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ORIGINAL ARTICLE

Hepatic Steatosis is the Most Common Finding in Abdominal Ultrasonography Performed in Patients with Psoriasis before Biological Agent Treatment

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Abstract: *Psoriasis has been associated with metabolic syndrome and nonalcoholic fatty liver disease. We wanted to investigate the abdominal ultrasonography results of psoriasis patients before biological agent treatment. Between April 2019 and February 2022, abdominal ultrasonography results of psoriasis patients which were performed before biological agent treatment were reviewed retrospectively. This study included 90 patients, 45 females, and 45 males with a mean age of 48.91±13.43 years. The most common ultrasonography finding was increased echogenicity of the liver parenchyma due to steatosis (58.9%) which was followed by an increase in liver size (25.6%), kidney cysts (17.8%), gallstones (8.9%) and increase in spleen size (7.8%). Hepatic steatosis was more frequent in older patients (p<0.001), patients with diabetes (p=0.007), and patients who were previously treated with biological agents (p=0.007). 70.4% of the patients with moderate or severe hepatic steatosis were female. Herein, hepatic steatosis was detected in 53 (58.9%) patients. Nonalcoholic fatty liver disease which presents as hepatic steatosis in early stages has an asymptomatic course and poor prognosis in psoriasis patients. We suggest that abdominal ultrasonography should be performed in psoriasis patients before biological agent treatment, especially in females, patients with advanced age, patients who were previously treated with biological agents, and patients with diabetes.*

Keywords: *abdomen; biological agents; hepatic steatosis; psoriasis; ultrasonography*

INTRODUCTION

Psoriasis is a systemic inflammatory disorder that primarily affects the skin and may present with various comorbidities such as psoriatic arthritis, nonalcoholic fatty liver disease, diabetes, metabolic syndrome, and inflammatory bowel disease [1]. Tumor necrosis factor-α (TNF-α), interleukin-17 (IL-17), and IL-23 are the cytokines mainly responsible for the inflammation in psoriasis [2]. Chronic inflammation has been implicated in the development of accompanying comorbidities. On the other hand, non-alcoholic fatty liver disease which is an important comorbidity of psoriasis due to its risk of progressing to cirrhosis has been associated with the development of severe psoriasis since it may lead to inflammatory cytokine production from the liver [3]. Biological agents affect specific pathways of the immune system that are implicated in the etiopathogenesis of psoriasis. Several biological agents have been developed and successfully used for the treatment of psoriasis. It has been suggested that biological agents were more effective and safer than conventional systemic treatments of psoriasis which lead to a broad immunosuppressive activity [4]. However, some safety concerns have been raised due to the widespread and long-term use of biological agents. Hepatotoxicity, reactivation of hepatitis B and latent tuberculosis infection, exacerbation of inflammatory bowel disease, and invasive fungal infections have been reported in psoriasis patients treated with biological agents. Side effects vary on each biological agent received [5]. For instance, administration of TNF-α inhibitors for long periods may lead to weight gain which has a negative impact on nonalcoholic fatty liver disease in patients with psoriasis [6].

Furthermore, it is controversial whether biological agent treatment increases the risk of malignancy in patients with psoriasis or not. Fiorentino et al. reported that the risk of malignancy might be increased in patients with psoriasis treated with TNF-α inhibitors for longer than a year [7]. On the

other hand, Mastorino et al. stated that the use of biological agents affecting TNF-α, IL-17, IL-12, and IL-23 for the treatment of psoriasis was safe even in patients with a past medical history of malignancy [8]. It has been suggested that abdominal ultrasonography might be performed in patients with psoriasis before the initiation of treatment with biological agents to exclude intraabdominal malignancy such as lymphoma and it might be repeated during the treatment [9]. However, abdominal ultrasonography is not included as a pretreatment test to be performed in psoriasis patients before the initiation of biological agents in major guidelines such as Joint American Academy of Dermatology – National Psoriasis Foundation (AAD-NPF) guidelines of care for the management and treatment of psoriasis with biologics and EuroGuiDerm guideline on the systemic treatment of psoriasis vulgaris [10, 11].

Within this study, we aimed to evaluate abdominal ultrasonography results of patients with psoriasis which were performed before the initiation of biological agent treatment**.**

MATERIALS AND METHODS

Gazi University Ethics Committee approval was obtained before this study (approval number: 2022-264). Between April 2019 and February 2022, medical records of patients with psoriasis who underwent abdominal ultrasonography before biological agent treatment were evaluated retrospectively. Psoriasis type, disease duration, psoriasis treatment, accompanying psoriatic arthritis, and systemic diseases were reviewed. All patients with psoriasis aged 18 years and over with complete data have been included in the study.

Statistical analysis was performed using SPSS version 20.0. Quantitative variables were represented as mean ± standard deviation or median and interquartile range, categorical variables were represented as counts and percentages. Kolmogorov-Smirnov test was used to determine whether variables were normally distributed or not. Differences in variables between the two groups were evaluated by chi-square test, independent sample t-test, and Mann-Whitney U test. P values less than 0.05 were considered statistically significant.

RESULTS

This study included 90 patients, 45 females and 45 males. The mean age of the patients was 48.91±13.43 years (range: 19-75 years). 79 (87.8%) patients had psoriasis vulgaris, 8 (8.9%) patients had generalized pustular psoriasis, and 3 (3.3%) patients had palmoplantar psoriasis. The mean disease duration was 19.35±11.93 years (range: 2-53 years). The median Psoriasis Area and Severity Index (PASI) was 7.2 (11.4) [12]. Psoriatic arthritis was detected in 34 (37.8%) patients. 34 (37.8%) patients were treated with ustekinumab, 29 (32.2%) patients were treated with IL-17 inhibitors such as secukinumab and ixekizumab, 23 (25.6%) patients were treated with TNF-α inhibitors such as adalimumab, infliximab and certolizumab pegol, 4 (4.4%) patients were treated with IL-23 inhibitors such as risankizumab and guselkumab. All patients previously received conventional treatments such as acitretin, cyclosporine, and methotrexate. 15 (16.7%) patients were previously treated with phototherapy. 37 (41.1%) patients were previously treated with biological agents whereas 53 (58.9%) patients were biologic-naive. None of the patients stated excessive alcohol consumption. Past medical history was unremarkable in 48 (53.3%) patients. However, 23 (25.6%) patients had hypertension, 17 (18.9%) patients had diabetes, 4 (4.4%) patients had chronic obstructive pulmonary disease, 4 (4.4%) patients had asthma, 4 (4.4%) patients had hypothyroidism, 4 (4.4%) patients had chronic hepatitis B virus infection, 3 (3.3%) patients had chronic kidney disease, 3 (3.3%) patients had coronary artery disease, 1 (1.1%) patient had nephrolithiasis, 1 (1.1%) patient had villous adenoma of the colon. In addition, 1 (1.1%) patient had a history of testicular seminoma, 1 (1.1%) patient had cervical cancer, and 1 (1.1%) patient had urothelial carcinoma.

Abdominal ultrasonography revealed an increase in liver size in 23 (25.6%) patients (the mean craniocaudal length in the midclavicular line: 16.69±0.96 mm, range: 15.5-20 mm). Among the patients with increased liver size, 17 (73.9%) were female and 6 (26.1%) were male (p=0.013). Increased liver size was observed in 14 (60.9%) patients with psoriatic arthritis and in 9 (39.1%) patients without arthritis (p=0.008) (Table 1). Increased liver size was more common in patients with hypertension (10, 43.5%) compared to patients without hypertension (13, 19.4%) (p=0.023). Increased liver size was observed in 6 (35.3%) patients with diabetes and 17 (23.3%) patients without diabetes (p=0.309).

The mean psoriasis duration was 22.15±12.47 years in patients with increased liver size and 18.39±11.68 years in patients with normal liver size (p=0.185). Among the patients with increased liver size, the mean craniocaudal length was 17.03±1.10 mm in those who were biologic-naive and 16.25±0.48 mm in those who received biological agents previously (p=0.037). All patients with increased liver size showed increased echogenicity of the liver parenchyma due to steatosis. An increase in echogenicity of the liver parenchyma due to steatosis was reported in 53 (58.9%) patients [mild: 26 (28.9%), moderate: 14 (15.6%), severe: 13 (14.4%)]. The mean age of the patients with and without increased echogenicity of the liver parenchyma due to steatosis was 53.62±11.71 years and 42.16±12.99 years, respectively (p<0.001).

Table 1: Patients with increased liver size and increased echogenicity of the liver parenchyma

	Increased liver size		P value
Patient characteristics (n, %)	Female (17, 73.9)	Male (6, 26.1)	0.013
	With psoriatic arthritis (14, 60.9)	Without psoriatic arthritis (9, 39.1)	0.008
	With hypertension (10, 43.5)	Without hypertension (13, 19.4)	0.023
Craniocaudal length (mm, mean±SD)	Biologic-naïve (17.03±1.10)	Previous biologic (16.25±0.48)	0.037
	Increased echogenicity of the liver parenchyma due to steatosis		
Patient characteristics (n, %)	Previous biologic (28, 75.7)	Biologic-naïve (25, 47.2)	0.007
	With diabetes (15, 88.2)	Without diabetes (38, 52.1)	0.007
Moderate/severe (n, %)	Female (19, 70.4)	Male (8, 29.6)	0.021

SD: Standard deviation. Increased liver size was more common in patients with psoriatic arthritis and hypertension. Moderate or severe increase in the echogenicity of the liver parenchyma due to steatosis was more common in female patients.

Among the patients with increased echogenicity of the liver parenchyma due to steatosis, 28 (75.7%) received biological agents previously and 25 (47.2%) were biologic-naive (p=0.007). Increased echogenicity of the liver parenchyma due to steatosis was detected in 15 (88.2%) patients with diabetes and in 38 (52.1%) patients without diabetes (p=0.007). Among the patients with a moderate or severe increase in the echogenicity of the liver parenchyma due to steatosis, 19 (70.4%) were female and 8 (29.6%) were male (p=0.021). In addition, heterogeneous liver parenchyma was reported in 5 (5.6%) patients, hypoechoic areas in the liver which might be compatible with focal fatty sparing in 4 (4.4%) patients, liver cyst in 3 (3.3%) patients, hyperechoic liver lesions which might be compatible with hemangioma in 3 (3.3%) patients and Chilaiditi syndrome was reported in 1 (1.1%) patient.

Moreover, gallstones were detected in 8 (8.9%) patients (the mean diameter: 15±7.05 mm, range: 3-20 mm) and gallbladder polyps in 3 (3.3%) patients (the mean diameter: 4.5±0.5 mm, range: 4-5 mm). Among the patients with gallstones and gallbladder polyps, 7 (63.6%) were female and 4 (36.4%) were male (p=0.141). The mean age was 53.73±13.32 years in patients with gallstones and gallbladder polyps and 48.24±13.40 years in those who had neither (p=0.094). Gallbladder wall thickening (4 mm) and echogenicities in the gallbladder wall (cholesterolosis) were detected in 1 (1.1%) patient. An increase in the transverse diameter of the gallbladder (42 mm) and accompanying gallbladder wall thickening (6 mm) were detected in 1 (1.1%) patient. Furthermore, kidney cysts were detected in 16 (17.8%) patients (the mean diameter: 26.5±15.8 mm, range: 8-50 mm). Increased echogenicity of kidney parenchyma was detected in 5 (5.5%) patients. The mean ages of the patients with and without kidney cysts were 56.81±7.54 years and 47.20±13.85 years, respectively (p=0.008). Kidney stones were detected in 4 (4.4%) patients (the mean diameter: 7.5±5.8 mm, range: 3-16 mm). Lobulated kidney contour was detected in 4 (4.4%) patients. Dilated renal collecting system was detected in 3 (3.3%) patients, focal caliectasis was detected in 1 (1.1%) patient, increase in kidney size was detected in 1 (1.1%) patient, decrease in kidney size was detected in 1 (1.1%) patient and a renal angiomyolipoma was detected in 1 (1.1%) patient. Abdominal ultrasonography also revealed increase in spleen size in 7 (7.8%) patients (the mean craniocaudal length: 13.87±1.05 mm, range: 13-16 mm), accessory spleen in 2 (2.2%) patients, splenic cyst with a diameter of 7 mm in 1 (1.1%) patient, situs inversus totalis in 1 (1.1%) patient, calcifications in prostatic parenchyma in 1 (1.1%) patient, heterogeneous prostatic parenchyma in 1 (1.1%) patient, an ovarian cyst measured 33x27 mm in size in 1 (1.1%) patient, uterine myoma with a diameter of 11 mm in 1 (1.1%) patient, increased bladder wall thickness (6 mm) in 1 (1.1%) patient, echogenic debris within the bladder which might be compatible with urinary tract infection in 1 (1.1%) patient (Table 2).

Based on ultrasonography findings, abdominal computed tomography (CT) was performed in 3 (3.3%) patients for further evaluation of kidney cysts and abdominal magnetic resonance imaging (MRI) in 2 (2.2%) patients for hypoechoic liver lesions and liver cysts. Renal scintigraphy was performed in 1 (1.1%) patient for the dilation of the renal collecting system.

DISCUSSION

Within this study, the most common abdominal ultrasonography finding in patients with psoriasis was increased echogenicity of the liver parenchyma due to steatosis (58.9%). Hepatic steatosis was more frequent in older patients, patients with diabetes, and patients who were previously treated with biological agents (p<0.001, p=0.007, p=0.007, respectively). These results may be related to the fact that patients previously treated with biologic agents were older than biologic-naive ones (p=0.021). In addition, increased echogenicity of the liver parenchyma due to steatosis was moderate or severe in 50.9% of the patients and

most of these patients (70.4%) were female. An increase in liver size (25.6%) was the other common abdominal ultrasonography finding followed by kidney cysts (17.8%), gallstones (8.9%), and an increase in spleen size (7.8%). The increased liver size was statistically significantly more prevalent in female patients, and patients with psoriatic arthritis and hypertension (p=0.013, p=0.008, p=0.023, respectively).

Table 2: Abdominal ultrasonography findings in patients with psoriasis before biological agent treatment

	Patients n (%)	Mean size±SD (mm)	Range (mm)
Increased liver parenchyma echogenicity	53 (58.9)		
Increased liver size	23 (25.6)	16.69±0.96	15.5-20
Kidney cysts	16 (17.8)	26.5±15.8	8-50
Gallstones	8 (8.9)	15±7.05	3-20
Increased spleen size	7 (7.8)	13.87±1.05	13-16
Increased kidney parenchyma echogenicity	5 (5.6)		
Heterogeneous liver parenchyma	5 (5.6)		
Kidney stones	4 (4.4)	7.5±5.8	3-16
Lobulated kidney contour	4 (4.4)		
Hypoechoic areas in the liver	4 (4.4)		
Liver cyst	3 (3.3)		
Liver hemangioma	3 (3.3)		
Gallbladder polyps	3 (3.3)	4.5±0.5	4-5
Dilated renal collecting system	3 (3.3)		
Accessory spleen	2 (2.2)		
Gallbladder wall thickening	2 (2.2)		
Echogenicities in the gallbladder wall	1 (1.1)		
Focal caliectasis	1 (1.1)		
Echogenic debris within the bladder	1 (1.1)		
Increased kidney size	1 (1.1)		
Decreased kidney size	1 (1.1)		
Renal angiomyolipoma	1 (1.1)		
Increased bladder wall thickness	1 (1.1)		
Splenic cyst	1 (1.1)		
Uterine myoma	1 (1.1)		
Ovarian cyst	1 (1.1)		
Heterogeneous prostatic parenchyma	1 (1.1)		
Calcifications in the prostatic parenchyma	1 (1.1)		
Chilaiditi syndrome	1 (1.1)		
Situs inversus totalis	1 (1.1)		

SD: Standard deviation. An increase in echogenicity of the liver parenchyma due to steatosis was the most common abdominal ultrasonography finding in patients with psoriasis.

Data on abdominal ultrasonography findings in patients with psoriasis treated with biological agents are scarce. Raudonis et al. reported that hepatic and pancreatic steatosis, hepatomegaly, kidney cyst, splenomegaly, gallbladder polyp, and pancreatic stiffness were commonly detected findings in abdominal ultrasonography which were annually performed in patients with psoriasis treated with infliximab, etanercept, and ustekinumab. Among them, hepatic steatosis (12.7%) and pancreatic steatosis (12.7%) were the most common [13].

Nonalcoholic fatty liver disease is a metabolic disorder that may present with steatosis, and nonalcoholic steatohepatitis and may result in cirrhosis or hepatocellular carcinoma [14-16]. Advanced age and diabetes are the risk factors for the development of nonalcoholic fatty liver disease, whereas the

effect of gender on disease remains controversial [17]. In addition, nonalcoholic fatty liver disease is more common in psoriasis patients with a prevalence of up to 65% compared to the general population [15]. Furthermore, poor prognosis has been reported in patients with nonalcoholic fatty liver disease accompanied by psoriasis [14,15]. Dermatologists are recommended to perform abdominal ultrasonography for screening fatty liver in patients with psoriasis, particularly in those who have metabolic syndrome even without elevated liver enzyme levels [6]. Dermatologists must determine accompanying nonalcoholic fatty liver disease in patients with psoriasis to choose appropriate treatment options. Dermatologists should also encourage patients for lifestyle changes or refer them to a gastroenterologist if needed [16]. For instance, Campanati et al. suggested that weight gain during anti-TNF-α treatment might increase the risk of hepatic fibrosis in psoriasis patients with nonalcoholic fatty liver disease [18]. Medications that may contribute to steatosis should be omitted in these patients. However, no specific treatment has been reported or primarily recommended for the treatment of psoriasis patients with nonalcoholic fatty liver disease [16]. On the other hand, TNF-α inhibitors such as adalimumab, etanercept, and infliximab may lead to hepatotoxicity. Among them, infliximab was the most commonly implicated one in the development of adverse effects on the liver such as jaundice, hepatitis, acute liver failure, cholestasis, and autoimmune hepatitis [19]. Even mild and rare, hepatotoxicity has been detected in patients who received ustekinumab [20].

Abdominal ultrasonography may be useful in patients with psoriasis since psoriasis has been associated with nonalcoholic fatty liver disease or intraabdominal malignancies such as hepatocellular carcinoma, gastric cancer, bladder cancer, lymphoma of the stomach and colon adenocarcinoma [21,22]. Intraabdominal malignancy and infections have also been reported in patients who received biological agents for the treatment of psoriasis. For instance, Nosotti et al. reported a 59-year-old male patient with psoriasis treated with adalimumab and diagnosed with B cell lymphoma with gastric, splenic, hepatic, abdominal lymph node, and vertebral involvement. Nosotti et al. suggested that the risk for the development of abdominal lymphoma should be kept in mind in patients with psoriasis under biological agent treatment. Nosotti et al. recommended performing abdominal ultrasonography before and during biological agent treatment for psoriasis [9]. Fortaleza et al. reported a 43-year-old male patient with psoriasis who developed splenic tuberculosis under infliximab treatment. Fortaleza et al. stated that close follow-up of patients treated with TNF-α inhibitors on the risk for extrapulmonary tuberculosis and disseminated tuberculosis was crucial [23]. Bud et al. reported peritoneal tuberculosis in a 32-year-old patient who received adalimumab for the treatment of psoriasis vulgaris. The patient had multiple splenic lesions on computed tomography of the abdomen and underwent surgery due to an initial diagnosis of a possible malignancy. Bud et al. suggested that Quantiferon test, abdominal ultrasonography, and computed tomography might be performed to exclude intestinal tuberculosis in patients with gastrointestinal symptoms treated with TNF-α inhibitors [24].

CONCLUSIONS

We suggest that patients with psoriasis should undergo abdominal ultrasonography before biological agent treatment not only to exclude intraabdominal malignancy and infections but also to determine hepatic steatosis. It should be kept in mind that nonalcoholic fatty liver disease has an asymptomatic course and poor prognosis in patients with psoriasis. Since lifestyle modification and weight loss can reverse early stages of nonalcoholic fatty liver disease such as steatosis [25], early detection of hepatic steatosis is crucial in the treatment of patients with psoriasis. Therefore, we suggest that abdominal ultrasonography should be performed in patients with psoriasis before biological agent treatment, especially in females, patients with advanced age, patients who were previously treated with biological agents, and patients with comorbidities such as diabetes. In addition, considering the high frequency of nonalcoholic fatty liver disease in patients with psoriasis, the most appropriate biological agent treatment should be determined in this population and stated in psoriasis treatment guidelines.

Conflicts of interest and sources of funding

The authors declare no conflict of interest. This research received no external funding.

Authors' contribution

Conceptualization, F.T., O.A., M.P., E.A.; methodology, F.T.; software, F.T.; validation, F.T., O.A., M.P., E.A.; formal analysis, F.T.; investigation, F.T., O.A.; resources, F.T., O.A., M.P., E.A.; data curation, F.T., O.A., M.P., E.A.; writing-original draft preparation, F.T.; writing-review and editing, M.P., E.A.; visualization, F.T.; supervision, M.P., E.A.; project administration, F.T., O.A., M.P., E.A. All authors have read and agreed to the published version of the manuscript.

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki, and local ethics committee approval for this study was obtained from Gazi University (approval number: 2022-264).

Patient consent for publication

Informed consent was obtained from all subjects involved in the study.

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