Diagnosis of fetal anterior abdominal wall defects by use of ultrasonography

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Omphalocele and gastroschisis involve protrusion of intestine through a defect in the abdominal wall. It is important to differentiate between the two because of a difference in the incidence of associated anomalies and of chromosomal abnormalities. The distinguishing characteristics are the location of umbilical cord insertion, the echogenicity of the contents of the protruding mass and, usually, the presence or absence of a sac surrounding the mass. Early detection is critical so that decisions can be made about the possibility of surgical correction and the outcome of the pregnancy. We describe an omphalocele detected by ultrasonography in the 20th week of gestation during a routine prenatal check-up.

(Key words: Omphalocele, gastroschisis, anterior abdominal wall defect, ultrasonography, pentalogy of Cantrell, Beckwith-Wiedemann syndrome)

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Omphalocele and gastroschisis are defects in the anterior part of the abdominal wall through which abdominovisceral organs protrude. The incidence of omphalocele is usually accepted as one in 5800 births, although it ranges from one in 1400 births in parts of Africa¹ to one in 10,000 births in Scandinavia.² Gastroschisis is more uncommon, occurring in one in 12,000 live births.³

Although the causes of omphalocele are unknown, this anomaly is thought to arise from the failure of fusion of the four lateral ectomesodermic folds during the third and fourth weeks of gestation. During this time, the normal midgut and superior mesenteric artery form a physiologic hernia, protruding from the anterior aspect of the developing fetal abdomen. By the 11th week of gestation and after a 270-degree rotation, the midgut returns rapidly to the normal intra-abdominal location. The failure of this reduction subsequently results in an omphalocele.⁴ If the caudal or cephalic folds fail to fuse, the pentalogy of Cantrell or cloacal exstrophy of the bladder results, respectively.

The surveillance of fetal growth and development by ultrasonography usually is performed between 18 to 22 weeks' gestation. During this time, neural tube defects, genitourinary and gastrointestinal defects, cardiac anomalies, and abdominal wall defects can be detected. Furthermore, early discovery of a congenital defect will give the family ample time to contemplate the choices available to them

concerning the outcome of the pregnancy.

When a fetal extra-abdominal mass is observed on ultrasound examination, the diagnosis of omphalocele is dependent on several structural entities:

- The location of the umbilical cord insertion in the fetus.
- The presence or absence of a sac surrounding the protruding mass, although, rarely, the sac can be absent secondary to premature rupture.
- The echogenicity of the contents of the protruding mass. The ultrasonogram demonstrates central insertion of the umbilical cord and a smooth-margined, encapsulated mass that frequently reveals homogeneous internal echoes (Table 1).

If these entities can be determined, then the correct diagnosis of omphalocele as opposed to other abdominal wall defects approaches 75%.⁵ A high degree of liver herniation and presence of fetal liver within the sac are indicators of poor prognosis for successful surgical correction.

Gastroschisis is characterized by normal cord placement with the wall defect lateral to the umbilicus, most often right-sided. The abdominal contents (mostly small intestine) will be seen free floating in the amniotic fluid with no evidence of encapsulation. Ultrasonography echoes demonstrate a lobulated margin representing the small intestine (Table 1).

These differences enable the physician to promptly and accurately diagnose an omphalocele.

Report of case

A 29-year-old gravida 2, para 0, aborta 1 white woman was seen for fetal ultrasonography. The history indicated no congenital defects in the family nor teratogen exposure during the pregnancy. As part of this patient's evaluation, two fetal ultrasound examinations were performed, one at a level 3 neonatal center. Both examinations revealed a 20-week intrauterine fetus of normal dimensions and movements. A homogeneous, encapsulated, spherical mass was observed protruding from the abdomen anteriorly (Figs 1 and 2). The diameter of the mass was essentially the same as that of the abdomen. The umbilical cord entered the mass centrally, with no other abdominal attachment of

the cord. The mass had increased homogeneous internal echoes, having the same texture and appearance of liver tissue. Various linear fluid-filled structures within the mass were observed; the volume of internal organs in the fetal abdomen was less than is normally encountered.

A diagnosis of omphalocele was made. After thorough counseling, the family decided to terminate the pregnancy. Six days after the second ultrasound study, labor was induced and the stillborn fetus was delivered without complications.

At pathologic consultation, the following were observed: an omphalocele 5.5 cm in diameter characterized by a semitransparent, thin, delicate membrane containing mostly the right lobe of a large liver; cleft lip and cleft palate; mild macroglossia; cystic dilation of the ring finger on the left hand; and a short and discolored little finger on the left hand (Fig 4). Microscopically, all tissues were normal for their age and revealed no inflammation or necrosis. Chromosomal analysis of abortus tissue revealed a normal 46,XX karyotype.

Discussion

Although not all babies with omphalocele have outcomes similar to that in the present case, certain factors indicate a poor prognosis. These indicators include coexisting physical and chromosomal anomalies (Table 2), the presence of the liver in the sac, and a large omphalocele. In contrast to gastroschisis, omphalocele is associated with an increased incidence of chromosomal abnormalities, most notably trisomies 13, 15, 16, and 18, and cardiac defects such as ventral septal defect, atrial septal defect, and tetralogy of Fallot (Table 2). In addition to these coexisting anomalies, omphalocele is associated with Beckwith-Wiedemann syndrome and the pentalogy of Cantrell. The latter syndrome, as the name implies, is associated with five anomalies: omphalocele, ectopia cordis, absent sternum, and absent portions of the diaphragm and pericardium. Beckwith-Wiedemann syndrome comprises omphalocele, macroglossia, adrenal cytomegaly, gigantism, and hyperplastic visceromegaly.

The case we report here represents the use of ultrasonography in the diagnosis of a potentially lethal birth defect during the second trimester of pregnancy. Once ultrasonography is performed and an anterior abdominal wall

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CONTRAINDICATIONS: Hypersensitivity to any component of this medication.
Active liver disease or unexplained persistent elevations of serum transaminases.

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Atherosclerosis is a chronic process and the discontinuation of lipid-lowering drugs during pregnancy should have little impact on the outcome of long-term therapy of primary hypercholesterolemia. Moreover, cholesterol and other products of the cholesterol biosynthesis pathway are essential components for fetal development, including synthesis of steroids and cell membranes. Because of the ability of inhibitors of HMG-CoA reductase such as MEVACOR® (Lovastatin, MSD) to decrease the synthesis of cholesterol and possibly other products of the cholesterol biosynthesis pathway, MEVACOR may cause fetal harm when administered to a pregnant woman. Therefore, lovastatin is contraindicated during pregnancy. Lovastatin should be administered to women of childbearing age only when such patients are highly unlikely to conceive. If the patient becomes pregnant while taking this drug, lovastatin should be discontinued and the patient should be apprised of the potential hazard to the fetus.

WARNINGS: Liver Dysfunction: Marked persistent increases (to more than 3 times the upper limit of normal) in serum transaminases occurred in 1.9% of adult patients who received lovastatin for at least one year in clinical trials (see ADVERSE REACTIONS). When the drug was interrupted or discontinued in these patients, the transaminase levels usually fell slowly to pretreatment levels. The increases usually appeared 3 to 12 months after the start of therapy with lovastatin and were not associated with jaundice or other clinical signs or symptoms. There was no evidence of hypersensitivity. A liver biopsy was done in one of these patients and showed areas of focal hepatitis. In this patient, transaminase levels returned to normal following discontinuation of therapy. Some of these patients had abnormal liver function tests prior to lovastatin therapy and/or consumed substantial quantities of alcohol.

It is recommended that liver function tests be performed before treatment begins, every 4 to 6 weeks during the first 15 months of therapy with lovastatin, and periodically thereafter in all patients. Special attention should be paid to patients who develop elevated serum transaminase levels, and in these patients, measurements should be repeated promptly and then performed more frequently. If the transaminase levels show evidence of progression, particularly if they rise to 3 times the upper limit of normal and are persistent, the drug should be discontinued. Liver biopsy should be considered if elevations are persistent beyond the discontinuation of the drug.

The drug should be used with caution in patients who consume substantial quantities of alcohol and/or have a past history of liver disease. Active liver disease or unexplained transaminase elevations are contraindications to the use of lovastatin.

As with other lipid-lowering agents, moderate (less than 3 times the upper limit of normal) elevations of serum transaminases have been reported following therapy with MEVACOR (see ADVERSE REACTIONS). These changes appeared soon after initiation of therapy with MEVACOR, were often transient, were not accompanied by any symptoms, and interruption of treatment was not required.

Skeletal Muscle: Several cases of rhabdomyolysis have been associated with lovastatin therapy alone, when combined with immunosuppressive therapy including cyclosporine in cardiac transplant patients, and when combined in non-transplant patients with either gemfibrozil or lipid-lowering doses (≥ 1 g/day) of nicotinic acid. Acute renal failure from rhabdomyolysis has been seen more commonly with the lovastatin-gemfibrozil combination and has also been reported in transplant patients receiving lovastatin plus cyclosporine.

Rhabdomyolysis with or without renal impairment has been reported in seriously ill patients receiving erythromycin concomitantly with lovastatin. Therefore, patients receiving concomitant lovastatin and erythromycin should be carefully monitored.

Fulminant rhabdomyolysis has been seen as early as 3 weeks after initiation of combined therapy with gemfibrozil and lovastatin but may be seen after several months. For these reasons, it is felt that, in most subjects who have had an unsatisfactory lipid response to either drug alone, the possible benefits of combined therapy with lovastatin and gemfibrozil do not outweigh the risks of severe myopathy, rhabdomyolysis, and acute renal failure. While it is not known whether this interaction occurs with fibrates other than gemfibrozil, myopathy and rhabdomyolysis have occasionally been associated with the use of other fibrates alone, including clofibrate. Therefore, the combined use of lovastatin with other fibrates should generally be avoided.

Physicians contemplating combined therapy with lovastatin and lipid-lowering doses of nicotinic acid or with immunosuppressive drugs should carefully weigh the potential benefits and risks and should carefully monitor patients for any signs and symptoms of muscle pain, tenderness, or weakness, particularly during the initial months of therapy and during any periods of upward dosage titration of either drug. Periodic CPK determinations may be considered in such situations, but there is no assurance that such monitoring will prevent the occurrence of severe myopathy. The monitoring of lovastatin drug and metabolite levels may be considered in transplant patients who are treated with immunosuppressives and lovastatin.

Lovastatin therapy should be temporarily withheld or discontinued in any patient with an acute, serious condition suggestive of a myopathy or having a risk factor predisposing to the development of renal failure secondary to rhabdomyolysis, including severe acute infection, hypotension, major surgery, trauma, severe metabolic, endocrine, and electrolyte disorders, and uncontrolled drug abuse.

Myalgia has been associated with lovastatin therapy. Transient, mildly elevated creatine phosphokinase levels are commonly seen in lovastatin-treated patients. However, in clinical trials, approximately 0.5% of patients developed a myopathy, i.e., myalgia or muscle weakness associated with markedly elevated CPK levels. Myopathy should be considered in any patient with diffuse myalgias, muscle tenderness, or weakness, and/or marked elevation of CPK. Patients should be advised to report promptly unexplained muscle pain, tenderness, or weakness, particularly if accompanied by malaise or fever. Lovastatin therapy should be discontinued if markedly elevated CPK levels occur or myopathy is diagnosed or suspected.

Most of the patients who have developed myopathy (including rhabdomyolysis) while taking lovastatin were receiving concomitant therapy with immunosuppressive drugs, gemfibrozil, or lipid-lowering doses of nicotinic acid. In clinical trials, about 30% of patients on concomitant immunosuppressive therapy including cyclosporine developed myopathy; the corresponding percentages for gemfibrozil and niacin were approximately 5% and 2%, respectively.

In 6 patients with cardiac transplants taking immunosuppressive therapy including cyclosporine concomitantly with lovastatin 20 mg/day, the average plasma level of active metabolites derived from lovastatin was elevated to approximately 4 times the expected levels. Because of an apparent relationship between increased plasma levels of active metabolites derived from lovastatin and myopathy, the daily dosage in patients taking immunosuppressants should not exceed 20 mg/day (see DOSAGE AND ADMINISTRATION). Even at this dosage, the benefits and risks of using lovastatin in patients taking immunosuppressants should be carefully considered.

PRECAUTIONS: General: When instituting therapy with MEVACOR® (Lovastatin, MSD), an attempt should be made to control hypercholesterolemia with appropriate diet, exercise, weight reduction in obese patients, and to treat other underlying medical problems (see INDICATIONS AND USAGE).

Lovastatin may elevate creatine phosphokinase and transaminase levels (see ADVERSE REACTIONS). This should be considered in the differential diagnosis of chest pain in a patient on therapy with lovastatin.

Eye: There was a high prevalence of baseline lenticular opacities in the patient population included in the clinical trials with lovastatin. During these trials the appearance of new opacities was noted. The causal relationship of lovastatin to these findings has not been established.

Of 431 patients examined with slit lamp at baseline and during therapy with lovastatin, 34 had opacities reported at the final examination (5 to 15 months after starting lovastatin) that were not noted at baseline. On the other hand, in 45 patients, opacities observed at baseline were not noted at the final examination, so that the prevalence did not increase. There was no clinically significant change in visual acuity in the patients who had new opacities reported, nor was any patient, including those with opacities noted at baseline, discontinued from therapy because of a decrease in visual acuity. Nevertheless, until further experience is obtained, it is recommended that patients placed on lovastatin therapy be examined with a slit lamp before or shortly after initiation of treatment and annually thereafter.

Homozygous Familial Hypercholesterolemia: MEVACOR is less effective in patients with the rare homozygous familial hypercholesterolemia, possibly because these patients have no functional LDL receptors. MEVACOR appears to be more likely to raise serum transaminases (see ADVERSE REACTIONS) in these homozygous patients.

Drug Interactions: Immunosuppressive Drugs, Gemfibrozil, Niacin (Nicotinic Acid), Erythromycin. See WARNINGS, Skeletal Muscle.

Coumarin Anticoagulants: In a clinical trial in warfarin-treated patients designed specifically to observe a potential effect of lovastatin on the prothrombin time, lovastatin in dosages up to 40 mg b.i.d. did not produce any consistent alteration of the anticoagulant action of warfarin. However, since the drug was marketed, clinically evident bleeding and/or increased prothrombin time have been reported in a few patients taking coumarin anticoagulants concomitantly with lovastatin. The causal relationship to lovastatin is unclear. Nevertheless, it is recommended that in patients taking anticoagulants, prothrombin time be determined before starting lovastatin and frequently enough during early therapy to insure that no significant alteration of prothrombin time occurs. Once a stable prothrombin time has been documented, prothrombin times can be monitored at the intervals usually recommended for patients on coumarin anticoagulants. If the dose of lovastatin is changed, the same procedure should be repeated. Lovastatin therapy has not been associated with bleeding or with changes in prothrombin time in patients not taking anticoagulants.

Antipyrine: Antipyrine is a model for drugs metabolized by the microsomal hepatic enzyme system (cytochrome P450 system). Because lovastatin had no effect on the pharmacokinetics of antipyrine, interactions with other drugs metabolized via this mechanism are not expected.

Propranolol: In normal volunteers, there was no clinically significant pharmacokinetic or pharmacodynamic interaction with concomitant administration of single doses of lovastatin and propranolol.

Digoxin: In patients with hypercholesterolemia, concomitant administration of lovastatin and digoxin resulted in no effect on digoxin plasma concentrations.

Other Concomitant Therapy: Although specific interaction studies were not performed, in clinical studies, lovastatin was used concomitantly with beta blockers, calcium channel blockers, diuretics, and nonsteroidal anti-inflammatory drugs (NSAIDs) without evidence of clinically significant adverse interactions.

Carcinogenesis, Mutagenesis, Impairment of Fertility: In a 21-month carcinogenic study in mice, a statistically significant ($p < 0.05$) increase in the incidence of hepatocellular carcinomas and adenomas was observed at doses of 500 mg/kg/day (312 times the maximum recommended human dose) of lovastatin. These changes were not seen in mice given doses of 20 and 100 mg/kg/day (12.5 and 62.5 times the maximum recommended human dose).

A statistically significant increase ($p < 0.05$) in the incidence of pulmonary adenomas was seen in female mice receiving 500 mg/kg/day (312 times the maximum recommended human dose); no similar changes were seen in males at any dose or in females receiving 20 or 100 mg/kg/day (12.5 or 62.5 times the maximum recommended human dose). Because the incidence of pulmonary tumors was within the range of untreated animals in studies of similar duration, the relationship of this latter change to treatment is not known.

In addition, an increase in the incidence of papilloma in the non-glandular mucosa of the stomach was observed in mice receiving 100 and 500 mg/kg/day (62.5 and 312 times the maximum recommended human dose); no increase was seen at a dosage of 20 mg/kg/day (12.5 times the maximum recommended human dose). The glandular mucosa was not affected. The human stomach contains only glandular mucosa. Importantly, there is a strong association between this change and hyperplasia of the squamous epithelium (acanthosis) in this region; acanthosis is a characteristic change observed in the non-glandular mucosa of rodents treated with HMG-CoA reductase inhibitors and is most probably a result of inhibition of the reductase in this tissue.

Similar squamous epithelium is found in the esophagus and anorectal junction of the mouse and rat; however, no evidence of a similar drug-induced hyperplastic response was observed in these tissues in studies of up to 21 months in the mouse given up to 500 mg/kg/day (312 times the maximum recommended human dose), or in a study of 24 months in the rat given 180 mg/kg/day (112 times the maximum recommended human dose).

In a 24-month carcinogenicity study in rats, there was a positive dose response relationship for hepatocellular carcinogenicity in males (unadjusted $p = 0.025$). However, because the incidence of hepatocellular carcinogenicity observed in male rats in this study is similar to that observed spontaneously in this strain of rat, the implications of this finding are unclear.

No evidence of mutagenicity was observed in a microbial mutagen test using mutant strains of *Salmonella typhimurium* with or without rat or mouse liver metabolic activation. In addition, no evidence of damage to genetic material was noted in an *in vitro* alkaline elution assay using rat or mouse hepatocytes, a V-79 mammalian cell forward mutation study, an *in vitro* chromosome aberration study in CHO cells, or an *in vivo* chromosomal aberration assay in mouse bone marrow.

No drug-related effects on fertility were found in studies with rats.

Pregnancy: Pregnancy Category X. See CONTRAINDICATIONS.

Lovastatin has been shown to produce skeletal malformations in the rat fetus at doses of 800 mg/kg/day (500 times the maximum recommended human dose). At similar doses in mice, an increase in skeletal malformations was observed. These individual changes are within the range of those observed spontaneously in this strain of mouse. No drug-induced changes were seen in either species at doses of up to 80 mg/kg/day (50 times the maximum recommended human dose). No evidence of malformations was noted in rabbits at up to 15 mg/kg/day (highest tolerated dose—about 9 times the maximum recommended human dose). There are no data in pregnant women.

Nursing Mothers: Studies in rats have shown that lovastatin is excreted in the milk. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from MEVACOR, women taking lovastatin should not nurse their infants (see CONTRAINDICATIONS).

Pediatric Use: Safety and effectiveness in children have not been established. Because children are not likely to benefit from cholesterol lowering for at least a decade and because experience with this drug is limited (no

studies in subjects below the age of 20 years), treatment of children with lovastatin is not recommended at this time.

ADVERSE REACTIONS: MEVACOR® (Lovastatin, MSD) is generally well tolerated; adverse reactions usually have been mild and transient. Less than 1% of patients were discontinued from controlled clinical studies due to adverse experiences attributable to MEVACOR. About 2% of patients were discontinued from all studies (controlled and uncontrolled) due to adverse experiences attributable to MEVACOR; about one-third of these patients were discontinued due to increases in serum transaminases.

Clinical Adverse Experiences: Adverse experiences reported in patients treated with MEVACOR in controlled clinical studies are shown in the table below:

	MEVACOR (N = 613) %	Placebo (N = 82) %	Cholestyramine (N = 88) %	Probucol (N = 97) %
Gastrointestinal				
Constipation	4.9	—	34.1	2.1
Diarrhea	5.5	4.9	8.0	10.3
Dyspepsia	3.9	—	13.6	3.1
Flatulence	6.4	2.4	21.6	2.1
Abdominal pain/cramps	5.7	2.4	5.7	5.2
Heartburn	1.6	—	—	—
Nausea	4.7	3.7	9.1	6.2
Musculoskeletal				
Muscle cramps	1.1	—	1.1	—
Myalgia	2.4	1.2	—	—
Nervous System/Psychiatric				
Dizziness	2.0	1.2	—	1.0
Headache	9.3	4.9	4.5	8.2
Skin				
Rash/pruritus	5.2	—	4.5	—
Special Senses				
Blurred vision	1.5	—	1.1	3.1
Dysgeusia	0.8	—	1.1	—

Laboratory Tests: Marked persistent increases of serum transaminases have been noted (see WARNINGS).

About 11% of patients had elevations of creatine phosphokinase (CPK) levels at least twice the normal value on one or more occasions. The corresponding values for the control agents were cholestyramine, 9% and probucol, 2%. This was attributable to the noncardiac fraction of CPK. Large increases in CPK have sometimes been reported (see WARNINGS, Skeletal Muscle).

Concomitant Therapy: In controlled clinical studies in which lovastatin was administered concomitantly with cholestyramine, no adverse reactions peculiar to this concomitant treatment were observed. The adverse reactions that occurred were limited to those reported previously with lovastatin or cholestyramine. Other lipid-lowering agents were not administered concomitantly with lovastatin during controlled clinical studies. In uncontrolled clinical studies, most of the patients who have developed myopathy were receiving concomitant therapy with immunosuppressive drugs, gemfibrozil, or niacin (nicotinic acid) (see WARNINGS, Skeletal Muscle).

Uncontrolled Clinical Studies: The adverse experiences observed in uncontrolled studies were similar to those seen in controlled clinical studies. Abnormal liver function tests were observed at a higher incidence than in the controlled studies (see WARNINGS, Liver Dysfunction). Myopathy (myalgia with marked CPK elevations) was reported in approximately 0.5% of patients (see WARNINGS, Skeletal Muscle).

Causal Relationship Unclear: Nervous System: Peripheral neuropathy has been reported; the relationship to lovastatin is unclear. Visual evoked response, nerve conduction measurements, and electromyography in over 30 patients showed no evidence of neurotoxic effects of lovastatin.

Special Senses: Of 431 patients examined with slit lamp at baseline and during therapy with lovastatin, 34 had opacities reported at the final examination (5 to 15 months after starting lovastatin) that were not noted at baseline. On the other hand, in 45 patients, opacities observed at baseline were not noted at the final examination, so that the prevalence did not increase (see PRECAUTIONS).

Post-marketing Experience: Additional adverse experiences occurring since the drug was marketed are listed below:

Clinical Adverse Experiences
Gastrointestinal: Hepatitis, cholestatic jaundice, anorexia, vomiting.

Hypersensitivity Reactions: An apparent hypersensitivity syndrome has been reported rarely which has included one or more of the following features: anaphylaxis, angioedema, lupus-like syndrome, polymyalgia rheumatica, thrombocytopenia, leukopenia, hemolytic anemia, positive ANA, ESR increase, arthritis, arthralgia, urticaria, asthenia, photosensitivity, fever, flushing, malaise, and dyspnea.

Nervous System/Psychiatric: Psychic disturbances, including anxiety, paresthesia.

Skin: Erythema multiforme, including Stevens-Johnson syndrome; toxic epidermal necrolysis.

Causal Relationship Unknown
Gastrointestinal: Pancreatitis, stomatitis.

Skin: Alopecia.

Nervous System/Psychiatric: Depression, insomnia.

Metabolic: Edema.

Clinical Laboratory Test Findings

Liver Function Tests: Liver function test abnormalities, including elevated alkaline phosphatase and bilirubin.

Thyroid Function Tests: Rare reports of thyroid function test abnormalities in patients taking concomitant thyroxine.

OVERDOSAGE: The oral LD₅₀ of MEVACOR in mice is 20 g/kg.

Five healthy human volunteers have received up to 200 mg of lovastatin as a single dose without clinically significant adverse experiences. A few cases of accidental overdosage have been reported; no patients had any specific symptoms, and all patients recovered without sequelae. The maximum dose taken was 5 to 6 g.

Until further experience is obtained, no specific treatment of overdosage with MEVACOR can be recommended.

The dialyzability of lovastatin and its metabolites in man is not known at present.

DOSAGE AND ADMINISTRATION: The patient should be placed on a standard cholesterol-lowering diet before receiving MEVACOR and should continue on this diet during treatment with MEVACOR. MEVACOR should be given with meals.

The recommended starting dose is 20 mg once a day given with the evening meal. The recommended dosing range is 20 to 80 mg/day in single or divided doses; the maximum recommended dose is 80 mg/day. Adjustments of dosage should be made at intervals of 4 weeks or more. Doses should be individualized according to the patient's response (see Tables I to IV under CLINICAL PHARMACOLOGY, Clinical Studies for dose response results).

For those patients with severely elevated serum cholesterol levels (i.e., >300 mg/dL [7.8 mmol/L] on diet), MEVACOR may be initiated at 40 mg/day.

In patients taking immunosuppressive drugs concomitantly with lovastatin (see WARNINGS, Skeletal Muscle), the maximum recommended dosage is 20 mg/day.

Cholesterol levels should be monitored periodically and consideration should be given to reducing the dosage of MEVACOR if cholesterol levels fall below the targeted range.

For more detailed information, consult your MSD Representative or see Prescribing Information, Merck Sharp & Dohme, Division of Merck & Co., Inc., West Point, PA 19486.

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Table 1
Ultrasonic and Gross Characteristics of Gastroschisis and Omphalocele

Characteristic	Gastroschisis	Omphalocele
<ul style="list-style-type: none"> • Umbilical cord Location • Insertion point 	Lateral to the defect Directly into abdomen	Central in the sac Protruding sac
<ul style="list-style-type: none"> • Encapsulation 	Absent	Present
<ul style="list-style-type: none"> • Echogenicity 	Lobulated with mixed internal echoes	Homogeneous internal echoes

defect is observed, it is vital that the diagnosis be made with speed and accuracy. The differential diagnosis for abdominal wall defects includes both omphalocele and gastroschisis. The differences between the two are distinct.⁶⁻⁸

The ultrasonographic differences are shown in Table 1 and Figures 1 through 3. An omphalocele is covered by a translucent membrane that is composed of an internal peritoneum and an external amnion. These two layers are separated by a thin layer of Wharton's jelly. The protruding sac can contain intestine, bladder, liver, stomach, or spleen (or a combination). The umbilical cord attaches to the apex of this mass and finds no other insertion in the fetus.

In contrast to omphalocele, gastroschisis has no sac surrounding the protruding abdominal contents. This leaves the extra-abdominal viscera, most often small intestine, to float freely in the amniotic fluid. The umbilical cord is attached lateral to the abdominal wall defect, most often to the left of the defect. In gastroschisis, this defect is usually much smaller. Associated anomalies are much less common and are mainly confined to the jejunoileal region in the forms of nonrotation, malrotation, and atresia of the bowel.

Some studies found that gastroschisis is caused by a teratogenic insult to the mother

Table 2
Congenital Anomalies Associated With Omphalocele

System	Common anomalies
<ul style="list-style-type: none"> • Chromosomal 	Trisomies 13, 15, 16, 18
<ul style="list-style-type: none"> • Cardiac 	Ventral septal defect Atrial septal defect Tetralogy of Fallot
<ul style="list-style-type: none"> • Genitourinary 	Polycystic kidney Renal agenesis
<ul style="list-style-type: none"> • Neural tube 	Anencephaly Hydrocephaly Microcephaly
<ul style="list-style-type: none"> • Gastrointestinal 	Cleft lip Cleft palate Malrotation of the gut

during pregnancy.⁹ It is also suggested that omphaloceles are the result of natural inborn errors, and possibly genetic aberrations. Because of the associated anomalies with omphalocele, there is some indication of genetic origin of the disorder.^{10,11} Many studies¹⁰⁻¹⁴ show a genetic predisposition for the etiology of omphalocele. One study¹² supports sex-linked recessive inheritance. An African study¹ reported that the incidence of omphalocele was approximately 1 in 1400 births in the country of Nigeria.

In contrast, other studies indicate no genetic predisposition greater than that of the general population. Studies from British Columbia and the Hungarian Register have indicated that the risk of having recurrent omphaloceles

Figure 1. Coronal view ultrasoundogram at 20 weeks' gestation. Notice the smooth, encapsulated protruding omphalocele (o).

Figure 2. Parasagittal view ultrasoundogram of same patient. o = omphalocele; b = body of the fetus.

within a family remains no higher than that of the general population.^{15,16} Possibly the reason for the few studies indicating a familial occurrence, that is the infrequency with which familial cases occur, makes them popular research subjects.

Conclusion

Careful surveillance and diligence in the diagnosis of this defect in utero is vital if the appropriate choices are to be made in the outcome of the pregnancy. Only after careful

searching by means of fetal ultrasonography can the family make such important decisions. The family physician must be knowledgeable about the capabilities and limitations of the diagnostic tools available. The family physician must be familiar with tertiary care centers and not hesitate to refer patients to specialized care in this field.

The case reported here in no way implies that termination is the only alternative to a pregnancy complicated by omphalocele. Both omphalocele and gastroschisis are amenable

Figure 3. Coronal view of a 20-week fetus with gastroschisis. Notice the free-floating small intestines in the amniotic sac, (g).

Figure 4. Gross specimen of stillborn 20-week fetus. Notice the prominent omphalocele, macroglossia, cleft lip and palate, and the cyst on left ring finger.

to corrective surgery. The outcome of the surgery has varying success based on several prognostic indicators, including those mentioned earlier in this report.¹⁷ Furthermore, karyotyping by means of umbilical blood sampling, transabdominal chorionic villi sampling, or amniocentesis should be performed to rule out any chromosomal abnormalities. In addition, careful fetal ultrasonography should be done, and repeated if necessary, to search for those anomalies (Table 2) and other syndromes most closely associated with omphalocele. If

karyotyping and ultrasound at a tertiary care center reveal no other gross abnormalities, pediatric surgical correction can be extremely successful. Because of the possible relationship to chromosomal inheritance, genetic counseling of affected women who wish to have more children is warranted.

The case described here is an example of a potentially life-threatening birth defect that requires rapid, but very careful, prenatal diagnosis. Such diagnosis is best handled by a team of healthcare personnel that includes geneti-

cists, radiologists, neonatologists, pediatricians, pathologists, and obstetricians.

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