CASE REPORT

Detection of hereditary bisalbuminemia in a Greek family by capillary zone electrophoresis

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Abstract

It is presented herein a case of a family, four members of which suffer from hereditary bisalbuminemia. The abnormality was initially detected in a 29-year old male, by serum protein electrophoresis (SPE), during the investigation for possible multiple sclerosis. SPE also revealed the presence of a double albumin band in sera of the patient's sister, father and grandmother, almost confirming the inherited (genetic) form of bisalbuminemia. Possible causes related with the acquired form of bisalbuminemia were excluded for all examined individuals. SPE was performed by both automatic capillary zone electrophoresis and agaroze gel electrophoresis. All tested samples were immunofixated with special antisera, in order to exclude the presence of monoclonal fractions. Total albumin, total proteins and immunoglobulins varied in normal ranges. The relative mobility of the albumin variant was determined by a simple mixing experiment, which gave evidence of the fast-type form of inherited bisalbuminemia. This is the first report of hereditary bisalbuminemia in Greece. Hippokratia 2008; 12 (2): 119-121

Keywords: albumin, bisalbuminemia, protein electrophoresis

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Bisalbuminemia or alloalbuminemia is an inherited or acquired serum protein abnormality characterized by the presence of 2 different albumin fractions, in equal or unequal amounts. This condition creates a typical electrophoretic image, in which albumin band presents as a doublet. The acquired (or transient) form of bisalbuminemia has been found in patients receiving high doses of β-lactamic antibiotics or suffering by pancreatic disease, usually complicated with ruptured pseudocysts[1,2]. Hereditary bisalbuminemia is a relatively rare genetic disorder, usually revealed by chance. The causative genetic lesion is a point mutation of human serum albumin gene, inherited in an autosomal codominant pattern[3]. Almost 70 discrete polymorphisms have been described worldwide. Albumin mutants (also called alloalbumins) exist in proportion 1:1 with normal albumin, and either have increased electrophoretic mobility (fast type variants) or decreased mobility (slow type variants)[4,5]. Geographic distribution of albumin variants is helpful in human genetics and anthropology studies[6]. Although bisalbuminemia has not been clearly associated with a specific disease, it seems that has, in some cases, clinical effects. There have been described point mutations responsible for familial dysalbuminemic hyperthyroxinemia[7] and familial dysalbuminemic hypertriiodothyroninemia[8].

Case report

We present herein a case of a family, four members of which were affected by hereditary bisalbuminemia. The abnormality was initially detected in a 29-years old male by serum protein electrophoresis, during the investigation for possible multiple sclerosis. Repeat of serum protein electrophoresis 2 days later in a consecutive sample gave the same result. Detailed medical history, clinical examination and biochemistry tests of the patient excluded the use of β-lactamic antibiotics and pancreatic or renal disease. With the suspicion of hereditary nature of disorder, and after informing the patient and receiving his consent, other members of his family were called in for testing: father (62 y), mother (57 y), sister (30 y) and grandmother (82 y). We performed protein electrophoresis by Capillary Zone Electrophoresis (CZE) (PARAGON 2000™, Beckman Instruments, USA) (Figure 1). The re-

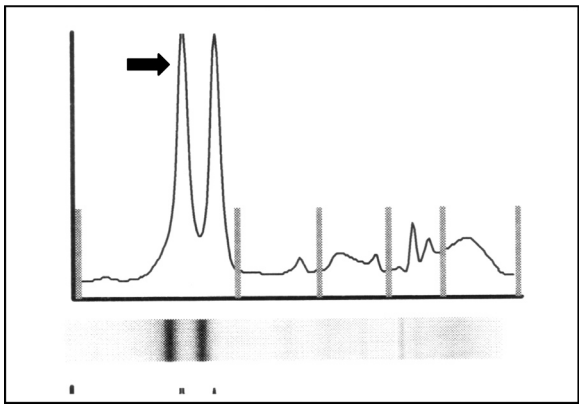

Figure 1. Serum protein CZE of the patient with hereditary bisalbuminemia (black arrow points the abnormal albumin band).

vealed presence of a double albumin band in sera of the patient's sister, father and grandmother, almost confirmed the inherited form of bisalbuminemia. We also tested the affected samples by agaroze gel electrophoresis (AGE) (Hydragel Protein reagent set, Sebia, France), according to the manufacturer's instructions. The two albumin fractions were split, although not very clearly. Repeat of AGE with increased migration time (30 min instead of 22 min) produced clearer separation of albumin fractions (Figure 2). Possible causes related with the acquired form of bisalbu-

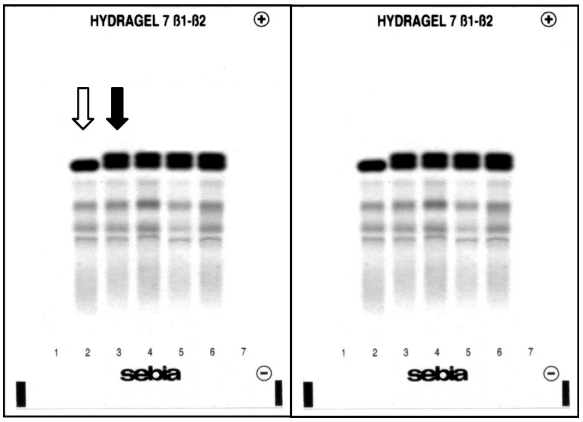

Figure 2. Agaroze gel electrophoresis of patients with hereditary bisalbuminemia (left: 22 min, right: 30 min). White arrow points a normal serum sample whereas black arrow points a sample with bisalbuminemia.

minemia were excluded for all examined individuals. All tested samples were immunofixated with special antisera, in order to exclude the presence of monoclonal fractions. Total albumin, total proteins and immunoglobulins varied in normal ranges. Albumin variant mobility, compared to that of normal albumin, was determined with a simple experiment. Five different mixtures of patient's serum and normal serum were produced, with gradually decreasing proportion of bisalbuminemic serum (4:1, 3:2, 1:1, 2:3 and 1:4). CZE of these mixtures was performed and the electrophoretic images were compared to a normal image of the instruments' database. It was found that mutant presented increased mobility, compared to normal albumin, as gradual decrease of abnormal serum proportion was responsible for lowering of the first albumin peak (Figure 3). This finding is indicative of fast type hereditary bisalbuminemia. The relative quantity of the fast and the normal albumin fraction was calculated to 53% and 47%, respectively.

Discussion

The frequency of hereditary bisalbuminemia, as it appears from international literature data, displays significant differences in terms of race, nationality and place of stay. Small, isolated population groups (like indigenous American Indians) present high incidence of the abnormality[9,10]. In Europe, heterozygocity in general population is estimated between 1:1000 and 1:10000[11,12]. In Greece, one single case of hereditary bisalbuminemia combined with monoclonal gammopathy has been reported so far[13], but it is the first time an affected family is studied.

In many laboratories CZE has replaced classical agaroze gel electrophoresis, due to its high discriminating ability. It has been reported that AGE fails to efficiently detect bisalbuminemia[14]. In our case CZE produced defi-

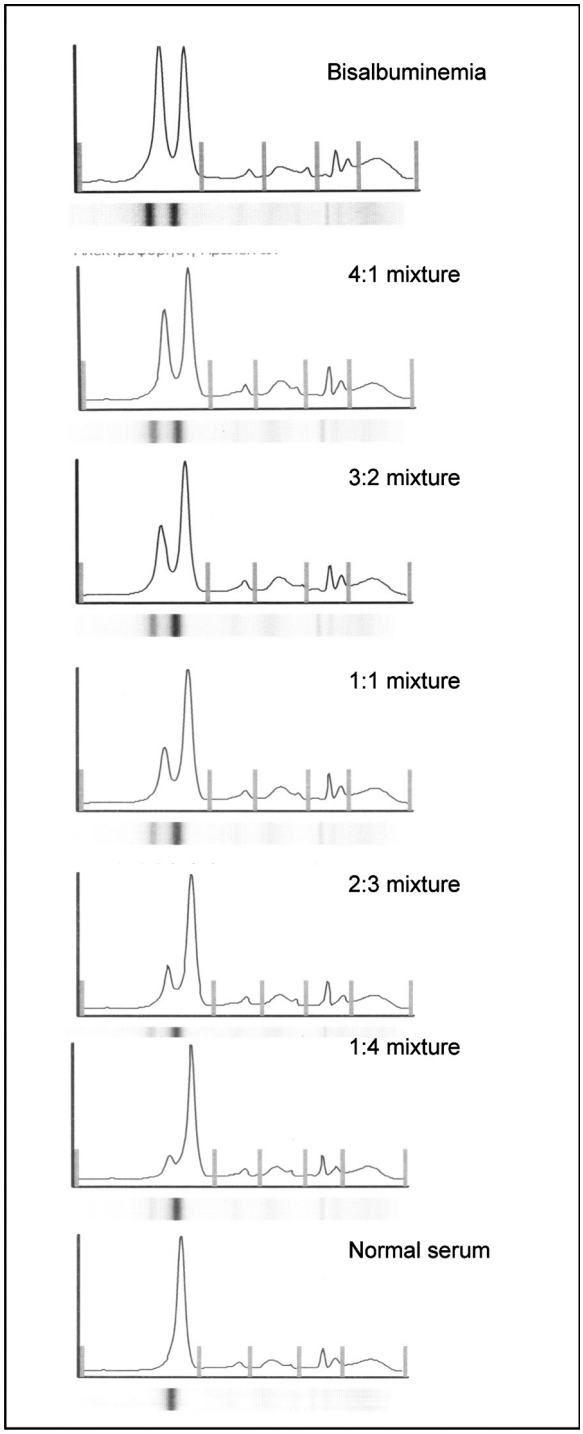

Figure 3. Mobility of albumin variant.

nite and unambiguous separation of the two nonidentical albumin fractions, although all CZE positive samples were also revealed with AGE. We suppose that additional positive individuals will be revealed after testing other members of the family. Great scale studies are needed, in order to estimate the exact incidence of the disorder in Greece and specify which form (slow or fast) is prevailing.

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