Sp18: What is the best method of assessment of response (clinical/ serological/ radiological) to conservative treatment in spinal tuberculosis?

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Response/Recommendation: Based on available data the assessment of response is based on a multifactorial approach utilising clinical features (pain, weight gain and appetite), sequential x-rays (excluding progression of kyphosis) and if available, MRI imaging. FDG PET CT has shown value in the research environment, and there is interesting work in peripheral blood biomarkers and genomics, but unlikely to be accessible to the population where spinal TB exists.

Level of Evidence: **Low**

Delegate Vote:

Rationale:

After a review of 188 abstracts, 24 were selected for full text review. Thirteen were appropriate to the topic in question.

Although most authors referred to clinical, blood and radiological parameters at variable time periods there was little explanation as to how they were interpreted. They were not assessed as to sensitivity or specificity or compared.

Authors generally used clinical parameters of resolution of presenting symptoms of pain, weight gain and return of appetite.[1-5]

Singh et al [4] presented the improvement of these factors over time in their 50 patients. Initially all patients reported severe back pain, with improvement over time. With 6 months treatment only 42% had moderate/ severe pain, 24% moderate at 9 months. By 12 months 88% reported mild or no pain.

Half had constitutional symptoms at presentation, with only 10% at 3 months and less than 5% by 6 months.

A ESR was generally used to confirm healing with some referring to CRP. ESR normalized by 12 months.[4]

All authors used x-rays at various time periods during the follow up. Boxer et al reported on the paravertebral soft tissue in the cervical and thoracic spine, which increased initially for the first 1.5 months and resolved over 12 months. It was not visible in the lumbar area.[6]

Earlier papers reported progressive boney destruction which developed within 3 months and progressed in 70% for 6.5 months thereafter, with body height loss for up to 14 months. There was increased sclerosis and disc height loss in 77% with anterior ankylosis in 75% at an average of 9 months.[6]

Zhang reports of an average 6.31° progression of kyphosis in what they refer to as mild spinal TB where the average kyphosis on presentation where the range was 10°–32°. [1]

In later studies, MRI was increasingly used to assess healing.[1, 5, 7, 8]. Factors such as reduced bone marrow oedema (reduced T2 and STIR signal), fatty replacement (increased T1), complete / partial resolutions of collections, reduced epidural and subligamentous spread and absence of contrast enhancement were regarded as healing.

Zhang [1] brought these factors together and introduced an outcome classification based on:

1. Normal body temperature and ESR, negative sign of all pretreatment symptoms
2. No presence of sinus or abscess
3. Intact neurological function
4. Complete regression or calcification of lesion focus on CT/MRI scan
5. Primary-line four-drug anti-tuberculosis medications, used throughout the 18 months
6. More than four drugs used, for longer than 18 months
7. Progression of kyphosis over 10° at affected level at the end of treatment
8. Failure of nonoperative treatment, requiring surgical intervention

Where an excellent result was complete resolution of disease with first-line anti-tuberculosis treatment for 18 months, with no residues or side effects of treatment (criteria 1, 2, 3, 4, 5). A good result: complete resolution of disease with first-line treatment for longer than 18 months, or with second-line drugs for 12 months or longer, with or without the occurrence of medically manageable side effects of drug therapy, such as gastrointestinal intolerance and drug-induced jaundice, necessitating frequent
manipulations in their doses and regimen, but with eventual complete resolution (criteria 1, 2, 4, 6). A fair result: complete resolution of disease, but with increased kyphosis of 10° or more at the affected level with no obvious or mild neurological compromising (criteria 1, 2, 3/4/5/6, 7). A poor result: cases that did not respond to conservative treatment, primary or secondary line, and had to be eventually operated (criteria 8)

In their 89 patients, they used this to report a excellent to good result in 70% and fair in 26%.

More recently there has been interest in FDG PET CT scanning. Mittel et al found this more useful than MRI especially when stainless steel implants were in situ. In their 28 patients, 11 were confirmed healed on both PET and MRI, 6 still active on MRI but healed on PET, 2 healed on MRI and active on PET, 9 unable to have MRI due to stainless steel or financial reasons [9].

Rai confirmed the FDG PET uptake in TB spine in their 25 cases. The SUVmax at baseline had a wide range making defining a cutoff for inflammation diagnosis challenging. However they reported a falling SUVmax with successful treatment, and suggest this change can be used as a biomarker of therapeutic response. In addition, it was valuable in assessing other sites of infection. [10]

Mann used PET in 28 patients who had completed >9 months treatment. They found that in a multiple regression model, CXCL10/IP-10, VEGFA, IFN-γ, CRP and Factor D/Adipsin biomarkers explained 52% of the variation in overall maximal FDG uptake. [11]

Agraval reported on the use of Technenium-ciprofloxacin in 15 cases as a promising tool for monitoring disease. In their 15 spTB cases, 9 had a positive scan, of which 7 became negative at 6 months which was accompanied with clinic-radiological resolution. [12]

Niu reported on genomic responses during the treatment of spTB compared to a healthy cohort. Although these patients were surgically debrided, the study does introduce an interesting option of using DNA microarray technology to detect and monitor the changes in gene expression in the peripheral blood cells. [13]

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