Should pulmonary computed tomography be performed in children with tuberculosis infection without apparent disease?

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Background

During early childhood, in particular, there is a continuum between tuberculosis infection and disease. When establishing the diagnosis in a child with suspected tuberculosis, the distinction between infection and disease frequently depends on the interpretation of the chest X-ray. Some studies have shown hilar and mediastinal lymphadenopathies on computed tomography (CT) in children with tuberculosis infection without apparent disease, i.e., asymptomatic children with a positive tuberculin skin test and normal chest X-ray. These observations raise the issue of whether pulmonary CT should be performed in children with tuberculosis infection without apparent disease and whether different types of therapy should be administered depending on the results.

Methods

We reviewed the physiopathology of tuberculosis infection and disease, diagnostic methods and treatment, and the literature on the use of pulmonary CT scan in pediatric tuberculosis.

Results

Modern CT scanners indicate hilar and mediastinal lymphadenopathies in many of the children with tuberculosis infection with no apparent disease on chest X-rays. However, neither the size nor the morphology of these adenopathies allows active tuberculosis to be diagnosed. The natural history of childhood tuberculosis indicates that most children show hilar lymphadenopathies after the primary infection, although progression to disease is rare and is characterized by the presence of clinical symptoms. The exceptions are children younger than 4 years old and those with immune alterations who more frequently show progression of infection to disease and who require close follow-up. In addition, the experience accumulated over many years in the treatment of tuberculosis infection with isoniazid has shown this drug to be effective in both short- and long-term prevention of active disease. Official guidelines and expert opinion do not recommend systematic pulmonary CT scan in these children or modification of treatment according to the results.

Conclusions

Hilar and mediastinal lymph nodes are frequently found in the CT scans of children with tuberculosis infection without apparent disease but there is no evidence that these adenopathies indicate active disease or that these children require different treatment. Consequently, until demonstrated otherwise, pulmonary CT scanning and changes in chemoprophylaxis are not justified in children with tuberculosis infection.

Key words:

Tuberculosis. Children. Computed tomography.

¿DEBE REALIZARSE UNA TOMOGRAFÍA COMPUTARIZADA TORÁCICA A LOS NIÑOS CON INFECCIÓN TUBERCULOSA SIN ENFERMEDAD APARENTE?

Antecedentes

En la infancia, la infección y la enfermedad tuberculosa forman parte de una acción continua. Cuando se hace la evaluación diagnóstica de un niño con sospecha de tuberculosis, la distinción entre infección o enfermedad recae con frecuencia en la interpretación de la radiografía de tórax. Algunos estudios han puesto de manifiesto mediante tomografía computarizada (TC) la presencia de adenopatías hiliares y mediastínicas en niños con infección tuberculosa sin aparente enfermedad, es decir, asintomáticos, con tuberculina positiva y con radiografía de tórax

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normal. Estos hallazgos abren el debate de si es necesario realizar TC torácica a niños con infección tuberculosa sin enfermedad aparente y si hay que administrar un tratamiento distinto según su resultado.

Métodos

Se analiza la fisiopatología de la infección y la enfermedad tuberculosa, su diagnóstico y tratamiento y la bibliografía existente sobre la utilización de la TC en la tuberculosis infantil.

Resultados

Las modernas TC helicoidales visualizan ganglios linfáticos hiliares y mediastínicos en muchos de los niños con infección tuberculosa sin aparente enfermedad. Sin embargo, ni por el tamaño ni por la morfología de estas adenopatías se puede afirmar que se correspondan con enfermedad activa. La historia natural de la tuberculosis indica que la mayoría de los niños presentan adenopatías hiliares tras la infección inicial y que la evolución a enfermedad es infrecuente y se caracteriza por la presencia de síntomas clínicos. La excepción la presentan los niños menores de 4 años y los niños con alteraciones de la inmunidad, en los que la infección progresa con mayor frecuencia a enfermedad y en los que habrá que hacer un estrecho seguimiento. Además, la experiencia acumulada durante muchos años en el tratamiento de la infección tuberculosa con isoniacida ha demostrado su eficacia a corto y a largo plazo en la prevención de la enfermedad activa. Los consensos oficiales y la opinión de expertos no recomiendan la realización de TC en estos niños ni adecuar el tratamiento a sus resultados.

Conclusiones

Con frecuencia se encuentran ganglios en zonas hiliares y mediastínicas al realizar una TC en niños con infección tuberculosa sin enfermedad aparente. Sin embargo, no existen evidencias de que estos hallazgos se correspondan con enfermedad activa ni de que haya que tratarlos como tal. Mientras no se demuestre lo contrario, a los niños con infección tuberculosa no es necesario realizarles una TC torácica y se les debe administrar el tratamiento actualmente recomendado.

Palabras clave:

Tuberculosis. Niños. Tomografía computarizada.

INTRODUCTION

Tuberculosis (TB) continues to be a worldwide problem. Of the 8.3 million new diagnosed cases of the disease in the year 2000, 11% were children[1]. In Spain, the arrival of immigrants, adults and children, from countries where disease from TB is endemic (rates of over 80 cases per 100,000) contributes significantly to the incidence of the disease[2,3]. The problems of tuberculosis infection are doubled in young children. Also there is a higher probability of progression to disease, with the possibility of severe and extrapulmonary forms. On the other hand, infected children make up a reservoir from which new future cases of the disease will arise[4]. Therefore, to control TB, the diagnosis and the correct treatment of infected children and those with the disease is important[5,6]. However, it can be difficult to differentiate between infection and disease in young children. In developed countries, often as a result of contact studies of an adult with TB, it is diagnosed in a child who has few or no symptoms. Bearing in mind that the most common presentation of TB in children is hilar or mediastinal lymph nodes, the interpretation of the chest X-ray is essential in the diagnosis and treatment of the infected or diseased child. For several years, there has been an open debate on whether *1)* a computed tomography (CT) should be performed on children with a tuberculosis infection and a normal chest X-ray, to detect hilar or mediastinal lymph nodes that may have gone unnoticed on the chest film; and *2)* in cases where they appear in the TC, whether the therapeutic approach has to be changed and administer several drugs as active disease treatment.

The physiopathological concepts of tuberculosis infection and disease, its diagnosis, and the existing evidence on the subject, are reviewed in this article.

TUBERCULOSIS INFECTION

When a child inhales a particle infected with *Mycobacterium tuberculosis* bacilli, a pulmonary parenchymal focus (Ghon focus) is produced. In the first 4-6 weeks, there is an uncontrolled multiplication of bacteria and a spreading to the regional lymph glands via the lymphatics. The upper lobes drain into the ipsilateral paratracheal glands, while the rest of the lung drains into the perihilar and subcarinal glands, mainly flowing from the left to the right[7]. The Ghon complex consists of the Ghon focus, local lymphangitis and the regional lymphatic glands. In this early phase, before cellular immunity is active, an occult haematogenous dissemination can also be produced.

In paediatrics, non-complicated hilar lymph nodes are the usual presentation of primary TB. Studies carried out before there were tuberculosis drugs, documented the existence of transient hilar lymph nodes in the majority of children with a recent primary pulmonary infection, of which only a few progressed to disease[8]. During the incubation period, the infection is generally controlled by the immune system, so that the progression to tuberculosis disease is very uncommon and mainly depends on the age of the child[8]. This is a fundamental difference to adult TB, which is often the re-activation of a latent infection. In early childhood, tuberculosis disease is usually a continuation of the primary infection and for this reason it can be difficult to differentiate between infection and disease.

TUBERCULOSIS DISEASE

The infection may evolve to the disease due to progression of the glandular or pulmonary involvement and

haematogenous dissemination. The initial parenchymatous lesion can progress to pneumonia. Cavity formation, although uncommon in children, can occur under certain circumstances: very young infants, children infected with HIV, adolescents with adult type disease, and when the affected lymphatic gland penetrates a neighbouring bronchus caused by caseating expansile pneumonia[9,10]. Another possible progression is if the affected regional lymphatics swell due to central caseation and peripheral inflammatory oedema. In children less than 5 years old, glandular disease is more common after the primary infection. The relatively small size of the airway makes them more vulnerable to the development of lymphobronchial TB, due to compression of the lymph nodes on the underlying bronchus, after drainage of the caseous material, formation of polyps and tissue granulation. If the bronchial obstruction is partial it causes valvular emphysema, whereas if it is complete the lobe or the pulmonary segment will collapse[11]. The pleura can be affected due to a hypersensitivity reaction, progression of the Ghon focus, or by haematogenous dissemination.

Tuberculosis disease occurs mainly in children who are, less than two years old, immunodeficient (including HIV-induced infection), or malnourished, all of them having a poor cellular immune response. More than 95% of children who progress to the disease do so in the first year of the primary infection. Young infants have a higher risk of progressing to lung disease (30-40%) or miliar TB and tubercular meningitis (10-20%), which is the most serious complication of this disease[8,12,13]. The incidence of lung or miliar and meningeal disease is still appreciable in the second year of life (10-20% and 2-5% respectively) and reaches a lower level between 5 and 10 years of age (2%).

Diagnosis of tuberculosis infection

The diagnosis of tuberculosis infection is made by the tuberculin test. In Spain, the positive threshold limit has been set at 5 mm, owing to the low incidence of atypical mycobacteria and at 15 mm in vaccinations with BCG[14]. However, the American Thoracic Society, advises a limit of 10 mm in children with no contact with a person with TB, with no symptoms and with no radiography compatible with the disease[15]. The tuberculin test may show false negatives in children with alterations in immunity and in the initial period of infection (≤ 12 weeks) and false positives due to atypical mycobacteria, the interpretation being difficult in children vaccinated with BCG.

Over the past few years, methods have been assessed based on the release of gamma interferon by T lymphocytes after *in vitro* stimulation with specific *M. tuberculosis* antigens, QuantiFERON®-TB Gold and T-SPOT-TB®. These techniques have a higher sensitivity in immunodepressed patients and in an initial anergic period, and a higher specificity with no false positives in infections caused by atypical mycobacteria or in children vaccinated with BCG[16]. However, up until now, in the absence of clinical signs and with a normal chest X-ray, these techniques have not shown to be able to differentiate the infection from the tubercular disease[12].

Diagnosis of tuberculosis disease

The definitive diagnosis of tuberculosis disease is determined by isolating by culture and identifying its causal agent, *M. tuberculosis*. In younger children, the sensitivity of the culture is low. On the one hand, the predominant forms of the disease are paucibacillary, and besides, clinical samples are not usually sputum, due to expectoration not being possible in many children. Traditionally, serial samples of gastric juice have been collected first thing in the morning, achieving a yield of 30-40%[17] and up to 80% in young infants and in cases with advanced endobronchial disease. Induced sputum or nasopharyngeal aspirated samples can be a valid alternative, particularly in out-patient children, although the sensitivity is similar to that of gastric juice[19,20]. Direct staining of the samples obtained provides a rapid probable diagnosis that enables specific treatment to be started, however, its sensitivity (< 15%) is significantly less than that of the culture[17,21]. Nucleic acid amplification techniques such as polymerase chain reaction (PCR), can provide rapid results within 1-2 days and increases the sensitivity to 60%[22]. PCR performed manually in the laboratory (In house PCR) is more sensitive and specific than commercial kits (Amplicor PCR)[23]. PCR, despite not being the ideal technique, when performed in centres with experience it can be useful in difficult to diagnose children[24].

In view of the difficulty in obtaining microbiological confirmation, the diagnosis is usually based on a positive tuberculin test, the contact history with an infected person, the presence of clinical symptoms or radiological changes. The clinical symptomatology, if present, is the best index in differentiating between tuberculosis infection and disease. However, in developed countries, children in contact with an adult with TB have few or no symptoms when they are diagnosed in the first phases of the disease. Therefore, the diagnosis of the disease often comes down to the interpretation of the chest X-ray when there is a positive tuberculin test[12].

Imaging techniques in the diagnosis of infantile tuberculosis

Among the usual forms of radiological presentation, the hilar or mediastinal lymph nodes and pulmonary infiltrates are noteworthy. Tuberculous lymph nodes show up on the chest X-ray as an increase in density with generally blurred limits due to the adjacent pulmonary parenchymal being affected, although when this is cured they can be seen with better defined borders[8]. In cases of lymphobronchial disease, bronchial compression can be

seen, as hyper-clear areas due to valvular emphysema or as atelectasis[11].

Different studies corroborate the difficulty and caution that must be used in interpreting a possible pulmonary lymph node on chest X-rays of children suspected of having TB. In one of these studies a wide intra- and inter-observer variability was observed in the viewing of lymph nodes when four paediatric pneumologists reviewed the X-rays of 100 children with a diagnosis of lung or pneumonia TB[25]. Another study compared the sensitivity and specificity of anteroposterior and/or lateral chest X-rays, interpreted by paediatricians and primary care doctors, in detecting pulmonary lymph nodes in 100 children who were suspected of having pulmonary TB[26]. Taking CT as reference, the sensitivity of the chest X-ray was 67 % and the specificity was 59 %. The family doctors had a higher sensitivity and lower specificity than the paediatricians. Therefore, the interpretation of chest X-rays to detect tuberculosis lymph nodes is not without problems. Computed tomography, magnetic resonance and chest echography, in the hands of a radiology expert, can also detect mediastinal lymph nodes and their progress during treatment[27-30].

CT in children with symptomatic tuberculosis disease

Computed tomography and high resolution CT can help in the investigation of lung involvement, occult cavities and the assessment of nodular and reticulonodular forms. With aid of intravenous contrast, lymph nodes are observed with a rim on the peripheral ring[27]. Its usefulness is unquestionable in the symptomatic child with a normal or doubtful X-ray, since it specifies the extent of the disease and helps to check if the patient symptoms are associated with TB.

CT in children with tuberculosis infection and with no apparent disease

In 1993 Delacourt[31] published a study of 15 children with tuberculosis infection with no evidence of disease, with a positive tuberculin test, normal chest X-ray and a negative gastric juice culture. A CT with intravenous contrast was performed on all of them, verifying an increase in the size of the lymph glands in 9 patients (60 %). The lymph nodes were mainly detected in children less than 4 years old and in the right paratracheal chains and hilars. Later, another group performed CT with intravenous contrast on 22 children with a positive tuberculin test, asymptomatic, normal chest X-ray and negative culture. In 14 of them (63 %) lymph nodes, mainly in the paratracheal chains, were found that had been missed on the chest X-ray; PCR was positive in 4 children with an abnormal CT and in none with a normal CT[32]. Subsequent studies have reported similar results in 50 % and 58 % of children with tuberculosis infection in whom an increases in the size of hilar or mediastinal lymph glands were detected by CT, which had not been seen in the chest X-ray (Sanchez y Altet en Comunicaciones a la XXIX Reunión de la SENP, Bilbao 2007).

Due to these results there is a dilemna on the need to perform a CT in cases of asymptomatic children, with a positive tuberculin test, and with a normal chest X-ray to differentiate a tuberculosis infection from the disease. To be able to support a recommendation, the following questions should be answered: A. What significance do lymph nodes have when discovered using CT and are they indicative of active tuberculosis disease? B. Is there an indication to treat the children who have them in a different way?

How is it known if children with lymph nodes in CT have an active disease?

The active glandular disease is verified with a histopathology/microbiology study. In the case of TB, the identification of *M. tuberculosis* confirms the diagnosis, and failing that, the identification of granulomas with caseous necrosis is very suggestive, although not very specific, of the disease. However, obtaining clinical samples of affected mediastinal nodes is complicated, requiring thoracotomy or thorascopy. A provisional diagnosis of active glandular disease by non-invasive means can be obtained by isolating *M. tuberculosis* in other clinical samples or using imaging methods such as CT, that previously establish the size and morphology of the nodes that have a histopathology that corresponds with active TB disease.

According to the size of the lymph glands

The criteria when considering if a mediastinal gland is pathological have been based on data from adults with cancer. In paediatrics, there are studies that correlate the size of the gland and the anatomical disease. Delacourt[31] took as a reference the normal size of the lymph glands of 10 children on whom a CT was being performed for other reasons. The normal size depending on age and the location were established: in children less than 4 years, from 5 mm in the right paratracheal area and 4 mm in the hilar area, and in those over 8 years: 7 mm and 6 mm, respectively. The presence of lymph glands in other locations was considered abnormal. Another study took as a reference 14 children who were being screened for lung metastases and considered a size greater than 5 mm as abnormal[32]. Some authors consider that any gland observed using CT as pathological[33-34]. However, with new scanning techniques, normal lymph glands are often seen. In fact, in one study lymph glands were seen in 92 of 100 children suspected of having TB, a much higher frequency than expected. On only taking glands greater than 10 mm as pathological, a lymph node was detected in 46 %[35].

It is evident that CT has a higher sensitivity than conventional X-ray in the diagnosis of tuberculous node involvement. However, it is worth knowing if CT can be considered as the diagnostic reference standard for tuberculous mediastinal lymph nodes. In a recent study, CT with contrast was carried out on 100 children clinically suspected of having TB, and four radiologists, including a paediatric radiologist, with experience in infantile TB were asked to identify lymph glands of any size[36]. The concordance in detecting lymph glands between the radiologists was only moderate, the biggest discrepancy being in those located in the anterior mediastinum and in the right hilar. They had difficulty distinguishing the normal thymus from a lymph node, and in differentiating normal glands from pathological ones, without having previously determined an abnormal cut-off point. The concordance was higher in the right hilar area and in locations around the carina.

These studies demonstrate that the pathological size of hilar and mediastinal glands are probably between 5 and 10 mm and that there is variability between different radiologists in identifying mediastinal lymph nodes in CT. Studies with histopathology correlation would be required to definitively establish what is the pathological size of the glands observed using CT, since with the improvements in equipment and radiological techniques, pathological lymph glands as well as normal ones are seen[36,37].

According to the morphology of the lymph glands

There are studies on adults that have correlated the morphology present in lymph nodes in CT and the histopathological findings reported after the analysis of gland biopsies[38,39]. The diagnosis of active nodal TB was defined by the isolation of *M. tuberculosis* in the culture or by the presence of caseous necrosis[39]. Patients with active TB had larger lymph nodes in CT with a central hypodensity and a peripheral rim. The hypodense areas corresponded to the caseation and liquefaction found in the biopsies, while the peripheral rim was associated with inflammatory hypervascularity of the granulation tissue[38,39]. On the other hand, patients with lymph nodes with no active disease had few or no symptoms, negative culture, and no histopathological evidence of caseous necrosis, smaller nodes in the CT and most importantly, none had central hypodense areas after the injection of intravenous contrast media. Calcification mainly appeared in patients with no active glandular disease, but it also was seen in some with active disease[39].

One study analysed the morphology of lymph nodes in children with active tuberculosis disease confirmed bacteriologically or clinically, with a positive tuberculin test, progression with treatment and a contagious person in the environment; the majority of children had hilar or mediastinal lymph nodes and 85% of cases showed a central hypodensity and a peripheral rim after injection of contrast[27]. Another recent study performed a CT on 100 children with clinically suspected TB due to pulmonary infiltrates and the presence of other expressions such as a positive tuberculin test, contact with TB, failure to thrive in the previous two months or cough for more than month. Surprisingly, in this group of children in whom it was clearly specified that they had active TB, the lymph nodes usually had a diffuse rim with no central hypodensity[35].

In adults, the presence of large lymph nodes in the CT, with central hypodensity and a peripheral rim is suggestive of active tuberculosis disease. On the other hand, the presence of small homogeneous lymph nodes with no central hypodensity after administration of an intravenous contrast are not suggestive of active disease. There are no conclusive studies in paediatric that correlate the appearance of tuberculosis lymph nodes with activity detected by histopathology/microbiology (caseous necrosis or bacterial growth).

Relationship between lymph glands in the CT and microbiological activity in clinical samples

Some studies have shown that up to 10% of children with active TB confirmed by culture have a normal chest X-ray[40]. On the other hand, when gastric juice samples were taken from children with tuberculosis infection with no apparent disease, *M. tuberculosis* was isolated in 8.5% of them[41]. There are no large studies that have analysed whether children with lymph nodes exclusively observed in CT have microbiological activity detected in normally collected clinical samples, gastric juice or bronchoalveolar lavage. It could be speculated that children with normal chest X-rays and a positive culture correspond to children with lymph nodes in the CT. However, it has also been argued that the existence of positive cultures in clinical samples from asymptomatic children might correspond to the spreading of the tuberculosis infection which happens in the initial proliferative phase before cellular immunity is active[7].

One study performed cultures and PCR on children with tuberculosis infection with no apparent disease and found one child with a positive culture and five with a positive PCR who had lymph nodes in the TC. On the other hand, all the children with a normal CT had positive cultures and a negative PCR[22]. Swaminathan[42] carried out thoracic CT on 9 children with a culture positive to *M. tuberculosis* in gastric juice samples and a normal chest X-ray (although two of them with visible calcifications). Eight patients had anomalies in the CT: thoracic lymph nodes (N = 5) or pulmonary lesions (N = 3). However, the CT was normal in one child despite having a positive culture. Therefore it is not possible to draw definite conclusions on whether children with a tuberculosis infection and a normal chest X-ray who have microbiological ac-

tivity detected by culture or PCR correspond to those who have lymph nodes in the CT.

How is it known if the children with lymph nodes in the CT should be treated differently?

Natural progression of the disease and experience before there was tuberculosis treatment.

In the period between 1920 and 1950, the availability of chest X-ray enabled descriptive studies to be performed on the natural history of TB without the influence of an effective treatment[8]. With these studies, it is documented that after the primary infection, 50-70 % of children had enlargement of hilar or mediastinal lymph nodes[43,44]. Serial radiological studies demonstrated that in 40 % of cases the lymph nodes disappeared in the first 6 months and in 30 % in the first year[45]. the spontaneous progression was favourable regardless of the size of the lymph nodes or there was a visible parenchymatous lesion[45]. On the other hand, age less than two years[43,44], as well as persistent clinical symptoms were risk factors of the progression of the disease, while the absence of symptoms was indicative of a good containment of the germ[12].

Physiopathological basis of treatment

From 1950 the discovery of several tuberculosis drugs achieved the first effective guidelines for the treatment of the disease. Tuberculosis treatment is based firstly, on the estimated bacilli population in the patient and secondly, on the probability of spontaneous resistant mutations to the tuberculosis drugs [46]. When there is a high bacilli population, as in the case of pneumonia or a cavity, the use of a single drug produces a selection of resistant mutations which become the dominant population and therefore cause the treatment to fail and makes the drug used ineffective, due to this resistance being chromosomic and irreversible[47]. When the estimated bacilli population is small, as in latent tuberculosis infection, the use of a single drug is sufficient. In the case of hilar or mediastinal lymph nodes, the estimated bacilli population is 10^2-10^5 while the probability of mutations resistant to isoniazid is 10^5-10^6. Therefore, theoretically, the use of isoniazid is sufficient to treat the bacilli population in cases of latent tuberculosis infection including those which have lymph nodes in the CT.

Clinical studies

The treatment of latent tuberculosis infection with isoniazid reduces the risk of progression to disease in more than 90 % of cases[48]. In children, this effectiveness is around 100 % and its effect lasts for at least 30 years[49]. The advised duration of treatment is 9 months[50] although the level of protection is probably similar with 6 months[51]. The consensus recommend using isoniazid for 6-9 months in the treatment of latent tuberculosis infection[15]. The administration of isoniazid and rifampicin for 3-4 months appears to have a similar efficacy[52,53], having few therapeutic failures, therefore it can be an alternative, mainly in cases where it may be necessary to reduce the treatment time[54].

In the child who has only a hilar lymph node in the chest X-ray, the same treatment as that for the active disease is recommended by consensus: at least 3 drugs, isoniazid, rifampicin and pyrazinamide for 2 months, followed by 4 months of isoniazid and rifampicin[55,56]. This is due to the innocuousness of the tuberculosis treatment in infants[57], although physiopathologically and microbiologically these cases are closer to the infection than the disease[8,46]. In fact, children with an isolated hilar lymph node on the chest X-ray or even with non-complicated pulmonary TB have shown a good response to the combination of isoniazid and rifampicin[58,59] and with no recurrences in two years of follow up[59]. For this reason, in children who have a hilar lymph node on the chest X-ray the use of only isoniazid and rifampicin for 6 months is acceptable, as long as there is not a high probability of drug resistance[60].

There are no studies that compare single drug therapy with the use of several drugs in asymptomatic children with latent tuberculosis infection who exclusively show lymph nodes in the CT.

CURRENT RECOMMENDATIONS

Is it recommended to perform a CT with intravenous contrast on all asymptomatic children, with a positive tuberculin test and normal chest X-ray, that is, without apparent disease?

The performing of a CT is indicated in the symptomatic child, with a normal or doubtful X-ray and in the assessment of the extent or complications of the tuberculosis disease or when the diagnosis of tuberculosis disease is doubtful or urgent[61]. None of the consensus recommend performing a CT on asymptomatic children with a positive tuberculin and a normal chest X-ray[52,55,56]. Delacourt, author of the first article on the detection of lymph nodes in children with tuberculosis without apparent disease, does not recommend the systematic use of CT in the immunocompetent child with a tuberculosis infection[62].

Arguments in favour of performing a CT

– Chest X-ray is too subjective and with limited sensitivity and specificity for detecting hilar or mediastinal lymph nodes. Lymph nodes located in the right hilar zone are easily recognised on the chest X-ray, while those in the paratracheal or subcarinal chains are difficult to see on the conventional X-ray.

– On occasions, X-ray also may not be able to detect small pulmonary infiltrations.

– CT is a more objective and precise method in the detection of hilar and mediastinal lymph nodes and pulmonary involvement. These lymph nodes and pulmonary infiltrates could represent a minimally active disease.

– It is precisely those children under 4 years who have a higher probability that the tuberculosis infection may progress to disease, and in whom pathological CT are more often found with normal X-rays.

Arguments against performing a CT

– The child has to be subjected to radiation, an intravenous contrast and sometimes sedation or anaesthesia.

– La CT can show false negatives and positives in the detection of hilar and mediastinal lymph nodes due to intra- and inter-observer variability between radiologists.

– It is not known exactly what size of lymph node must be considered pathological in infants.

– The morphology of the hilar and mediastinal lymph nodes present in CT is also unknown in cases of active disease. Studies carried out in adults indicate that the lymph nodes have central hypodensity and a peripheral rim in the active disease; this is not the predominant pattern in children.

Does the child who has lymph nodes in the CT have to be treated differently to the asymptomatic child, with a normal chest X-ray?

– Delacourt[31] in his preliminary study, recommends the use of isoniazid and rifampicin in small children due to them more often having lymph nodes in the CT. He actually considers that it is not justified to change the therapeutic scheme in asymptomatic children based on finding lymph nodes in the CT, since the normal treatment of tuberculosis infection with a normal chest X-ray is effective[62].

– The consensus recommend treating hilar lymph nodes seen on the chest X-ray as active disease. Therefore it could be doubtful whether it is necessary to perform a CT and treat as active disease if there are lymph nodes present in the CT. However, in the asymptomatic child, the lymph glands as well as the small pulmonary infiltrates represent the primary tuberculosis infection. The natural history of the disease indicates that hilar lymph nodes very often appear in infected children, but in the majority of them they resolve spontaneously and progression to disease is characterised by the association with clinical symptoms. The relative innocuousness of tuberculosis treatment in the infant leads to a tendency to over-treat children with hilar lymph nodes on the chest X-ray, although these cases are nearer the infection than the disease[8,46,63].

– It could also be speculated, although without justification, that these forms of minimally active disease discovered using CT would be under-treated on receiving isoniazid only, thus responsible for the progression from infection to disease or long-term reactivations, due to incomplete sterilisation of the lesions. However, treatment with isoniazid has been effective in almost 100 % of children[48] with latent tuberculosis infection, although it is not known whether lymph nodes were present in the CT or not, since the existing bacilli population is less than the probability of resistant mutations to the drug appearing[46]. The experience of more than 30 years has also demonstrated that isoniazid has been effective in the long-term prevention of tuberculosis disease[49].

In the asymptomatic child with tuberculosis infection and a normal chest X-ray, mediastinal lymph nodes are often seen in the CT. However, there is no evidence that their size and morphology correspond with the active disease, and the natural history of the disease suggests that they may be a part of the primary tuberculosis infection. The official national and international recommendations and opinions of prestigious authors do not recommend performing CT on the asymptomatic child, with a positive tuberculin test and with a normal chest X-ray, or to take a particular therapeutic path depending on their results. Also, the experience accumulated with isoniazid has demonstrated its effectiveness in the prevention of tuberculosis disease. Therefore, whilst it may not be demonstrated that the clinical progress of children with lymph nodes only visible on the CT is different from those who do not have any, it is not necessary to perform a CT on children with a positive tuberculin test, asymptomatic and with a normal chest X-ray, and any of the accepted treatments for tuberculosis infection should be recommended.

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