Case Report

Biclonal Gammapathies

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Biclonal Gammapathies

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Abstract: Bi-clonal gammopathy is distinguished by the presence of two different or distinct monoclonal proteins, due to a proliferation of two distinct monoclonal plasma cell clones. A single monoclonal clone can give rise to two different monoclonal proteins. In this report, we present three cases of biclonal multiple myeloma and one case of Waldenstrom's disease that exhibits two biclonal peaks. Serum protein electrophoresis showed two M bands on serum protein electrophoresis.

Keywords: biclonal gammapathy; serum protein electrophoresis; multiple myeloma; Waldenström disease

Introduction

Biclonal gammopathy (BG) is a rare condition with an incidence ranging from 1 to 5% of the patients presenting clonal plasma-cell proliferations [1]. The biclonal gammopathy may occur with two separate distinct bands on the serum protein electrophoresis or a single band that resolves into two distinct bands on the serum immunofixation. (BG) is a pathology characterized by the proliferation of one or two clones of lymphocyte resulting in the appearance of 2 abnormal immunoglobulins in excess in the serum called paraproteins or "M" proteins[2]. In this study we report the epidemiological, biological and etiological aspect of the biclonal gammopathies diagnosed in 4 cases at the HUHC of Casablanca in Morocco during the period from 01.01.2018 to 01.01.2019.

Material and methods

This is a retrospective study including 4 case of biclonal gammopathies diagnosed in HUHC biochemistry laboratory between January 2018 and January 2019 by the presence of two monoclonal bands on serum immunofixation. The technique of capillary electrophoresis (Capillarys® (Sébia)) is based on the principle in free solution offering rapid separation or even complete automation of the analysis. The CAPILLARYS system contains 8 capillaries in parallel, which allows 8 simultaneous analyses. The injection into the capillaries of the sample is made at the anode by suction. On this system, the separation is carried out, while applying a potential difference of thousands of volts from each terminal of the capillary. Direct protein detection is performed from 200 nm to the cathode side. After washing the capillaries with a washing solution and with the buffer at basic pH, six protein fractions are obtained in this order: γ-globulins, β2 and β1-globulins, α2 and α1-globulins, and albumin. The qualitative reconstruction of the proteinogram is done by the software. Dosage of serum total protein sera collected was carried out by the biuret colorimetric test on the Architecte ci-8200 automaton. The monoclonal component was quantified.

We collected epidemiological data, such as as age and gender, and information about the underlying disease based on review of medical records. Finally we analysed the clinical evolution of patients.

Results

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Association of the serum protein profile of the bi-clonal peak with the biological parameters revealed by serum electrophoresis

Table 1. VALUES OF THE DIFFERENT SERUM PROTEIN FRACTIONS OF THE BI-CLONAL PEAK.

Types of protein profile	N	Albumin (g/l)	α1-globulins (g/l)	α2-globulins (g/l)	β1-globulins (g/l)	B2-globulins (g/l)	y-globulins (g/l)
Peak Biclonal	4	25,15±6,35	3,20±1,28	4,52±2,56	3,02±1,22	24,90±23,06	15,42±11,68

According to this table, hypoalbuminemia and a very significant increase in the fraction of beta-2 globulin and gammaglobulinemia are noted.

The biclonal peak was recorded in a woman and three men, aged 54.50±4.55 years old. With a gamma globulin level of 15.42±11.68 g/L, the beta-2 globulin level is 24.90±23.06 g/L, and the albumin level is 25,15±6.35g/L. This reflects hypergammaglobulinemia, hypoalbuminemia and an increase in beta-2 globulin due to the migration of monoclonal immunoglobulin to the beta-globulin zone. Serum protein electrophoresis revealed two distinct bands in the gamma globulin zone giving a qualitative aspect of the biclonal peak, in a 58-year-old woman. The gammaglobulin level is 33 g/L, the quantification of the first monoclonal peak is 10.8 g/L and the second peak is 8.5 g/L. The diagnosis revealed Waldenstrom's disease. The three patients are aged 56.25 ± 3.76 years old; present a serum protein electrophoresis with two peaks at the level of the gammaglobulin fraction. A final diagnosis of biclonal multiple myeloma was made for these three cases. Unfortunately, the patients could not be followed for their treatment and subsequent follow-up.

Discussion

The protein profile of the biclonal peak is often revealed in patients with Waldenström's macroglobulinemia due to the polymerization of this molecule. Also, the bi-clonal peak is frequently linked with immunoglobulin type M gammapathies [3] , this disease is a malignant lymphoplasmacytic medullary proliferation characterized by the secretion of type M immunoglobulin. Eventually two clones produce the IgM resulting in a bi-clonal gammopathy [4]. The protein profile of the biclonal peak is often revealed in patients with Waldenström's macroglobulinemia due to the polymerization of this molecule. The bi-clonal peak is frequently linked with type M immunoglobulin gammopathies [5]. Its clinical significance is not yet apparent given the lack of studies that address the protein profile of a bi-clonal spike. However, the bi-clonal gammopathy presents more evocative symptoms than the monoclonal gammopathy, but without having a significant difference concerning the clinical specificities. Indeed, the clinical signs of biclonal gammopathy are no different from those of monoclonal gammopathy [6].

Multiple myeloma is a neoplastic clonal disease characterised morphologically by plasma cell infiltration of the medullary space and involvement of extra osseous tissues in a multi-focal fashion [7]. Monoclonal gammopathy is a B cell disorder that is known to produce a specific and unique M component. So, biclonal gammopathies are defined by the simultaneous appearance of different M components, two distinct or different monoclonal proteins[8]. However, bi-clonal multiple myeloma represents only 1 to 5% of all myelomas [9]. A study by Banerjee et al. described a bi-clonal spike in a 64-year-old woman with multiple myeloma [10]. Again study of Pallavi and al. described an atypical case of IgA-kappa multiple myeloma, two M-bands (one in the globulin region and one in

the beta globulin region) were found by serum electrophoresis. This showed a picture of biclonal gammopathy [11]. Our study presented three cases of bi-clonal multiple myeloma, against a single case of bi-clonal peak related to Waldenstrom's disease. The study by Nafia Al-Riyami and al. described biclonal gammopathy in a 66-year-old man with chronic lymphocytic leukemia (CLL) [12]. In addition, a study by Trey et al. revealed that 22 out of 393 patients presented with bi-clonal gammopathy of undetermined significance [13]. Further, Pooja and al. reported a case of severe COVID-19 in a 60 year old male subject with bioclonal [14]. According, the study described a series of 7 cases of COVID-19 with MGUS [15].

Conclusions

The etiology of bi-clonal gammopathy is not yet elucidated; suddenly it is necessary to follow the evolution of the clones by more advanced research focused on the genetic study of these clones to better understand the physiopathology of the bi-clonal peak.

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Conflicts of Interest: The authors declare that they have no conflicts of interest.

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