without organomegaly as an early form of SLVL.

In case of the patient's brother, presence of splenomegaly, refractoriness to chemotherapy and a possible transformation to large cell lymphoma would be consistent with a diagnosis of SLVL. Demonstration of CD5 antigen co-expression on B cells is not diagnostic of B-CLL. In a recent study of 100 SLVL cases, Matutes *et al*¹² found CD5 expression in 19% of the cases. Therefore, in the absence of detailed immunophenotypic and ultrastructural studies, we cannot exclude the possibility of SLVL in the patient's relatives.

We conclude that a detailed work up of small B-cell lymphoproliferative disorders can help accurately classify these disorders and these distinctions may have important therapeutic implications.¹³

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J Clin Pathol 1995;48:587-589

Lipoprotein composition and serum Lp(a) lipoprotein in hypobetalipoproteinaemia

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Abstract

A family with hypobetalipoproteinaemia was studied to examine the Lp(a) lipoprotein, lipoprotein cholesterol, and triglyceride composition of the serum lipids. Lp(a) lipoprotein was measured by immunoassay. Serum lipoproteins were separated by ultracentrifugation. Cholesterol and triglycerides were measured using standard enzymatic assays. Serum apolipoprotein B was low and Lp(a) undetectable in the index patient and in her father and son. Separation of the lipoproteins by ultracentrifugation showed a low cholesterol content of serum low density lipoprotein in the affected family members and also a low triglyceride content of high density lipoprotein particles in two affected members. It is concluded that serum lipoprotein cholesterol is altered in hypobetalipoproteinaemia, and family

members of index cases have undetectable serum Lp(a) lipoprotein concentrations.

(*J Clin Pathol* 1995;48:587-589)

Keywords: Hypobetalipoproteinaemia, Lp(a) lipoprotein, lipoprotein composition.

Hypobetalipoproteinaemia is a rare autosomal dominant condition characterised by low serum cholesterol concentrations. The exact biochemical defect is not known although truncated forms of apolipoprotein B (ApoB) have been described.¹ Heterozygotes tend to be asymptomatic, whereas homozygous individuals may present with neurological sequelae similar to individuals with abetalipoproteinaemia. Lp(a) lipoprotein is considered to be a cardiovascular risk factor, yet how it exerts this action is unclear; possibly it acts in part by counteracting the fibrinolytic system.²⁻⁴ There are few published data upon Lp(a) lipo-

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Accepted for publication 26 September 1994

Table 1 Serum lipids and apolipoproteins A1, B, and (a) in the patient and other family members

	Patient*	Father*	Mother	Daughter	Son*	Reference range
Age (years)	41	68	70	15	22	
Cholesterol (mmol/l)	1.35	2.42	4.97	3.02	1.91	
Triglyceride (mmol/l)	0.67	0.41	0.98	0.63	0.53	
HDL (mmol/l)	0.27	1.37	1.68	0.83	1.11	
ApoA1 (mg/dl)	67.4	155.2	168.6	93.6	132.2	114–209
ApoB (mg/dl)	22.1	26.9	89.5	58.4	21.6	49–141
Lp(a) lipoprotein (mg/dl)	ND	ND	25	ND	ND	

* Affected family members

HDL = high density lipoprotein; Apo = apolipoprotein; ND = not detectable.

Table 2 Serum lipoprotein cholesterol and triglyceride concentrations in the subjects with hypobetalipoproteinaemia. Values are mmol/l

	Cholesterol			Triglycerides		
	LDL	VLDL	HDL	LDL	VLDL	HDL
Patient	0.69	0.16	0.27	0.14	0.34	0.12
Father	0.69	0.10	1.37	0.08	0.15	0.08
Mother	2.74	0.21	1.68	0.38	0.38	0.22
Daughter	2.07	0.12	0.83	0.04	0.42	0.17
Son	0.42	0.14	1.11	0.06	0.33	0.09
Reference ranges, mean (SD):						
Male	3.5 (1.02)	0.44 (0.38)	1.23 (0.29)	0.31 (0.13)	0.80 (0.76)	0.15 (0.06)
Female	3.66 (0.98)	0.20 (0.13)	1.61 (0.27)	0.30 (0.08)	0.36 (0.20)	0.14 (0.04)

protein concentrations or the distribution of cholesterol or triglyceride within the major serum lipoprotein particles in hypobetalipoproteinaemia. We present a family with hypobetalipoproteinaemia in whom serum Lp(a) lipoprotein and the distribution of serum lipoprotein cholesterol and triglyceride were studied.

Case history

A 41 year old woman presented to the hospital lipid clinic because routine lipid screening in general practice had shown a serum cholesterol of less than 2 mmol/l. There was little of note in her medical history except for rheumatoid arthritis which was now quiescent. She was not taking any medication apart from self prescribed evening primrose oil for her arthritis. The patient was asymptomatic and there was nothing of note upon physical examination, including neurological assessment. Several blood tests were performed to exclude secondary causes of hypocholesterolaemia. Thyroid, renal, and liver function tests were all normal, as was a full blood count. A fasting serum biochemical lipid profile was also performed at presentation and showed a cholesterol of 1.0 mmol/l, triglyceride 0.48 mmol/l, and high density lipoprotein (HDL) cholesterol 0.30 mmol/l. In view of these findings other family members were investigated including the patient's father, mother, daughter, and son. Physical examination was unremarkable in each of these asymptomatic family members and there was no evidence of hyperthyroidism, malabsorption, or any other secondary causes of hypocholesterolaemia in any of the subjects.

A more detailed biochemical investigation of the serum apolipoproteins in the family members and also the distribution of cholesterol and triglyceride in their lipid subfractions was later undertaken. Serum apolipoproteins (ApoB100 and A1) were measured, using an immunoturbidimetric immunoassay on a Cobas Mira analyser (Roche). The intrabatch coefficient of variation is less than 4%. Serum

Lp(a) lipoprotein was assayed using an enzyme linked immunosorbent assay (ELISA) method (Immuno) with an intra-batch coefficient of variation of less than 6%. Cholesterol and triglyceride were assayed enzymatically (Boehringer Mannheim) on a Cobas-Bio analyser with intra-assay coefficients of variation of less than 2%. Ultracentrifugation was performed to prepare serum low density lipoprotein (LDL), very low density lipoprotein (VLDL), and HDL using a Fisons MSE Pegasus 65 ultracentrifuge.⁵ Cholesterol and triglyceride were assayed in the LDL, VLDL, and HDL lipoprotein subfractions.

Results

The results of the serum lipids and apolipoproteins in the family members are given in table 1. The index patient, her father, and her children had undetectable serum Lp(a) lipoprotein. Serum apo-B was low in the index patient, and in her father and son. The cholesterol and triglyceride content of serum lipoprotein particles of the family members is shown in table 2. Of note is the low cholesterol content of serum LDL from the affected family members and also the low triglyceride content of the HDL particles in the patient's father and son, both of whom had the condition.

Discussion

Recently, several different mutations of the ApoB gene have been shown to result in familial hypobetalipoproteinaemia; most of these are either frameshift or nonsense mutations that interrupt the translation of a complete ApoB100 molecule.⁶ From this family study we assume that the patient is a heterozygote for this autosomal dominant condition.

Undetectable serum concentrations of Lp(a) lipoprotein in subjects with hypobetalipoproteinaemia have to our knowledge not been described before. However, the LDL cholesterol (from the ultracentrifuge determinations) in each of the affected subjects was

clearly low and their serum ApoB concentrations about half that of normal subjects. The patient's daughter also had an undetectable serum Lp(a) lipoprotein concentration. Lp(a) lipoprotein has been shown to be a cardiovascular risk factor.²⁻⁴ The observation of undetectable serum Lp(a) lipoprotein concentrations in heterozygotes for hypobetalipoproteinaemia merits further study as to the underlying biochemical mechanisms for its in vivo control. It is suggested that ApoB is in some way involved in the production of the Lp(a) particle.

It has been reported that subjects with this condition have a lower incidence of coronary artery disease than would be expected for the general population.⁷ This could in part be due to their low LDL cholesterol, as well as to a low serum Lp(a) lipoprotein concentration.

Herbert *et al*⁷ noted that HDL cholesterol concentrations in hypobetalipoproteinaemia are variable, with some subjects having low HDL cholesterol concentrations and others normal levels. In our family the index patient had a low HDL cholesterol concentration,

whereas her son and father had normal levels. It is also of note that the triglyceride content of the HDL particles of the affected family members was low.

We are grateful to Dr S Amiel for kind permission to report this patient and to Dr M Mattock and the Metabolic Medicine Department for their help with this study.

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Gastric polyposis caused by multiple carcinoids and early carcinoma

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Abstract

A case of gastric polyposis caused by multiple carcinoids with concurrent gastric carcinoma is reported in a 70 year old woman with severe atrophic gastritis and intestinal metaplasia. On microscopic examination, the carcinoids and gastric carcinoma arose separately thus representing "double primaries". Long-standing hypergastrinaemia probably plays a causative role in the development of carcinoma and carcinoids. Carcinoid tumours, although of low malignant potential, may be important as indicators of other unrelated high risk malignancies. Patients with carcinoids should be followed closely, especially as the incidence of these tumours seems to be on the increase.

(*J Clin Pathol* 1995;48:589-591)

Keywords: Stomach, carcinoid, adenocarcinoma.

The stomach is an uncommon site for carcinoids and multiplicity of carcinoid tumours

is even rarer. Coexistence of adenocarcinoma with these multiple carcinoids is very rare indeed and very few such cases have been reported in the literature.¹⁻³

Case report

A 70 year old Polish woman was admitted with a history of weight loss of over two stones over two years and occasional chest pains. There was a family history of malignancy. Her brother and father had both died of gastric carcinoma, a sister had died of hepatic carcinoma, and a daughter had carcinoma of the uterus. A barium enema was negative but barium meal examination revealed multiple gastric polyps. Intestinal polyposis was not present.

Methods

Endoscopic biopsy specimens ranging in size from 0.3 to 0.5 cm were obtained from three polyps. A larger polyp measuring 2.3 × 1.6 × 1.2 cm was also removed for histological assessment.

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Accepted for publication
13 October 1994