combined with the low total bile salt concentration in the biles surrounding brown stones, could decrease cholesterol solubility and account for the high percentage of this sterol in the stones. Second, addition of lecithin enhances interaction of calcium with bile salt micelles (3), so that hydrolysis of lecithin *might* enhance Ca^{++} activity in bile, promoting precipitation of calcium-sensitive anions like bile salts (2). On the other hand, contrary to the discussion in this paper, lecithin decreases solubilization of bilirubin by bile salt micelles (10), so that hydrolysis of lecithin *might* decrease the activity of bilirubinate anions, inhibiting their precipitation. These latter possibilities need to be assessed by studies of the relative effects of (lysolecithin + palmitate) vs. lecithin on the binding of Ca^{++} and bilirubinates by bile salt micelles. It is of interest that the combined hydrolytic products are just as effective as lecithin in enhancing the solubilization of cholesterol by mixed bile salt micelles (11).

Finally, the studies were conducted on brown pigment stones obtained from the gallbladders of 28 Japanese patients, but it was not stated whether ductal stones were present concomitantly. It is thus uncertain whether the results can be applied to the brown stones that are more often found in the bile ducts alone than the gallbladder. Moreover, no information was given regarding the presence of ductal obstruction and/or acute cholangitis/cholecystitis in these patients, factors that might have accounted for some of the observed abnormalities in bile composition.

In summary, more such carefully performed studies are needed, but their value in understanding gallstone formation will be diminished if ionized Ca^{++} activity is not measured also.

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REFERENCES

1. Ostrow JD. The etiology of pigment gallstones. HEPATOLOGY 1984; 4:215S-222S.
2. Moore EW. Biliary calcium and gallstone formation. HEPATOLOGY 1990;12 (suppl.):206S-218S.
3. Jones CA, Hofmann AF, Mysels KJ, Roda A. The effect of calcium and sodium ion concentration on the properties of dilute aqueous solutions of glycine conjugated bile salts: phase behavior and solubility products of the calcium salts of the common glycine conjugated bile acids. J Colloid Inter Sci 1986;114:452-470.
4. Bills PM. The precipitation of calcium carbonate polymorphs *in vitro* at 37° C. Calcif Tissue Int 1985;37:174-177.
5. Marteau C, Portugal H, Pauli AM, Gerolami A. Effect of glycoursodeoxycholate on precipitation of calcium carbonate. HEPATOLOGY 1985;5:1209-1212.
6. Van der Meer R, De Vries HT. Differential binding of glycine and taurine conjugated bile acids to insoluble calcium phosphate. Biochem J 1985;229:265-268.
7. Smith BF, LaMont JT. Hydrophobic binding properties of bovine gallbladder mucin. J Biol Chem 1984;259:12170-12177.
8. Ostrow JD. Unconjugated bilirubin and cholesterol gallstone formation. HEPATOLOGY 1990;12 (suppl.):219S-226S.
9. Nakano T, Yanagisawa J, Nakayama F. Phospholipase activity in human bile. HEPATOLOGY 1988;8:1560-1564.
10. Carey MC, Spivak W. Physical chemistry of bile pigments and porphyrins with particular reference to bile. In: Ostrow JD, ed. Bile pigments and jaundice: molecular, metabolic and medical aspects. New York: Marcel Dekker, 1986:81-132.
11. Neiderhiser DH, Roth HP. Effect of phospholipase A on cholesterol solubilization by lecithin in a bile salt solution. Gastroenterology 1970;58:26-31.

LICHEN PLANUS AND THE LIVER

Gruppo Italiano Studi Epidemiologici in Dermatologia (GISED). Lichen planus and liver diseases: a multicenter case-control study. BMJ 1990;300:227-230.

ABSTRACT

***Objective*—To assess the association of lichen planus with liver complaints and with known etiological factors of liver diseases.**

***Design*—A multicentre case-control study. Interviews were conducted by trained medical investigators on the basis of a structured questionnaire. At the interview patients and controls were asked for consent to blood samples being taken to determine transaminase activities and the presence of hepatitis B virus surface antigen.**

***Setting*—Outpatient departments of 27 Italian general and teaching hospitals that were collaborating in the Gruppo Italiano Studi Epidemiologici in Dermatologia (GISED).**

***Subjects*—Incident cases and controls were eligible. A total of 577 patients with lichen planus and 1031 controls with dermatological diseases other than lichen planus were interviewed. Less than 1% of the people contacted refused to participate. Patients and controls were matched for sex and age in 5 year intervals.**

***Results*—The risk of lichen planus was higher in patients with a history of liver diseases requiring hospital admission or specialist consultation (relative risk = 1.6; 95% confidence interval = 1.2 to 2.2), those who had had liver biopsy (5.5; 1.9 to 15.6) and those with a history of viral hepatitis (1.9; 1.1 to 3.1). High activities of liver enzymes and positive results of tests for hepatitis B virus surface antigen were also associated with lichen planus. The association with alcohol consumption was not clearly confirmed by a dose-risk relationship.**

***Conclusion*—This study adds quantitative epidemiological evidence to the clinical observation that liver disease is a risk factor for lichen planus although not a specific marker of it.**

COMMENTS

Lichen planus (LP) is one of the skin conditions that delight dermatologists. Since its classical description by Willan in 1869, the spectrum of this flat-topped, shiny, violaceous eruption of polygonal papules, symmetrically distributed and surmounted by fine white linear striations, has been expanded with a splendid array of elaborately descriptive terminology by many authors. The sun-induced *LP actinicus,* and the blistering from *LP pemphigoides* are aptly named, as are *LP annularis*

and *LP atrophicus*. *LP follicularis* involves primarily the hair follicles, whereas *LP hypertrophicus* is a thickened variant that occurs primarily on the lower legs. Other forms include *LP planopilaris, LP tropicus, LP subtropicus, guttate LP, LP pigmentosus, LP linearis* and *LP erythrodermicus*. Some astute observers have even reported *"invisible LP"*. To further color this eruption, distinguished names such as Max Joseph, Wickham, Koebner, Nekam and Brocq have been associated with various clinical or histological features of the disease.

Because of the broad spectrum of this disease, clinical diagnosis, at times, can be difficult. Fortunately, the histological findings in developed lesions of LP are distinctive, showing a dense, bandlike infiltrate of predominantly T lymphocytes at the dermoepidermal junction and epidermal changes, including degeneration of basal cells, hyperkeratosis, and irregular hypergranulosis.

The cause of LP remains unknown. There appears to be a genetic predisposition in some patients as evidenced by reports of familial cases and the occurrence of human leukocyte antigen DRI in 80% of LP patients compared with 25% of control subjects (1).

Cutaneous eruptions similar to LP can occur with exposure to gold, certain drugs (mepacrine, para-amino salicylic acid and streptomycin, for example) and, strangely, after contact with developers used in processing color photographs. More recently, the description of LP eruptions in the chronic phase of graft-versus-host disease has restimulated interest in a possible autoimmune pathogenesis of this disease, further supported by the occurrence of LP in patients with lupus erythematosus, vitiligo and alopecia areata. Despite these indications, the cause of LP for most patients remains a mystery.

Dermatologists have also attempted to link other medical disorders with this fascinating eruption, and the growing list of associated conditions includes ulcerative colitis, thymoma, myasthenia gravis and hypogammaglobulinemia. The liver and its diseases are, at present, under scrutiny. Initially described in patients with PBC receiving D-penicillamine therapy (2), LP was subsequently reported in PBC patients unrelated to therapy (Graham-Brown RAC, et al. Lancet 1981;2:1046, Correspondence), although this association was recognized to occur only rarely (7 of 268 patients with PBC developed LP unrelated to therapy) (3).

Investigators from Italy, however, reported a startling 13.5% of patients affected by LP who did not have PBC but rather CAH (4). This strong association could not be confirmed by investigators from Sweden (5), the United Kingdom (Monk B. J Am Acad Dermatol 1985;12:122-123, Correspondence) or the United States (Powell FC, et al. J Am Acad Dermatol 1984;10:840-841, Correspondence). This paper is an additional study suggesting an association between LP and "liver disease." It comes from 27 predominantly northern Italian outpatient dermatology departments and involves 56 regional coordinators. Although this study is thought provoking, it fails to provide solid evidence of an association between LP and hepatic disorders.

A number of questions must be raised about this study and its results. Of the 577 LP patients studied, histological confirmation of the diagnosis was required only in certain subsets, with the crucial diagnosis of cutaneous disease accepted on clinical features alone for most patients, a totally unsatisfactory basis for patient selection. Information was then obtained from these patients and 1,031 control subjects by interviewers with "biomedical training" using a structured questionnaire. Analysis of the questionnaire results revealed that patients with LP had more "liver complaints requiring a specialist consultation," more frequent history of acute viral hepatitis and more liver biopsies, although information relating to history of liver biopsy was missing for 31 of the control subjects.

Unfortunately, the kinds of "liver complaints" related by these patients are not defined. The patients' criteria for the diagnosis of acute viral hepatitis are not listed, and the reason why liver biopsies were carried out is unclear. In a previous report (6), one of the participants in this study described liver biopsy findings in some patients with LP. Inclusion of LP patients being investigated in a unit interested in this possible association would naturally affect these results. Indeed, it would be important to know whether previously identified patients with LP and liver disease (6; Rebora A, et al. J Am Acad Dermatol 1985;12:123-124, Correspondence) are included in this investigation. If so, the data could be recalculated excluding such patients. The findings on liver biopsy in the 16 LP patients included 5 who had fatty infiltration of the liver and only 3 with CAH. The conclusion that "a history of having had a liver biopsy gave an estimated risk of LP of about 5," seems unjustified on the basis of such scanty data.

Levels of ALT and AST activities were elevated more often in the LP group, but no details of concomitant drug therapy, alcohol exposure or other medical conditions in the patients with elevated levels are given, so the significance of these abnormal findings is impossible to evaluate. Twenty-six of the 561 LP patients tested (4.6%) were positive for HBsAg, a finding appreciably higher than control subjects in this report, but far lower than the occurrence of 34% positivity for one or more hepatitis B virus markers in the population of Genoa cited by one of the coauthors of this study in previously published correspondence (Rebora A, Rongeoletti F. J Am Acad Dermatol 1985;12:123-124, Reply), and a center for recruitment of patients for this study.

It is noteworthy, in this regard, that in six contributing centers, only one control patient was selected for each of 123 patients, a factor that could be significant because the frequency of HBsAg positivity seems to vary significantly with the Italian population.

What does this study tell us about the association of LP and liver disease? Unfortunately, very little. As the authors themselves state, "liver disease" was a "poorly defined entity," and a selection of abnormal blood tests or the history of having had a liver biopsy is no substitute for clearly identified disease criteria. The suggestion that LP could be caused by a "stereotypic

cell-mediated reaction to either a specific virus or several viruses, some of them hepatotropic" is unwarranted on the evidence provided. In the authors' own words, these data are "too vague or speculative" to provide any real insight into the enigma of the relationship of lichen planus and hepatic disease.

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REFERENCES

1. Powell FC, Rogers RS, Dickson ER, Moore SB. An association between HLA DRI and lichen planus. Br J Dermatol 1986;114: 473-478.
2. Seehafer JR, Rogers RS, Fleming CR, Dickson ER. Lichen planus–like lesions caused by penicillamine in primary biliary cirrhosis. Arch Dermatol 1981;117:140-142.
3. Powell FC, Rogers RS, and Dickson ER. Primary biliary cirrhosis and lichen planus. J Am Acad Dermatol 1983;9:540-545.
4. Rebora A, Rongioletti F, Canepa A. Chronic active hepatitis and lichen planus. Acta Dermatol 1982;62:351-352.
5. Mobacken H, Nilsson LA, Olsson R, Sloberg K. Incidence of liver disease in chronic lichen planus of the mouth. Acta Derm Venerol (Stockh) 1984;64:70-73.
6. Rebora A, Rongioletti F. Lichen planus and chronic active hepatitis: a retrospective study. Acta Derm Venerol (Stockh) 1984;64:52-56.

HOW DOES ENDOSCOPIC SCLEROTHERAPY ALTER SPLANCHNIC HEMODYNAMICS?

Bourbon P, Zarski JP, Kitmacher P, Bourlard P, Machecourt J, Denis B, Rachail M. Esophageal varice sclerotherapy: influence on portal pressure and azygos blood flow. Gastroenterol Clin Biol 1990;14:244-247.

ABSTRACT

Endoscopic sclerotherapy is widely employed for esophageal variceal hemorrhage. However it has side effects and can aggravate portal hypertension by suppression of portosystemic shunt. The purpose of the present investigation was to study the effect of variceal thrombosis on hepatic venous pressure gradient and azygos blood flow. Eight alcoholic cirrhotic patients with a first variceal hemorrhage were included. According to Child Pugh's classification, 4 patients were group A, 2 group B and 2 group C. At each session 40 to 60 ml of 1 p. 100 polidocanol were injected into the varices. A hemodynamic study was performed in each patient before and about 1 week after variceal obliteration (mean 3.3 procedures). Mean value of hepatic venous pressure gradient was 16.6 ± 5.5 mm Hg and 17.0 ± 3.8, respectively, before sclerotherapy and after eradication of varices; azygos blood flow 663 ± 506 ml/min before and 682 ± 522 after; cardiac output was 6.5 ± 0.7 ml/min before and 6.5 ± 0.8 after. None of these differences were significant. These results suggest that endoscopic sclerotherapy using polidocanol does not change hepatic venous pressure gradient and azygos blood flow, and does not lower blood flow through the gastroesophageal collaterals draining into the azygos vein. This is consistent with the hypothesis that thrombosis remains localized.

COMMENTS

In his first report of endoscopic sclerotherapy (EST) of esophageal varices (EV) in 1947, Moersch suggested that EST may increase the risk of bleeding from gastric varices, and he considered that the presence of gastric fundal varices was a contraindication to the use of EST. Since then, the potential hazard of EST in aggravating the consequences of portal hypertension has been debated. The hypothesis is that EST, by occluding EV and, perhaps, para-EV, could thereby reduce the collateral vessels that shunt blood from the gastric veins. Another hazard of EST that has been suggested is the occurrence of thrombosis in a major vessel of the portal venous system, which could increase the portal venous pressure.

Bourbon et al. suggested, in the work under discussion, that EST using polidocanol did not significantly alter the hepatic venous pressure gradient and azygos blood flow in eight patients with alcoholic cirrhosis who had recently bled from ruptured EV. This interesting study deserves several comments. First, no control group existed. As stated by the authors, this was not thought possible for ethical reasons. However, it greatly limits the conclusions achievable because it has been suggested that a progressive decrease in portal pressure occurs after a bleeding event (1) and that portal venous pressure falls spontaneously in alcoholic cirrhotic patients who have not bled from varices, especially in those patients who abstained from alcohol (2). Second, the number of patients is low, and large intraindividual variations were observed (e.g., portal venous pressure fell by 59% in one patient. Third, the use of the thermal dilution method for prolonged periods to detect chronic variations in azygos blood flow has not been established. This measurement is technically difficult, and the displacement of the catheter between serial measurements may introduce methodological errors because it is not clear that blood flow is measured in precisely the same way. Finally, the authors' results cannot be extrapolated to those with other sclerosing agents because it has been suggested that EST with ethanolamine decreases azygos blood flow by almost one fourth after eradication of EV (3). It has also been suggested that ethanolamine is superior to polidocanol for the eradication of EV and the prevention of rebleeding (4), even though it has also been suggested that the recurrence of EV in patients receiving EST with ethanolamine is caused by incomplete obliteration of the venous feeders of the varices (5).

In three other studies, EST did not significantly alter portal venous pressure (6). On the other hand, several reports have noted gastric or ectopic variceal bleeding after EST (6), and it has been suggested that EST significantly increases the prevalence of large spleno-