Sp30: Is there a difference in the duration of drug therapy between patients who are conservatively treated and those who undergo surgical debridement and stabilization?

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Response/Recommendation: Based on available data for spinal tuberculosis (TB) treatment, a short-course of 6 months triple or quadruple therapy is adequate for favorable outcomes in terms of disease eradication, bony fusion, avoiding recurrence and regaining function. In terms of surgery, radical surgery may yield better outcomes for more severe disease but not drug duration.

Performance of surgery does not alter the duration or dosage of chemotherapy.

Level of Evidence: Moderate

Delegate Vote:

Rationale:

For spinal TB, longer courses of antitubercular treatment regimens are to be expected due to poor penetration of antitubercular drugs to bone. However, with surgical removal of the microbial load, there is potential for reduced chemotherapy duration to have similar eradication action. As more aggressive surgical debridement, bone grafting and instrumentation are commonly adopted to achieve better outcomes like alignment and fusion rates, the duration of chemotherapy treatment should also be re-explored. In addition, there are concerns for longer duration of drug treatment with drug interactions, side effects, and hence worse patient tolerance and adherence to the treatment.

Some of the best evidence for answering this question stems from the Medical Research Council (MRC) trials. For the fourteenth report by the MRC[1], a five-year assessment of 3 randomized trials of 6, 9 and 18 months of TB chemotherapy was studied. Outcomes included physical ability, quiescent disease, kyphosis angle and bony fusion. Three countries were involved. Hong Kong patients were randomized to 6 or 9 months of isoniazid and rifampicin following radical resection and bone grafting and streptomycin for 6 months. Madras patients were randomized to 6 or 9 months of isoniazid and rifampicin or 6 months with surgical resection; and Korea to 6 or 9 months or 9- or 18-months isoniazid plus ethambutol or isoniazid plus para-aminosalicyclic acid (PAS). Through these studies, radical resection provided excellent results and all centers with 6- and 9-month regimens were excellent and similar to 18-month regimens. The only regimen that fared poorly was the 9-month isoniazid plus PAS group.

For the Hong Kong group of individuals (n=114) who were part of the MRC trial as noted above, a long-term follow-up of minimum 10 years was studied in 1996[2]. These were individuals who received 6, 9 or 18 months of treatment. The 6- and 9-month groups received streptomycin, rifampicin and isoniazid with streptomycin given for the first 3 months. For the 18-month group, similarly 3 months of streptomycin was given initially with 18-months of PAS and isoniazid. There were similar clinical results with no recurrence or reactivation of TB between 6-month, 9 month and 18-month treatment groups. The severity of remnant deformity was similar between groups. From this study, a 6-month regimen with surgical excision and bone grafting was adequate to achieve successful eradication of the disease with comparable radiological fusion and deformity maintenance.

Dai et al. [3] showed in a retrospective study of 57 consecutive patients with anterior radical debridement, autogenous bone grafting, and instrumentation that postoperative chemotherapy for 9 months using isoniazid, rifampicin and ethambutol was adequate for treatment. The TB was eradicated, there was no recurrence and bony fusion was achieved in all patients. However, the patients in this study had different preoperative regimen, ranging from 1 week to 2 years using isoniazid, rifampicin and ethambutol.

A retrospective study[4] from 7 Korean hospitals (n=137) showed that between patients who received 6 or 9 months of isoniazid, rifampicin and ethambutol, and patients with more than 12 months of treatment, there was no difference in favorable outcomes. However, a favorable outcome was related to surgery (p=0.043; OR = 3.047) and age (p=0.025; OR = 0.963). For short-course regimens, severe disease had more negative outcomes of limited physical activity due to the kyphosis. With radical surgery, patients were in worse preoperative state such as greater number of thoracic vertebrae (37.8% vs 20.0%; p=0.052; OR = 0.161) and neural compression (36.5% vs 15.6%; p=0.017; OR = 0.321) than for non-radical surgery.

In a more recent retrospective study[5], 45 patients allocated into a short course of less than 12 months of isoniazid, rifampicin and ethambutol, and long course of more than 12 months treatment. 27 underwent surgery (21 with radical resection) and this group had more neural compression and abscess formation. With radical surgery, patients were more likely to have a better outcome (p=0.010). There was no advantage in long course treatment in terms of remaining sinus or abscess, fusion status, radiological quiescence and functional ability.

A meta-analysis[6] of 6 trials in the Chinese population (n=851) showed that there is no difference between 6 months or less chemotherapy versus 9-18 months of chemotherapy for patients undergoing surgery. There were no significant differences between the two groups for clinical cure rates, bone graft fusion rates, change in erythrocyte sedimentation rate and C-reactive protein, kyphosis correction, and functional scores.

In a more recent randomized controlled trial[7] of 6 versus 12 months of treatment with isoniazid, rifampicin, ethambutol and pyrazinamide, no difference was identified in terms of clinical and radiological resolution of disease. Regardless of surgery, 6 months of treatment provides no worse outcomes at 24 months of follow-up. Patients in general had surgery for more severe pain and radiologic at-risk signs. It is important to note that more modern surgical approaches using instrumentation is adopted in this study.

One additional study[8] of 185 patients showed that with radical surgery and instrumentation, drug treatment can be at an average of 4.5 months with no difference in healing, alignment and functional outcomes up to 5 years follow-up. These patients utilized isoniazid, rifampicin and pyrazinamide of 2-month intensification phase followed by consolidation phase of 2-4 months. However, this study was observational without clear

understanding of why some patients had 2 months or 4 months of treatment. Furthermore, it was unclear when surgical intervention was required.

Conclusions:

Most data were from retrospective studies except for the trials run by the Medical Research Council (MRC) and 1 recent randomized controlled trial. The data suggests two main conclusions. Firstly, 6 months of chemotherapy is adequate regardless of surgical or non-surgical approaches to eradicate the disease, achieve bony fusion, regain function and avoid recurrence. Secondly, in certain severe cases such as pre-existing myelopathy and deformity, radical debridement and bone grafting may provide better outcomes. For this statement, the evidence is of lower quality and only pertains to a comparison between performing radical surgery or not for severe disease. It is not relevant to the duration of chemotherapy.

References:

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