Letters to the Editor

Clarifications to the Consensus Document on the Diagnosis, Treatment and Prevention of Tuberculosis

Aclaraciones al documento de consenso sobre diagnóstico, tratamiento y prevención de la tuberculosis

To the Editor:

“Consensus” means agreement among the members of one or more groups. It implies the abandonment of individual positions in order to arrive at a common ground, and therefore the result of the assent cannot be optimal. The excellent document on tuberculosis by the SEIMC and SEPAR reflects the strengths of this approach, although I will not discuss the details as they are evident. I will instead focus on the inherent weaknesses of this type of agreement, which lead to the inclusion in the text of assertions or omissions that may be surprising. The following are those that strike me the most:

1. Regarding the tuberculin skin test (PPD), it is stated that in patients with strong immunosuppression “any induration is considered positive”. This affirmation is based on two citations from SEPAR documents. This low cut-point for positive PPD does not have much support in the literature, nor is it accepted in southern Spain or outside our borders. In contrast, the final recommendations conclude that the minimal positive value for PPD in severely immunodepressed patients is also the widely-accepted value of ≥5 mm.

2. Continuing with latent TB infection (LTBI), the treatment section specifies that “If the clinical situation indicates taking cultures, it is necessary to wait for the results. This is an appropriate recommendation directed at avoiding unsuitable monotherapies that induce resistances. In my opinion, this prudent advice merits an addendum: initiating complete tuberculosis treatment while waiting for the culture differentiating between LTBI and active disease can be quite recommendable in some cases. This would have the added advantage that a 3-month regimen of R+H is a good option for LTBI treatment.

3. The authors opt for a duration of H of 6 months, in tune with British recommendations and those of the WHO. The recommendations in the US and Canada opt for 9 months. Six months may seem better from the perspective of public health-care programs that prioritize cost-effectiveness, but from the standpoint of patient benefit, which should be the priority of the physician, nine months is better. In any case, the possibility put forth by the authors of equaling 9 and 12 months in treatment duration has not had many supporters in recent years.

4. As for the number of drugs used to initiate TB treatment, the 4-drug regimen (RHEZ) is emphatically preferred. Treatment with 3 medications (RHZ) could only be used exceptionally in paucibacillary cases. It seems to be deduced that, for the authors, the deciding factor for the choice of drugs (3 vs. 4) resides in the amount of the bacillary load. This opinion also does not represent a majority. The addition of ethambutol to the triple-drug regimen does not increase either the bactericidal or sterilizing capacity, and is only indicated in situations of suspected resistance to one of the other medications or when the primary resistance rate to H is greater than 4%.

Then, the deciding element for choosing either 3 or 4 preparations is resistance and not bacillary load. This second variable does influence, however, the duration of the treatment. Substitutive markers used for high bacillary loads are the presence of cavitations plus positive culture after 2 months. Under these circumstances, the recommended duration is 9 months in total.

As primary resistance rates to H vary from one place to another and even between different population groups (natives vs. immigrants, etc.) of a same city, it is logical for treatment recommendation to vary from area to area. Therefore, the recommendation for initiating 4-drug treatment in all new TB cases (which seems wise to this writer) would be more solidly justified if the authors provided detailed current studies that showed primary resistance rates to H > 4%. Moreover, this would also avoid headaches for our southern colleagues who are now going to have to decide between conflicting recommendations.

5. In treating patients with HIV infection, no mention is made that the duration of anti-tuberculosis therapy could or should be different. The key for accepting a new guideline for a certain population group lies in a demonstrated lower recurrence rate. Observational studies show that the recurrence rate of tuberculosis in patients infected with HIV is greater in patients that received 6 months of treatment than those who received 9 months, which leaves this point open until results of comparative clinical essays are made available.

6. In finishing, I would like to say that it caught my attention that so much emphasis is made in not exceeding the maximum daily dosage of R (600 mg), H (300 mg) etc., meanwhile offering as an option three dosages of combination preparations that exceed the limits of R and H in up to 25%. I do not wish to be misinterpreted: this is not a criticism of the concept of this type of preparations, as we all agree that they are fundamental in the treatment of tuberculosis.

References

Lung neoplasia can debut as paraneoplastic neurological syndromes, among these being Eaton-Lambert syndrome, encephalomyelopathy, cerebellar degeneration, subacute sensory neuropathy and autonomic neuropathy but rarely has Guillain Barré syndrome been described. It is an autoimmune demyelinating polyneuropathy that affects the peripheral nervous system and frequently presents as ascending paralysis together with complete loss of deep tendon reflexes. Guillain Barré syndrome as an initial manifestation of lung neoplasia is quite exceptional.

Our patient was a 45-year-old male who smoked 65 packs/year and was diagnosed with schizophrenia. He was admitted for anorexia, asthenia, low-grade fever and weight loss over the previous three months, in addition to dyspnea upon mild effort. Two months before, he had begun with symptoms of ascending progressive muscular weakness, and was incapable of walking during the prior week. Physical examination discovered abolition of the vesicular murmur in the upper 2/3 of the right hemithorax, intense tetrparesis (proximal 1/5 and distal 2/5) with areflexia and generalized amyotrophy with maintained sensitivity. Posteroanterior and lateral chest radiograph (fig. 1A) showed a well-defined mass occupying the right upper lobe (RUL). Thoracic computed axial tomography was ordered (fig. 1B), which confirmed the presence of a lung mass of 15 × 11 cm in the RUL, with infiltration of the right pulmonary artery, tracheal compression and pathological adenopathies in the mediastinum. Bronchoscopy revealed an obstruction of the RUL bronchus with tumor infiltration. Bronchoaspiration, brushing and bronchial biopsy were compatible with small-cell carcinoma. Electromyogram showed neurographic findings compatible with Guillain Barré syndrome while the anti Hu, anti Yo, anti Ri, and anti calcium channel antibodies were negative. Treatment was initiated with chemotherapy and intravenous immunoglobulin and the neurological symptoms progressively improved for 15 days. The patient died three months later due to tumor progression.

Patients with cancer can develop signs and symptoms of peripheral nervous dysfunction, although more frequently related to chemotherapy; in some cases, neuron antigens expressed by the tumor stimulate an immune response characterized by T-cells, antibodies or both, that attack not only the tumor but also the nervous tissue. The Guillain Barré syndrome is a very infrequent initial manifestation and is rarely associated with lung carcinoma. To our knowledge, just one case has been published in Spain associating squamous carcinoma, and in the literature 3 sporadic cases of small-cell carcinoma are described. Although infrequent, the syndrome is estimated to appear in 1% of cancer patients. Non-Hodgkin lymphoma is the cancer that is most frequently associated, but the relationship with other malignant diseases is less clear. In a series of 435 patients with Guillain Barré syndrome, 9 developed neoplasia in the following 6 months, 3 of which were non-small cell lung cancer while the others were chronic lymphocytic leukemia, non-Hodgkin lymphoma, kidney cancer, esophageal cancer, cancer of the vocal chords and metastatic disease of unknown etiology. The prognosis of patients with neoplasia and Guillain Barré was poorer, with higher mortality than those with Guillain Barré syndrome alone.

We conclude that, given a patient with Guillain Barré syndrome, lung cancer should be included in the etiological study.

References