Bacterial meningitis in the elderly patient Review of cases of the Department of Infectious Diseases of the Hospital de Santa Maria, from 1988 to 1993

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Abstract

In view of the usual severity of bacterial meningitis in the elderly, the authors carried this study to compare the current results with those of another work on the same theme, carried out even years ago by one of the authors. The new study confirmed the undisputed severity of this disease, as demonstrated by the mortality rate of 30.3% found in this study, compared with 45% in the previous one. One of the reasons given by the authors for this improvement is more accurate and earlier diagnosis, the use of a monoantibiotic drug regimen, mainly with betalactamic drugs, and a series of therapeutic measures to prevent and correct metabolic and hydro-electrolytic imbalances. The authors also point out that Streptococcus pneumoniae was the most commonly isolated etiological agent, as is also reported in the literature. They also call attention to the low percentage of positive results, whether in the cerebrospinal fluid or in the blood cultures.

Key words: bacterial meningitis, elderly, betalactamic antibiotics, Streptococcus pneumoniae.

Introduction

Over the years, bacterial meningitis (BM) has been one of the most severe and feared infectious diseases, due to its high morbidity and mortality rates, regardless of the age group of the individuals affected.[1,2,3] This situation, however, assumes even more worrying proportions in patients at either end of the age spectrum, due to the biological, anatomic and immunological characteristics of these patients.[4,5,6,7,8,9]As regards the elderly population, it is added that due to the indisputable medical progress seen in recent years, the number of elderly individuals has increased continually so that today, of the 4.5 billion people currently living on the planet, 8.5% are over 60 years of age, and that this number is expected to increase 57% by the end of this century.[10]

Prompted by these statistics, one of the authors carried out a retrospective study on this pathology several years ago, together with other colleagues, which we believe was the first study of its kind to be carried out in Portugal.[11] Today, seven years after the publication of that study, and convinced of the interest in revaluating the problem, particularly with regard to some of the surprising results obtained, such as the predominance of Neisseria meningitidis as an etiologic agent of meningitis among the elderly, the authors present this new study on this extremely important disease.

Material and methods

The organizers considered all the processes of patients aged 65 years or over, admitted to the Department of Infectious Diseases of the Hospital de Santa Maria (HSM) between the 1st January 1988 and the 31st December 1993, totaling 33 patients, with a diagnosis on discharge of Bacterial Meningitis (MB), based on suggestive clinical symptoms and complementary diagnostic exams, particularly lumbar puncture (LP) and/or serial blood cultures, and in some cases, post-mortem examination.

Patients with completely normalized clinical alterations on discharge from hospital, and in the complementary diagnostic exams, were considered cured.

Situations in which any psychic or permanent neurological alteration was verified, either through

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clinical observation and/or the complementary diagnostic exams, were considered sequelae, even through the infectious problem had been resolved. The results were studied statistically.

Results

In the six-year period of this study, 33 patients aged 65 years or over with a final diagnosis of BM were hospitalized. Of these, 15 were male and 18 female. All the patients were White. As regards ages, the total mean age was 73.9 years, with 72.1 years for the female patients and 75.1 for the male patients. The oldest patient was 87 years of age.

In relation to the patients' occupations, it was not possible to determine any findings of clinical or epidemiological interest.

The distribution of cases of meningitis occurring over the six years of the study, and for the different months of each year, was very uniform, and it was not possible to draw any statistically valid conclusion.

In terms of the clinical manifestations that preceded hospitalization *(Table I)*, the most common symptoms were fever, in 93.9% of the cases, alterations in consciousness, in 81.8%, headaches, in 78.8% and vomiting in 36.4%. In addition to these, which are widely acknowledged to be the classic signs and symptoms of leptomeninges infections, symptoms of the respiratory system also occurred in 15.2% of the patients. In mean terms, all these manifestations emerged about three days before hospital admission, with the exception of respiratory complaints, which emerged, on average, seven days prior to admission.

Antibiotic therapy prior to hospitalization is a conditioning factor of the evolution and possibilities of etiological diagnosis of infectious diseases, and when introduced at the wrong time, can be a highly negative factor in these aspects. In our study, eleven patients (33.3%) had been medicated with antibiotics before hospitalization. It was not possible to establish any correlation between this practice and the isolation of the etiologic agent and/or clinical evolution of the disease,[7] particularly in relation to sequelae and deaths.

The objective examination of the patients upon admission (*Table II*) showed that 100% of these patients had positive meningeal signs. 90.9% were febrile, 81.8% presented alterations in consciousness, with the patients in various states of coma, and 9 of the 33 patients included in the study (27.3%) presented focal signs in the neurological examination.

In view of this data, it is not surprising that the provisional diagnosis on admission was BM in all the patients.

In terms of the laboratory data obtained on admission or during the first few days of hospitalization (*Table III*), it was verified that the white blood cell count was above 10,000 for leukocytes in 81.8% of

TABLE I

Clinical manifestations prior to admission

Pathology	No. patients	%
Fever	31	93.9
Alterations in consciousness	27	81.8
Headaches	26	78.8
Vomiting	12	36.4
Respiratory symptoms	5	15.2
Focal alterations of the CNS	2	6.0
Others	14	42.4

TABLE II

Clinical state on admission

Pathology	No. patients	%
Alterations in consciousness	27	81.8
Meningeal signs	33	100
Fever	30	90.9
Focal alterations of the CNS	9	27.3
Exanthem	3	9.1
Convulsions	3	9.1
Others	14	42.4

TABLE II

Laboratory alterations at the start of hospitalization

Laboratory alterations	no. patients	%
Leucocytosis w/neutrophilia (L>10,000 and N>70%)	25	75.6
ESR	18	54.5
CRP	20	60.6
Hyperglycemia	27	81.8

the patients, with neutrophils above 70% in 75.6% of the patients. The erythrocyte sedimentation rate (ESR) was also 54.6% higher (values above 20mm in the first hour). This value was not determined for eleven patients. C-reactive protein (CRP) was positive in 60.6% (this was not determined in eleven patients), and these values were very high values in 81.8% of the patients, but urea at 51.5%, and the creatinine and serum ionogram, were within the normal values in the majority of the patients.

LP was determined for all the patients, and it was verified that all had cytobiochemical alterations compatible with a clinical diagnosis of BM. In 87.9% there was pleocytosis with predominance of polymorphonuclear neutrophils (PMN). In all but one patient, Pandy's reaction was positive, and protein levels were high in 21 patients. Glycorrhachia, performed on 27 of the 33 patients of the study group, showed below-normal values in 23 patients.

Through the cerebrospinal fluid (CSF) it was possible to obtain the etiologic agent of the meningeal infectious process in 9 patients (27.3%), with streptococcus pneumoniae, isolated six times, being the most frequent causal agent of these meningitis. Neisseria meningitides was isolated twice and group B Streptococcus once (*Table IV*).

The serial blood cultures taken from all the patients, led to the detection of the etiologic agents in 10 cases, where Streptococcus pneumoniae, isolated in 3 patients, was also the most frequent.

Among the complementary diagnostic exams, electroencephalogram (EEG) was performed on 16 patients, showing alterations of various types in 11 of them: diffuse retardation of cerebral electrogenesis in all of these, and predominantly bifrontal paroxystic activity in 3 cases. Cranioencephalic computed axial tomography (CAT scan) was performed on 29 patients, with 16 showing various alterations, such as cerebral edema, hydrocephalia, ischemic lesions, either encephalic or of the cerebral trunk, cerebral atrophy and maxillary, ethmoidal and sphenoidal sinusopathy. In one clinical case there was mastoiditis and in another, cerebral abscess.

The clinical and epidemiological precedents were also investigated, as these are recognized as very important factors in the occurrence and development of BM.

We verified that 51.5% of the patients suffered from arterial hypertension (AHT), 24.2% were diabetic, 18.2% had cerebrovascular pathology, 12.1% presented problems of the ENT, and only one case of respiratory pathology (3.0%). Two patients (6.0%) had a history of previous meningitis (*Table V*).

TABLE IV

Etiologic agents isolated in the CSF

Agent	No. patients	%
Pneumococcus	6	66.7
Meningococcus	2	22.2
Streptococcus haemolyticus	1	11.1

TABLE V

Precedents (associated and/or conditioning pathology)

Pathology	No. patients	%
AHT	17	51.52
Cardiac path.	9	27.27
Diabetes	8	24.2
Cerebrovascular path.	6	18.2
ENT	4	12.1
Previous meningitis	2	6.0
Respiratory pathology	1	3.0
Others	8	24.2

As regards treatment, it was verified that all except for three of the patients had undergone antibiotic therapy, although it was not possible to determine the reason why three did not. The antibiotic therapy approaches were varied, but monotherapy and the use of betalactamic antibiotics (penicillin, ampicillin, third-generation cephalosporins) was prevalent, corresponding to 84.8% of all the antibiotics prescribed. The physicians prescribed an association of antibiotics in only a few cases, with ampicillin + gentamicin being most frequent.

In addition to antibiotics, 9 patients (27.0%) took mannitol and 7 (21.2%) potent diuretics. Hydroelectrolytic correction was performed on 23 patients (63.6%), and corticoids were prescribed in only 9 (27.3%). 6 patients (18.2%) required assisted ventilation.

The overall final results of our study, measured through the quantifiable clinical and laboratory parameters, showed that 16 patients (72.7% - 9 female and 7 male) were completely cured on discharge.

TABLE VI

Alterations in the parameters of the last LP performed

Parameters	No. patients	%
Cytology	2 2	66.7
Pandy	19	57.6
Glycorrachia	14	42.4
Proteins	17	51.5

Six patients, three female and three male, were discharged with different types of neurological sequelae, as shown in the table below.

Ten patients (30.3% - 6 female and 4 male) died. One patient was transferred to the ENT department for surgery for cholesteatoma. The final evolution is not known.

The mean time to apyrexia was 15.5 days, with a maximum of 48 days in one case and minimum of 3 days in another. Eight patients were continually febrile, while three had no fever at all.

The mean hospitalization time was 24.2 days, with a maximum of 60 days and a minimum of 2.

In the different laboratory tests of the patients who were discharged, a clear improvement was seen among almost all them, compared with the admission values. Only the results of the cytology, Pandy's reaction, glycorrachia and proteins, in the last LPs performed also exhibited some alterations in a significant number of cases, as shown in *Table VI*.

Seeking to find factors that favor or determine the deaths recorded, we investigated age, sex, previous antibiotic therapy, initial state of consciousness and associated pathology in the deceased population. We verified that the distribution of deaths by sex does not have any significant difference, especially if we bear in mind the existence of a larger elderly female population in our country, as evidenced by the various population censuses, and also in this study, which had 15 men and 18 women.

In relation to the antibiotic therapeutic approach prior to hospitalization, only 3 patients had taken antibiotics, which is without statistical significance. Regarding the state of consciousness upon admission, 8 of the 10 deceased patients presented severe alterations in consciousness (different degrees of coma). All the deceased patients were febrile at all times and the average stay in the department was statistically significant, with only 5.0 days versus 35.0 days for the rest of the surviving population. Of the deceased patients, 4 were hospitalized for less than 24 hours, and the maximum hospital stay was 17 days, in one case.

Among the various types of associated pathology we emphasize that all the patients had concomitant diseases that favored and/or determined the appearance of symptoms and the poor evolution of BM. These included 5 cases of AHT, 3 cases of diabetes, 3 cases of heart disease, 1 case of chronic liver disease, 1 case of rheumatoid arthritis and 1 case of Hodgkin's lymphoma. Curiously, there were no cases of alcoholism and only in one patient was reference made to heavy smoking habits, situations that are traditionally correlated with a poor or worse prognosis.[1,2,3,4,5,6,7,8,9,11,13,14]

Final commentary and conclusions

Although this study is a retrospective review of clinical processes, with a relatively small number of researchers, in our opinion it presents aspects of undeniable interest and enables us to draw some conclusions that we consider important in the approach to these patients.

Accordingly, we have proven once again, as in our previous study and in accordance with the literature[4,11], that bacterial meningitis in the elderly still constitutes a disease of considerable severity, as shown by the high morbidity and mortality rates, and despite all the advances in the areas of diagnosis and treatment, it continues to show results that are clearly worse than most bacterial meningitis in other age groups. The biological and immunological alterations in elderly individuals, which are very difficult or impossible to overcome, and which make these patients particularly susceptible to bacterial infections, certainly contribute to this fact[4,9,11]. However, without seeking to emphasize this aspect, an improvement was seen from the mortality rate of the first study (1968-1987), of 45% [11], to 30.3% in the second study (1988-1993), although these figures are not statistically significant.

Though we cannot state categorically, we believe this "improvement" to be the result of a series of factors, including increased awareness and better information among physicians in general, in relation to the clinical characteristics, particularly the form of presentation of bacterial meningitis in the elderly,

which is often oligosymptomatic[4,9,11]. Supporting this belief, to some extent, is the fact that in this study, the provisional diagnosis of BM upon admission was correct for all the patients. But in addition to a correct initial diagnosis, it is also important to state that in a significant percentage of cases (72%, 24/33), the potential severity of the clinical situation was admitted *ab initio,* leading to admission of the patients to the Intensive Care Unit for Infectious Diseases (ICU-ID). We also admit that the relatively small percentage of cases of "untimely" antibiotic therapy prior to hospital admission played an important role. As is well known, this is an aspect that often has negative consequences in the clinical and etiologic characterization and evolution of the symptoms of meningeal infection.

Alongside the aforementioned reasons, we also believe that the therapeutic attitudes taken by the hospital, not only in terms of antibiotic therapy, were determining factors in the final outcome.[11,12,13,14,15] Accordingly, we believe it is necessary to emphasize some aspects that we consider highly positive, which are: predominance of antibiotic monotherapy; use of antibiotics of the betalactamic group in 84.8% of cases; frequent use of mannitol and potent diuretics as a means of combating cerebral edema and the subsequent intracranial hypertension; frequent hydroelectrolytic correction, particularly of hyponatraemia, an equally important attitude in the prevention and correction of cerebral edema; and regular correction of metabolic imbalances.

As stated in the introduction, one of the reasons that led us to conduct this study was the verification of the most frequent etiological agent in these meningitides, since in the previous study, we had evidenced a surprising and inexplicable predominance of Neisseria meningitides[11]. Indeed, in all the series published on this topic, that we are aware of and used as reference material, Streptococcus pneumoniae is always the main etiologic agent.[1,9] In our series, as shown above in the chapter on results, this rule is now been confirmed, with Streptococcus pneumoniae being the most frequently isolated agent. What is surprising in our present results is the low rate of microbiological isolation, whether in the CSF or in the serial blood cultures. We were unable to find an acceptable explanation for this fact.

In relation to the other complementary diagnostic exams, we suggest that these were, as is common in acute bacterial processes: leucocytosis with neutrophilia, very high erythrocyte sedimentation rate and high CRP values. In the CSF, Cytochemical alterations inherent to bacterial infections of the leptomeninges, that is, PMN pleocytosis, hyperproteinorrachia and positive Pandy's reaction, were predominant. Glycorrachia was also below normal values in the majority of cases. We consider it equally important to mention that as in the first study, where 63% of the patients presented high values, glycaemia levels were also higher than normal in 81.8% of the patients in the present study. Hence we believe it is possible to conclude that these metabolic alterations might somehow contribute to the appearance of the disease and/or that over the course of the meningeal infection, there are frequent alterations in glucidic metabolism.

The fact that the clinical and epidemiological precedents of our patients showed 26.7% and 24.2% of diabetics in the first and second studies, respectively, is in accordance with these data as well. In relation to the same clinical and epidemiological precedents, we believe it is interesting that in this study, we found that only 51.5% of the patients suffered from AHT, and that contrary to what normally happens; only 1 patient (3%) had precedents of lower respiratory tract pathology, while in our previous series, 25% of patients had this disorder.[11]

Considering the overall final results obtained, we reaffirm that despite the improved mortality rate in this study compared to the previous study, 30.3% of deaths is nevertheless still very high value in the context of mortality from acute bacterial meningitis as a whole, although it is equivalent to the values reported in the majority of foreign series published on BM in the elderly individual.[1,11,16,17,18,19,20,21,22,23] We also emphasize that underlying these poor results is a whole range of "limitations" and/or insufficiencies of a biological, immunological and even anatomic nature[4,9]. Given the fact that these limitations are difficult to resolve, it is the task of the general practitioner to overcome them, going the extra mile, i.e. keeping in mind and being totally proficient in all the clinical and epidemiological particularities of BM in the elderly, in order to make the correct diagnosis as soon as possible, enabling the subsequent establishment of the therapeutic approach that is best suited to each case. To this effect, and in relation to our own results, we draw attention to some of the aspects that are commonly linked to a worse prognosis. One of the aspects of a less favorable clinical evolution is

the persistence of fever, regardless of the therapeutic measures taken. In our study, we were able to confirm this fact, as all the deceased patients were constantly febrile. Likewise, the first days of disease, the suddenness of the onset of the meningeal infection process, the concomitance of another type of pathology that may be present, and the more marked alteration of the state of consciousness on admission to hospital, are all unfavorable aspects in this prognosis. In our patients, we verified that death occurred in all the cases but one during the first week of hospitalization, and that they all simultaneously presented other severe pathologies that facilitated or determined the poor evolution of meningitis. Lastly, and in accordance with literature,[1,9] we were able to confirm that the patients' state of consciousness upon hospitalization is an important prognostic factor of CNS infections. Therefore, of the ten deceased patients, eight presented very severe alterations of consciousness upon admission, and the four that were in a profound coma upon admission all died, which is of real statistical significance.

Finally, as in the previous study, we state that if death is an inexorable fact, everybody should fight within their specific field of activity to prolong and improve the conditions and the quality of life of citizens and particularly, in this case, elderly individuals. ■

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