that the predominant source of plasma DNA was hematopoietic. No significant difference was observed among the total DNA concentrations in plasma samples obtained by use of different centrifugation protocols. Thus, this present work supports the view that the release of plasma DNA in our previous study was a genuine in vivo phenomenon and that hematopoietic cells represent the predominant origin of plasma cell-free DNA (1). Our work also provides information about the compatibility of studies of plasma DNA that used different centrifugation speeds.

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References

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Inherited Bisalbuminemia with Benign Monoclonal Gammapathy Detected by Capillary but not Agarose Gel Electrophoresis

To the Editor:

Bisalbuminemia (or alloalbuminemia) is characterized by the presence of two albumin components (in equal or unequal amounts) on serum protein electrophoresis (1). Bisalbuminemia may be inherited (genetic) or acquired. The cumulative frequency of inherited bisalbuminemia is typically 1:10000 to 1:1000 (2–4), with inheritance showing an autosomal codominant pattern (5). Inherited bisalbuminemia has no pathologic or therapeutic consequences, but it is of interest for investigations of the evolution of functional differences in the protein, including altered affinity for steroid hormones, thyroxine, and several dyes (6). An acquired or transient form has been described that usually has a faster mobility (1, 7, 8). The faster form may be seen in patients who receive large amounts of β-lactam antibiotics or have pancreatic diseases, usually complicated by a ruptured false cyst (9). Acquired bisalbuminemia has been reported as a rare occurrence in patients with myeloma (10) or in nephrotic syndrome (1).

We recently encountered a patient with both bisalbuminemia and monoclonal paraprotein. Capillary zone electrophoresis (CZE) of serum proteins from this 78-year-old male is shown in Fig. 1A. The paraprotein was IgG-k with a concentration of 20 g/L; IgA and IgM concentrations were within the appropriate reference intervals. The patient had moderate anemia with total serum protein, serum albumin, calcium, and β2-microglobulin concentrations within the appropriate reference intervals. There was no osteolysis, and the bone marrow biopsy showed a plasma cell infiltration of 7%, confirming the diagnosis of monoclonal gammapathy of uncertain origin, and findings very suspect of myelodysplastic syndrome. A double albumin band was also detected in one of the patient’s three daughters, with no other electroforetic abnormalities, supporting the inherited (genetic) form of bisalbuminemia (Fig. 1C). Serum protein electrophoresis was normal in another daughter; the third daughter and the remaining family members declined to be examined. Situations that might lead to acquired bisalbuminemia were excluded for all examined members.

Routine protein electrophoresis was performed in the PARAGON 2000™ CZE system (Beckman Instruments). The mobility of the albumin variant relative to the normal albumin was determined by comparison with the normal protein peak in the instrument database and by electrophoresis of a mixture of the patient’s serum sample and normal serum in different proportions. The samples that showed a double albumin band were also analyzed by agarose gel electrophoresis (TITAN Protein reagent set (HELENA) and Hydragel Protein reagent set (SE-BIA)). The type of monoclonal component was identified with immunofixation by immunosubtraction using beads coated with anti-IgG, -IgA, -IgM-κ, and -IgM-λ in the PARAGON 2000.

On CZE the two albumin bands were 48% and 52% of the total albumin. One band had a slower mobility than that of the normal albumin in the instrument database. The mixing experiment confirmed that the abnormal band was the one with slower mobility (Fig. 1B). We assume that this finding is indicative of a so-called fast-type form of inherited bisalbuminemia because the mobility in agarose gel electrophoresis is in the opposite direction of that in capillary electrophoresis. The two agarose gel electrophoresis methods failed to separate the two albumin bands detected by CZE, even when the electrophoresis time was doubled (Fig. 1, insets).

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CZE is reported to be superior to agarose gel electrophoresis for the separation of albumin and to allow detection of more cases of bisalbuminemia (11).

The present case of bisalbuminemia and benign monoclonal gammopathy appears to be the second description of such an association. Both patients had IgG-κ (8). Bisalbuminemia occurring with paraprotein has also been reported rarely in patients with myeloma and plasmacytoma, but the genetic origin was not investigated in these cases (8, 10). Bisalbuminemia in these cases may be a coincidental finding. In our patient, myelodysplastic syndrome was also suspected; the occurrence of this disorder with bisalbuminemia has not been reported.

Our observations further support the previous report (11) that CZE has an advantage over agarose gel electrophoresis in albumin separation, allowing the detection of more cases of bisalbuminemia.

Fig. 1. Capillary electrophoresis of serum proteins from the patient showing monoclonal gammopathy and hereditary bisalbuminemia (A), a 3:7 mixture of normal serum and the patient’s serum (B), and serum from the daughter of the patient shown in panel A (C). The lines divide the electrophoreograms into five fractions, Ab, albumin; α1, α2-globulin fraction; β, β-globulin fraction; γ, γ-globulin fraction. The arrows show the characteristic peaks: N, albumin peak with normal mobility; AN, albumin peak with abnormal (lower) mobility; MG, monoclonal immunoglobulin. (Insets), agarose gel electrophoresis (Hydragel Protein reagent set) of serum proteins from the patient (A) and the patient’s daughter (C).

References

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To the Editor:

There is currently substantial debate about how cardiac troponin concentrations should be reported. We would like to offer an alternative strategy to two recent recommendations.

In a recent editorial, Apple and Wu (1) proposed that the concentration of cardiac troponin that corresponds to an analytical imprecision (CV) of 10% be used as a medical diagnostic guide.

Panteghini et al. (2), in their document on quality specifications for cardiac troponin assays, state that “the detection limit . . . of cardiac troponin should be significantly lower than the clinical discrimination limit used”. The main reason for this is that patient risk stratification based on results generated by assays not meeting this requirement would be compromised by considerable imprecision.

In contrast, a recent article on the proposed new definition of myocar-

dial infarction states that “A review of currently available data demonstra-
tes no discernible threshold below which an increased value for cardiac troponin would be deemed harmless” (3). Thus, the first two views (1, 2) focus on ensuring that reported results are real, and the third (3) is intent on extracting the maximum clinically useful informa-