile pneumonia. The patients were treated for 28 days with steroids and a four-drug anti-TB regimen and re-assessed. If clinical or radiological evidence of airway obstruction persisted, the patients underwent flexible bronchoscopy and CT scan of the chest as routine management to investigate the cause and the level of obstruction. CT scans were either performed on a 4 slice multi-detector scanner; later scans were performed on 40 slice multi-detector scanner. A routine chest protocol for children was used with 120 kVp tube voltage and 50 mA tube current. Intravenous contrast was routinely administered at a dose of 2ml/kg bodyweight by hand injection. The standard image reconstruction yielded ‘soft-tissue’ images, standard lung images as well as ‘high-resolution lung’ images.

The range of abnormalities was categorised according to predetermined CT features in categories and organised according to the severity classification, based on existing pathological principles of post obstructive lung disease discussed above [13,22,24,25].

Stage I to III all demonstrate enhancing lung tissue (vital lung) irrespective of the content of the airways or the volume of the involved lung. This underscores the importance of intravenous contrast in making the distinction of reversible and non-reversible lung injury. Stages IV and V represent irreversible lung change (non-salvageable lung tissue - note that other parts of the same lung may be salvageable). The differentiating features of non-vital lung are therefore non-enhancement and cavitation.

Limitations of this classification system

No biopsies of the lung parenchyma are available which **precludes pathological proof** of the CT findings and what they represent. A biopsy is an invasive procedure, and in patients who are under 1-year of age (the majority of patients in this database), this will lead to a bronchopleural fistula.

Very few patients had follow-up CT scans and therefore it is only assumed that progression of lung parenchymal changes is inevitable and sequential if left untreated. We cannot prove that post obstructive lung disease progresses sequentially through all the stages described in the proposed classification or whether parenchymal changes skip stages or make any comment on the duration of each stage.

The converse is also true, that we cannot disprove that a process of self-healing may occur with regressions to a prior stage without an iatrogenic intervention, but it is well accepted that bronchial obstruction requires treatment to avoid inevitable distal lung destruction.

Conclusion:

Using prior publications on LBTB and post obstructive lung injury we have used an image bank of CT scans in children with pulmonary TB, presenting with airway symptoms, to create a CT severity

staging of lung injury in LBTB. The staging focuses on distinguishing non-salvageable destruction [non-enhancing or cavitated lung] from salvageable lung parenchymal disease [enhancing and non-cavitated] to inform the management decisions, which range from bronchoscopic airway clearance to surgical decompression of the compressing nodes.

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Legends to Figures

Figure 1

Coronal CT reformat of the chest in a child with diagnosed pulmonary TB demonstrating the right middle and lower lobe air-trapping (visualised as expanded lobes of lower density than the contralateral lung) due to compression of the bronchus intermedius by sub-carinal and right hilar lymphadenopathy.

Figure 2

Sequential pathogenetic mechanism and the available treatment options at each pathologic stage.

Figure 3

The proposed stage 0 – V CT severity classification for parenchymal injury in paediatric LBTB distinguishing reversible change (*salvageable* lung) in blue from irreversible change (*non-salvageable* lung) in green.

Key to Definitions

Air trapping: The affected lobe shows a decrease in CT density as well as an increase in volume (as indicated by bulging fissures and splayed vascularity).

Air-space consolidation: The affected lobe shows increase in CT density, which enhances on the post contrast scan and demonstrates air-bronchograms, and either fills a lobe or has ill-defined edges within a lobe. This may exist with or without volume gain. In the situation where a consolidation exists with a decrease in volume of the affected segment/lobe, this will be termed a 'collapse'.

Drowned lung: A consolidated segment that shows fluid-bronchograms (i.e. fluid in the bronchi instead of air). The lung enhances normally on the post contrast scan.

Necrosis: No perfusion of the affected segment/lobe as evidenced by non-enhancement on the post contrast scan.

Breakdown or cavitation: Irregular air-filled or fluid-filled cavities in the affected segment/lobe

Expansile: Any areas of above pathology showing an increased volume will be considered as expansile. "Air trapping" is expansile by definition and unrelated to the parenchymal changes and will therefore not be included in this category.