Familial Occurrence of Diminished Pancreatic Amylase in Serum—a "Silent" Amy-2 Allelic Variant?

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We describe a family of 32 subjects, including two healthy siblings without detectable pancreatic amylase in serum and five healthy relatives (one of them a sister) exhibiting subnormal pancreatic amylase activities. Comparisons of immunoreactive amylase concentrations with the corresponding amylase activities may justify the assumption of a "silent" Amy-2 allelic variant.

Additional Keyphrases: immunoreactive amylase · genetics · heritable disorders

Human α-amylases (EC 3.2.1.1) are synthesized from two closely related structural genes (I) on chromosome no. 1, Amy-1 (nonpancreatic amylase) and Amy-2 (pancreatic amylase). In healthy individuals the pancreatic type will constitute about half of the total amylase activity in serum. Generally, a diminished activity of the pancreatic amylase in serum is supposed to reflect a decreased exocrine pancreatic function.

Case Report

We accidentally discovered the case of a healthy woman, age 26 years, with an extremely low (<10 U/L) serum pancreatic amylase activity [method: electrophoresis in agarose gel (2, 3), pH 8.6; reference interval: 40–150 U/L; precision: 6 U/L]. The findings were confirmed by measurements repeated half a year later. From information provided by the proband a pedigree was constructed, and 32 of 33 subjects older than 10 years (siblings, parents, parental cousins, and cousins' children) were interviewed and blood tested. The pedigree and the results for total amylase activity, pancreatic amylase activity, and concentration of immunoreactive trypsin were published in an earlier paper (4).

Besides the proband, her healthy brother, age 37 years, also exhibited a pancreatic amylase activity <10 U/L in serum. Their only sister, healthy and 35 years old, showed a subnormal serum pancreatic amylase activity (38 U/L). Neither sibling had offspring. Their healthy, non-consanguineous parents exhibited serum pancreatic amylase activities within the lower part of the reference interval (66 U/L and 82 U/L). None of the parental siblings, cousins, and cousins' children older than 10 years (in total 27 persons) showed clinical symptoms of pancreatic disease, but four of them (a father's sister, a granddaughter of another sister of their father's, a daughter of a mother's sister, and a son of hers) exhibited low activities of serum pancreatic amylase (24–38 U/L). All seven subjects with subnormal pancreatic amylase activity showed normal concentrations of immunoreactive trypsin (reference interval: 140–400 µg/L) in serum, which was taken as an indication of an unimpaired exocrine pancreatic function (5). Of the 32 persons studied, 31 had values for total serum amylase activity within the reference interval (70–300 U/L, Phadebas, 37 °C). One subject, a man 22 years of age, had a total amylase activity of 414 U/L and a concentration of immunoreactive trypsin >1300 µg/L.

Since our first communication (4) an ELISA assay for quantification of immunoreactive amylase has been developed (3). This assay, based on polyclonal rabbit antibodies raised against a highly purified human amylase (3), was used for measurement of immunoreactive amylase in the 31 serum samples with total amylase activity within the reference interval. Figure 1 shows the linear relationship \[ y = 0.42 \pm 0.06x + 14 \pm 10 \] (SE: 13, \[ r^2 = 0.73 \], n = 31) between catalytic activities and corresponding concentrations of immunoreactive amylase in this family. The observed relationship did not differ significantly from what was found (6) for serum from 140 healthy blood donors \[ y = 0.46 \pm 0.03x + 6 \pm 6 \].

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Fig. 1. Concentration of immunoreactive amylase (µg/L) in serum compared with total serum amylase activity in a family with decreased serum pancreatic amylase

Discussion

Comparing concentrations of immunoreactive amylase [information not available in our first communication (4)] with the corresponding amylase activities may permit assumptions concerning a possible molecular mechanism. Thus, the unimpaired relationship between catalytic activity and concentration of immunoreactive amylase in the blood samples from the two siblings without detectable pancreatic amylase and from their five relatives with low activity of pancreatic amylase might reflect a "silent" Amy-2 allelic variant (not previously reported) rather than the presence of a noncatalytic gene product. However, two other theories may also explain the observed phenomenon: (a) pancreatic amylase may for some unknown reason fail to enter the vascular system or (b) the blood may contain an Amy-2 amylase that cannot be resolved from the Amy-1 amylase forms by the methods we used.

Neither of the two (homozygotic?) persons without detectable serum pancreatic amylase activity showed any clinical symptoms of impaired carbohydrate digestion, which is not necessarily a concomitant (7), and both of them refused further investigations. Therefore, duodenal aspirates were not available, and we were not able to make more conclusive studies.

References