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Clinical Response to Treatment of Infectious Rachiditis

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Abstract: ***Introduction: Spondylodiscites treatment is one of the most difficult aspect of Infectious Rachiditis (IR) management. The aim of the study is to recognize the efficacy of drug therapy and associated side effects of the treatment of IR. Material and methods: The study included 103 patients who presented to Service of Infectious Diseases, at University Hospital Centre in Tirana, Albania over the period January 2006 – December 2015. The diagnosis of infectious rachiditis was made according to clinical, radiological and microbiological criteria. Results: The mean age of patients was 58.1(±10.4) years with a range 16-75 years. 62% were males and 38% females. Male to female ratio is 1.6:1. The clinical neurological signs of patients are presented in table 1. Spondilodiscitis and discitis were most frequent signs in 37.9% and 16.5% patients respectively (p<0.01). Side effects were manifested in 56 (54.4%) of patients. Most frequent ones were gastrointestinal disturbances (17.5%), dermatoses (9.7%), hepatopathy (7.8%), glossitis (4.9%). Two cases (1.9%) had a fatal outcome, one of them had a periaortal abscess complicated to septic shock, while the other case suffered also from acquired immunodeficiency syndrome. Sequelae manifested 4 (3.9%) of the total patients. One case developed tetraplegia, two cases (1.9%) developed inferior unilateral paraplegia, one case (1%) had neurogenic bladder. Two (1.9%) cases manifested relapse of the disease. Conclusion: These findings are similar to those presented in different studies sugesting that IR treatment is a complex and a significant issue in many countries.***

Keywords: infectious rachiditis, spondylodiscites, treatment

1. Introduction

Spondylodiscites treatment is one of the most difficult aspect of Infectious Rachiditis (IR)management (1).The difficulty is related to the choice of antibiotics for the etiologic treatment especially if the agent is identified along with the pathogenetic and symptomatic therapy, as well as defining the duration of their administration, real-time surgical intervention, neurosurgical and orthopedic treatment, taking into account patient tolerance and cost of the overall treatment (2). The problem is more difficult in individuals with compromizedimmune system and hepatic, renal, hematological and other pathologies that may be aggravated by the side effects of the above preparations, which are due to be given for a very long time (3).The aim of the study is to recognize the efficacy of drug therapy and associated side effects of the treatment of IR.

2. Matherial and Methods

The study included 103 patients who presented to Service of Infectious Diseases, at University Hospital Centre in Tirana, Albania over the period January 2006 – December 2015. The diagnosis of infectious rachiditis was made according to clinical, radiological and microbiological criteria (3).

The etiologic treatment comprised a number of antibiotics, administered empirically., various antipyretics, analgesis and anti-inflammatory drugs have been used for the treatment relieve of fever and pain. Their daily doses were defined according to current literature (). Also, supportive therapy has been applied as appropriate. Patients were followed for 12 to 18 months after the hospital discharge, depending on their condition, the progression of the disease and personal compliance. Evaluation of therapeutic efficacy was based on the dynamic follow-up of clinical indicators:daily measurement of temperature and evaluation of mobility andspontaneous pain; biological indicators, every 1 to 2 weeks (leukocytes, VES, PCR, fibrinogen); microbiological (hemocultures, after 7 to 15 days, serological tests after 1.5 to 3 months); imaging images (CT, MR, Ro graph at different intervals, according to progression. Each patient repeated the above examination at least tree times.Side effects according to treatment schemes were evaluated. Regarding the etiology the majority of patients had a known cause but for some patients the cause of the disease remained unknown. The course of disease and various clinical features has been followed to evaluate therapeutic failure and relapse (2).

SPSS 20.0 software was used for the statistikal analysis of data. Chi square test was used to test the differencies in ptoportions. A p-value ≤0.05 was considered statistically significant.

3. Results

The mean age of patients was 58.1(±10.4) years with a range 16-75 years. 62% were males and 38% females. Male to female ratio is 1.6:1. The clinical neurological signs of patients are presented in table 1. Spondilodiscitis and discitis were most frequent signs in 37.9% and 16.5% patients respectively (p<0.01).

Table 1: Frequency of clinical signs

Clinical signs	*N*	*%*
Spondilodiscitis	39	37.9
Discitis	17	16.5
Disitis + paravertebral abscess	13	12.6
Disitis + paravertebral echinococcal	12	11.7
Spondylitis	8	7.8
Epiduritis	4	3.9
Disitis + perivertebral edema	2	1.9
Disitis + transvers mielitis	2	1.9
Disitis + epidural empiemae	2	1.9
Disitis + perivertebral myositis	2	1.9
Disitis + psoas abscces	2	1.9
Total	10	100.0

Hemocultures, bronchoalveolar lavagea and agopunction of rachides were used to establish the etiology of the infection. The most frequent agent was *Brucella* in 36 (35%) of

patients, followed by *Staphylococcus aureus* in 17 (16.5%) of patients, and *Mycobacterium tuberculosis* in 10 (9.7%) ($p<0.01$). For 23 (22.3%) of patients the cause of infection was unknown (table 2).

Table 2: Frequency of etiological agents

Etiologic agent	*N*	*%*
Brucella	36	35.0
Staphylococcus aureus	17	16.5
Mycobacterium tuberculosis	10	9.7
Escherichia coli	4	3.9
Streptococcus spp.	3	2.9
Echinococcus	2	1.9
Salmonella typhi	1	1.0
Pseudomonas aeruginosa	2	1.9
Roseomonas gilardii	1	1.0
Eikenellacorrodens	1	1.0
Sphiingomonas spp	1	1.0
Enteroccocus spp.	1	1.0
Aspergillus flavus	1	1.0
Unknown	23	22.3
Total	103	100.0

Forteen antibiotics were used in combination as a first or second line after anticrobial ssusceptibility test for known agents and empirically for the unknown cause: (*Rifadin; Doxycycline; Gentamicin; Bactrim; Ciprofloxacin; Ceftriaxone; Cefazolin;Metronidazole; Levofloxacin; Vancomycin; Meropenem; Imipenem; Ampicilin; Cefotaxime*). Three different schemes were used for the empiric treatment if the first scheme failed to yield results.

Regarding the efficacy of treatment, fever decreased and was normalized with a range from three to twenty three days. The pain persisted less than six month in 7 (6.8%) of patients, until one year in 92 (89%) and over one year in 4 (3.9%) patients, ($p<0.01$).

Indicators of inflammation: leucocytes, fibrinogen, PCR and VES were normalized over a period from one to two week after treatment.

Serological tests Wright and ELISA were repeated after 4 to 16 weeks for patients with *brucellosis*etiology.

Side effects were manifested in 56 (54.4%) of patients. Most frequent ones were gastrointestinal disturbances (17.5%), dermatoses (9.7%), hepatopathy (7.8%), glossitis (4.9%) (table 3).

Table 3: Frequency of side effects

Side effects	*N*	*%*
Gastrointestinal disturbances	18	17.5
Dermatoses	10	9.7
Hepatopathy	8	7.8
Glossitis	5	4.9
Hyperbilirubinemia	3	2.9
Candidalvulvovaginsitis	3	2.9
Renal dysfunction	2	1.9
Photodermatitis	2	1.9
Pruritus	2	1.9
Hyperazotemia	1	1.0
Vestibular neruritis	1	1.0
Gutta	1	1.0
Total	56	54.4

In 14 (25%) out of 56 cases, imagery guided punction was done to empty the purulent perivertebral abscesses and 3 (5.4%) cases underwent surgical intervention of whom two cases with echinococal and one case with aspergillus etiology.

Two cases (1.9%) had a fatal outcome; one of them had a periaortal abscess complicated to septic shock, while the other case suffered also from acquired immunodeficiency syndrome.

Sequelae manifested 4 (3.9%) of the total patients.One case developed tetraplegia, two cases (1.9%) developed inferior unilateral paraplegia, one case (1%) had neurogenic bladder.

Two (1.9%) cases manifested relapse of the disease.

4. Discussion

We obtained various results in our study. In the case of brucellosis rachiditis it is noted that clinical and biological manifestations were normalized in all cases treated, as reported also by other researchers (2,3,4). We noted a variation in the percentage of efficacy of the various therapeutic treatment schemes used. The first line combination *Rifadin/ Doxycycline/ Gentamicin* was efficient in 50% of cases, while the combination of the second line *Rifadin/Doxycycline/ Ciprofloxacin* reached a 75% efficacy and *Doxycycline/Bactrim/Ciprofloxacin*combination in 66.6%. The second line of medication in question resulted quite efficiently.

So with the combination *Rifadin/ Doxycycline/ Ciprofloxacin/Gentamicin*and*Cefazolin/Ciprofloxacin/Doxycycline/Gentamicin* we managed to cure all of our cases.

This is a very useful finding that needs to be taken into account in practice when dealing with brucellosis-related infectious rachiditis.Literature data in this regard, despite being scarce, support our results regardin the efficacy of anti brucellosis treatment (2,3,20). Our data suggest that we should start the treatment with the second line antimicrobials to ensure the result in the treatment of brucellosis indued infectios rachiditis.Also, very interesting are the findings related to the treatment of staphylococcal rachiditis. Numerous studies are reported in literature for staphylococcal infections (6,11-14).

Clear distinctions of the effectiveness of various therapeutic preparations / schemes were noted among these patients. Thus, the combinations of the first antistaphylococcal line line were effective in 20% of the cases; *Ceftriaxone /Ciprofloxacin /Metronidazole* in 42.8%; *Ceftriaxone/ Ciprofloxacin* 50%; Cf */Ciprofloxacin/Gentamicin*in 100% and *Cefazolin / Levofloxacin*in 100% of cases treated. The antimicrobials of the second line as also were effective in 100% of the cases used. In the case of staphylococcal rachiditis, in contrast to the brucellosis ones, we found a highe efficacy even with two antibacterial combinations of the first line. These data suggest that staphylococcal rachiditis should be initially treated either with one of the four combinations of the second line or with the last two combinations of the first line. However, in the case of

staphylococcal rachiditis, clinicians should insist on the isolation and antimicrobial susceptibility of the isolated strain due to the known multidrug resistance of of staphylococci not only in hospital setings but also in community (8, 9-12).

Different antimicrobial efficacy was observed in streptococcal IR cases: both schemes used by us were effective. This is related to the fact that streptococci are still susceptible to certain antibiotics routinely used in daily practice (11,12).

Our experience with tuberculosis related rachiditis therapy was more specific. Its efficacy was soon apparent in the treatment of four febrile cases, when the fever delined after 19 to 21 days, while in six cases without fever, the improvement was obvious later because pain is a long-lasting symptom. However, in our ten cases, long-lasting medication proved to be very useful, as reporded by various researchers too (1,15,16).

The therapy against IR form agents other than tuberculosis and brucellosis, namely from*Roseomonas gilardii, Eikenellacorrodens, Sphiingomonas spp.*and*Aspergillus flavus* proved to be efficacious. This is also due to susceptibility of these agents towatds to ciprofloxacin, cefotaxime, levofloxacin and vankomycin that are often administered in the empirical therapy of IR. (17,18). Our results show that the first clinical sign that is affected by therapy is temperature. It subsidized and was normalized at different intervals from the onset of treatment: respectively it declined from day 3 to 19 and after 5 to 25 days returned to normal. This was due to different factor are related to the cause, the affected components of the rachid, the immune status of the subject as well as the antimicrobial used. We think that these data are valuable to prevent us from rapidly changing etiologic treatment: the decline of fever in IR requires a prolonged time.As far as inflammatory syndrome is concerned, it also responded to etiologic treatment.Leukocytosis presented an downward trend, usually after 1to 2 weeksand was normalized in most cases within 4 to 5 weeks.Fibrinogen started to decline in week 1-4 and normalized on week 3 to 6. PCR began to decrease in week 1 to 3 and normalized on week 2 to 9; VES began to decrease in week 2 to 4 and normalized on week 4 to 25. These data are important because theliterature lacks the data regarding the efficacy of the therapy over inflammation indicators.

Also, interesting are findings on the influence of antimicrobial therapy on the microbiological aspects of IR. In all our cases with positive hemoculture, it returned negative in the second week after the start of the treatment. Serological tests of Wrighs and ELISA had a low sensitivity. Even these data are very important, as in the literature there are no studies of this topic for the treatment of infectious rakiditis.

This study indicates that 54.4% of cases manifestetd undesirable effectsby etiologic treatment. It is considered that the treatment of IR is extremely prolonged and of course, that such phenomena are expected. We noted side effects from 21 different preparations, of which 7 anti-inflammatory / antipyretic / analgesic and 14 antibacterial.

5. Conclusions

Jatrogenic manifestations were associated with the involvement of the the digestive tract in 41.8% of them. In 16.5% of the patients the treatment had to be discontinued and replaced by other preparations. In 10.67% of them had medically needed surgery. Sequelae manifested 4 (3.9%) of the total cases. Recurrence was found to be 1.9%. Lethality resulted 1.9%. These findings are similar to those presented in different studies (1,2,3,5,7), sugesting that IR treatment is a complex and a significant issue in many countries.

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