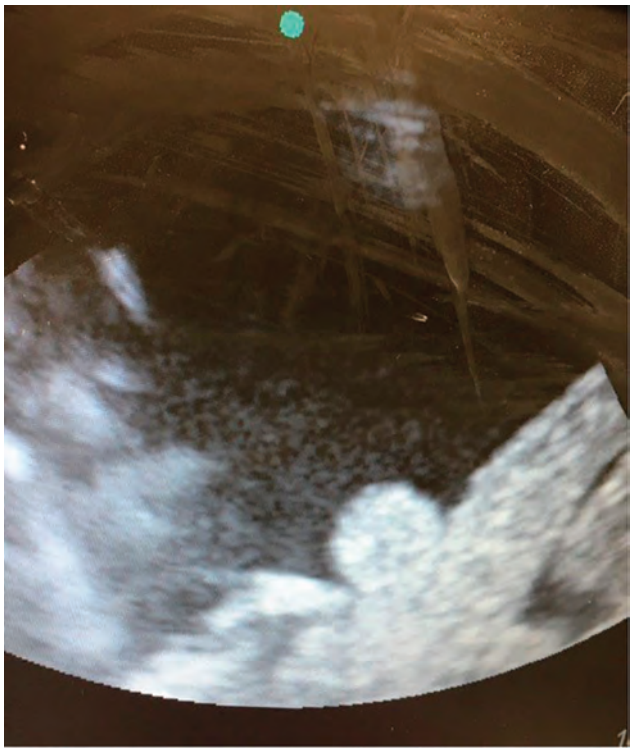
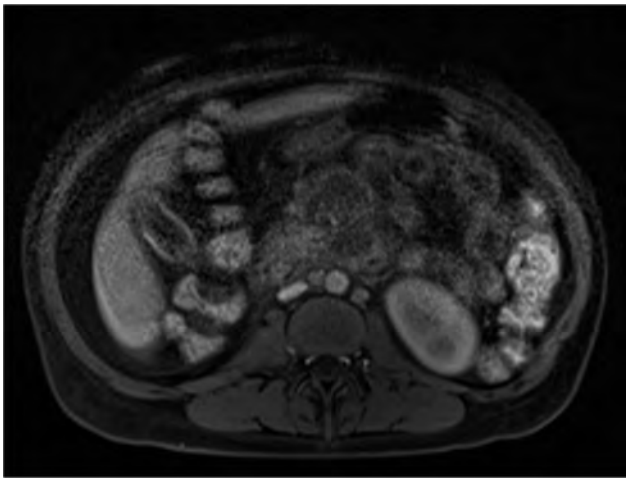


[2372A] Ascites visualized on ultrasound imaging.

[2372B] Extraction of chylous abdominal fluid on bedside paracentesis.



[2372C] Necrotic mesenteric adenopathy as nidus for chylous ascites.

2373

Kava Kava, Not for the Anxious: A Case of Fulminant Hepatic Failure After Kava Kava Supplementation

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A 28 female without significant past medical history presented as a transfer to our tertiary referral center for acute liver failure. She presented to her primary care clinic with a two-week history of dark colored urine, nausea, and right upper quadrant abdominal pain. The patient reported no alcohol intake and denied risk factors for viral hepatitis. Over the past year, she had been drinking Kava root tea daily for anxiety. She was found to be jaundiced with a hepatocellular pattern of liver dysfunction. Her total bilirubin was 12 mg/dL and liver enzymes peaked at an AST of 2400 U/L, ALT of 3000 U/L, and alkaline phosphatase of 183 U/L. Unfortunately, during the workup she developed alerted mental status, slurred speech, and epigastric abdominal pain and was hospitalized for evaluation. She was found to have acute liver failure with grade 2 hepatic encephalopathy and coagulopathy with a peak INR of 3.58. Viral serology was negative as well as plasma acetaminophen levels. An abdominal ultrasound revealed normal liver morphology with normal flow in the hepatic vessels. She was transferred and subsequently underwent urgent evaluation for liver transplantation. She required extracorporeal liver support with molecular absorbent recirculation system (MARS) therapy as a bridge to transplant. Ten days following transfer from the outside facility and twenty-nine days following symptom onset, she received orthotopic liver transplantation. Post-transplant course was uncomplicated and the patient was discharged five days later. Acute liver failure is a life threatening critical condition that may occur in patients without underlying liver pathology. Drug induced liver injury (DILI) is the most common cause of acute liver failure in the United States and incidence is rising. Approximately 2-11% of patients with DILI reported taking non-FDA regulated herbal supplements as adjunctive therapy. One such product is Kava kava, which is derived from the roots of the plant *Piper methysticum* and has an active relaxing property due to kavalactones. Supplements containing this derivative are marketed to treat anxiety and insomnia. The exact incidence of clinically apparent liver injury due to kava kava remains unknown and the pathophysiology underlying the subsequent hepatotoxicity is unclear. Further investigation remains to elucidate the underlying mechanism of injury. This case highlights the increasing concern in the US for herbal hepatotoxicity induced acute liver failure.

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Spontaneous Rupture of Hepatocellular Carcinoma in a Non-Cirrhotic Patient Managed by Robot-Assisted Hepatectomy: A Case Report

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A 65 year-old woman with a history of diabetes presented with a sudden onset of sharp abdominal pain. There was no history of trauma. Abdominal examination revealed tenderness and rebound guarding on the right side; laboratory tests were unremarkable (Table). Computed tomography scan of abdomen showed a heterogeneously hypodense mass in hepatic segment V (Figure A). A contrast-enhanced magnetic resonance imaging (MRI) further characterized the mass as a T2 hyperintense lesion with an arterial enhancement but no washout (Figure B). Surgery revealed a ruptured bleeding mass and she underwent a robot-assisted partial hepatectomy. Pathology was consistent with moderately differentiated hepatocellular carcinoma (HCC) with disrupted capsular surface, without evidence of fibrosis or steatosis (Figure C). She remains recurrence-free, and follows with surveillance cross-sectional imaging every 3 months without need for chemotherapy. HCC is the seventh most commonly diagnosed malignancy and the sixth leading cause of cancer deaths in women worldwide. It is commonly associated with cirrhosis, but can also occur in patients with non-alcoholic fatty liver disease and hepatitis B in the absence of liver fibrosis. Spontaneous rupture of HCC is a rare complication with an incidence of only 3% but with mortality ranging from 25-100%2. Physical exam and laboratory findings can be nonspecific. Transarterial embolization (TAE) is performed if the patient has ongoing bleeding. Emergency hepatectomy or staged hepatectomy following TAE leads to significantly better survival than TAE alone3.The median survival is significantly better in non-cirrhotic patients (20 months)3. This is the first case of ruptured HCC in a non-cirrhotic patient with no known risk factors managed by robot-assisted hepatectomy. 1. Yoshida H, MamadaY, Taniai N, and Uchida E. (2016) Spontaneous ruptured hepatocellular carcinoma. Hepatol Res, 46: 13–21.

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ACUTE SEVERE PSYCHOSIS FOLLOWING TESTOSTERONE SUBSTITUTION IN KLINEFELTER SYNDROME

I. Püntmann, H. Wille, B. Mühlbauer

Male Klinefelter Syndrome (KS) is implicated with hypogonadism, and testosterone substitution is used around puberty to prevent physical and psychological sequelae. Individuals diagnosed with KS in adult age may also benefit from testosterone substitution. Intramuscular injection of depot formulations is the most common form of testosterone substitution in accordance to the patient's clinical appearance. Assessment of testosterone and luteinizing hormone serum levels is recommended before but not on a regular basis during treatment. Adverse effects associated with androgen substances should lead to dose reduction. Psychotic disorders have been described for both KS and long term administration of testosterone.

We report the case of an 18 year old adolescent with KS (47, XXY), who developed a dramatic aggressive and paranoid personality change within hours after the first testosterone injection. Symptoms vanished slowly resulting in a reactive depression with suicidal attempts. Similar psychotic reactions occurred following the next two injections resulting in delinquency (fire setting). After intensive inhouse psychiatric treatment and discontinuation of the hormone replacement the patient is now following normal life activities.

Side effects of anabolic steroids include aggressiveness and induction of manic or psychotic episodes. So far, such effects have been reported for long term hormone application while acute psychotic effects have been ascribed to androgen intoxication. As stated above, KS in itself may be associated with neuropsychological disorders. Since no hostile or psychotic attitudes were noted before substitution, testosterone may have increased the patient's specific susceptibility to develop psychotic disorder.

Though testosterone administration is of benefit in KS males, it may also induce psychological symptoms, especially if dosage is not adjusted to the individual situation.

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DIABETES MELLITUS AND THYREOIDITIS IN A PEDIATRIC PATIENT DURING THERAPY FOR CHRONIC HEPATITIS C WITH PEGYLATED INTERFERONE-α AND RIBAVIRIN

D. Langheit, H. Wille, B. Mühlbauer

Treatment of chronic hepatitis C in children with interferon (IFN)-alpha monotherapy yielded poor results in the past. In clinical trials, combined treatment with ribavirin is studied. IFN-alpha therapy may be associated with a number of immunological adverse events, including various forms of autoimmune disease, e.g. Hashimoto thyreoiditis, autoimmune hepatitis and insulin-dependent diabetes mellitus. Several reports describe the induction of one of the autoimmune disorders above. So far Ribavirin is not associated with these adverse reactions.

We report the case of a 11-year-old girl with chronic hepatitis C infection who was treated with pegylated IFN-alpha plus ribavirin. Therapy was effective, viral load was reduced from 5.46*10E5 IU/ml (≈1100000 copies/ml) to < 600 IU/ml within two months. Nine months after the start of treatment she presented with polyuria, polydipsia and fatigue. After hospital admission insulin dependent diabetes mellitus was diagnosed. The girl had no positive family history of diabetes mellitus. Laboratory investigations revealed plasma glucose of 392 mg/dl and C-peptide level of 0.4 µg/ml (normal range 0.5-3 ng/ml). In addition, she had severe thyroid hypofunction with TSH value of 22 mU/l (normal range 0.36-5.8 mU/l) which was ascribed to autoimmune thyreoiditis, since several thyreoid autoantibodies were tested positive but had been negativ before initiation of therapy.

Although hepatitis C itself may induce immunological endocrine disorders we conclude that the time course in this case suggests a crucial role of IFN-alpha therapy in triggering autoimmune endocrine failure. To our knowledge, the coincidence of two autoimmune endocrine disorders in children during IFN-alpha therapy has not been reported before.

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FSME-IMMUNISATION-INDUCED POLYMYOSITIS

K. Boomgaarden-Brandes, H. Wille, B. Mühlbauer

Drug-induced muscle disorders are characterized by a broad clinical spectrum from asymptomatic elevation of creatine kinase to life threatening myopathies. An increasing number of drugs are suspected or identified as myotoxic. The clinical and histopathological features depend on the causative agent and individual susceptibility to a given compound. Various drugs such as non-steroidal antirheumatics, D-penicillinamin, and lipid-lowering drugs such as statins may cause myopathy. Polymyositis occurring as an adverse event, in contrast, is rare. We present a case of polymyositis following FSME-immunisation.

A 75 year-old woman was admitted to the hospital because of sudden onset of progressive bilateral weakness of the proximal extremities, arthalgia and myalgia. Symptoms occurred three days after she had seen her general practioner for FSME-immunisation with an inactivated parental vaccine. Until than the patient was well.

Clinical laboratory investigation performed on admission and the results of a muscle biopsy were consistent with polymyositis. The patient was started on corticosteroids. Symptoms subsided and the patient could be mobilised shortly thereafter. Further extensive diagnostic testing was performed. No malignancies could be detected.

Because of (1) the temporal coincidence of clinical event and vaccination and (2) lack of other plausible factors such as concurrent diseases or other xenobiotics, FSME-immunisation is thought to be the probable/ likely cause of polymyositis in this case.

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MISTLETOE-INDUCED AUTOIMMUNE-HEPATITIS

B. Mühlbauer, H. Wille, I. Püntmann

Introduction: Mistletoe (viscum album) extracts are widely used in the treatment of cancer. Therapeutic efficacy has not been proved and the mode of application is inconsistent due to the variety of products available. The more alerting should be serious adverse events occurring with mistletoe.

Case: A 40 year old woman diagnosed with adeno-carcinoma of the appendix (pT3/GIII,N0,M0,R0) received injections of aqueous solution of viscum album after resection of the tumour. Treatment was terminated after the fifth application because of local reactions at the injection sites. 4 weeks later, a 100-fold elevation of alanine aminotransferase (ALT) and a 50-fold elevation of aspartate aminotransferase (AST) were noticed, followed by a 6-fold elevation of the gamma-Glutamyltransferase (gGT). C-reactive protein, white blood cells, and alkaline phosphatase stayed within normal ranges. The patient did not complain of any clinical symptoms. Diagnosis of a virus hepatitis of either type was excluded by negative serology and PCR. Titre of antinuclear antibodies (ANCA) was highly positive (1:5120) while anti-neutrophil cytoplasmic antibodies as well as antimitochondrial antibodies (ANCA and AMA) were negative. Liver biopsy showed pericentral necrosis and signs of inflammation interpreted to be drug-induced. An autoimmune genesis was discussed as a concomitant factor. No medication other than the mistletoe extracts had been used and no travels to foreign countries had been undertaken within the last months.

Research: Only few case reports which suspected mistletoe extracts to cause hepatitis have been published. In one case lymphocyte transformation test confirmed that sarcoidosis was induced by a subcutaneous administered aqueous solution of viscum album.

Conclusion: Regarding time course and lack of other plausible factors, e.g. liver metastases, concomitant diseases, drugs and chemicals, we conclude that autoimmune hepatitis most probably/likely was triggered by mistletoe extract.

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CLINICAL VIGNETTE

Acute Hepatotoxicity: A Complication of Chaparral Ingestion

Nicholas Tangchaivang, M.D., and Rumi Cader, M.D., MPH, FACP

Case Presentation

A 65-year-old Caucasian man with no significant past medical history presented to the Emergency Department with a one week history of chills and fevers up to 39°C. He reported myalgias, nausea, anorexia, night sweats, and fatigue. He denied abdominal pain, diarrhea, melena, weight loss, or recent travel. The patient was not taking any medications, supplements, or herbals. He was seeing an acupuncturist regularly. Physical exam was notable for a temperature of 38.1°C, blood pressure of 78/58, heart rate of 130, a jaundiced general appearance, scleral icterus, dry mucous membranes, and hepatomegaly. The patient was given IV fluids with improvement in blood pressure to 116/73 and heart rate to 113.

Laboratory work-up revealed elevated liver tests with an AST of 178 U/L, ALT of 342 U/L, Total Bilirubin of 4.3 mg/dL, and Alk Phos of 257 U/L. CBC, basic metabolic panel, and INR were within the normal range. An abdominal ultrasound revealed an enlarged liver with mild perihepatic ascites and marked gallbladder wall thickening with no evidence of cholecystitis. A CT abdomen and pelvis with contrast confirmed these findings. There was no evidence of drainable fluid collections.

IV fluid resuscitation was continued. Empiric antibiotics were not given due to a lack of an infectious source, normal WBC, and hemodynamic stability following fluid resuscitation. Hepatitis A, Hepatitis B, and Hepatitis C serologies were negative. Serum IgG 4 and smooth muscle antibody were both negative, effectively ruling out autoimmune hepatitis as an etiology. Acetaminophen level was normal ruling out acetaminophen toxicity. An abdominal ultrasound with doppler was negative for vascular occlusion.

Over the next 48 hours, the patient had complete resolution of his symptoms without additional intervention. Bacterial cultures returned negative, and his liver tests were downtrending. A call to the patient's acupuncturist revealed that the patient had been taking Chaparral to promote liver health.

Discussion

The prevalence of herbal product use and incidence of acute herbal hepatotoxicity are unknown. Herbal products are implicated as a cause of hepatotoxicity in up to 10% of drug-induced liver injury and acute liver failure cases.[1] Chaparral-induced hepatotoxicity typically manifests with symptoms that include fatigue, abdominal pain, dark urine, light stools, nausea, and diarrhea. Most patients have marked jaundice and elevated liver tests.[2] Although most cases of hepatotoxicity resolve following cessation of Chaparral ingestion, some evolve into cirrhosis or acute liver failure.

Chaparral is made from the leaves of the Creosote bush or Greasewood bush endemic to California and the Northern Baja Peninsula of Mexico.[3] It has been used for its claimed antioxidant and anti-aging properties as well as for treatment of various conditions such as cancer and AIDS. The mechanism of Chaparral-induced hepatotoxicity is not known but may be related to inhibition of lipoxygenase and cyclooxygenase pathways, cytochrome P450 inhibition, or the estrogen activity of chaparral metabolites.[4]

In this case, the patient presented with acute hepatotoxicity with marked hypotension. This may have led to acute liver failure had prompt IV fluid resuscitation not been employed. Awareness that the ingestion of alternative medicines can lead to severe hepatotoxicity is essential in cases of unclear liver disease. This case also reminds us that inquiring about the use of alternative medicines is an important aspect of taking a thorough medication history.

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CASE REPORT

JIACM 2019; 20(2): 125-27

A Deadly Alternative

Niraj Bohania, Sumeet Singla**, Sanjay Pandit***, S Anuradha****, Heemanshu Lodhi*****, Puja Sakhuja*******

Abstract

Solanum nigrum is a species in the genus Solanum. It is also known as black night shade. It has been widely used as food in various parts of the plant world. In South India, its leaves and berries are routinely consumed as food (Mannathakalli keerai, Red Makoi). Senna occidentalis is a species in the family Fabaceae. In India, the weed is widely prevalent (known locally as Bana chakunda). Both S. occidentalis and S. nigrum are used commonly in the alternative system of medicine for various chronic conditions. Both of them can cause liver failure in high doses. We are reporting a case of Solanum nigrum and Senna occidentalis overdose presenting as subacute liver failure, tachyarrythmia and ultimately leading to death.

Key words: Solanum nigrum; Senna occidentalis; alternative medicines; hepatotoxicity; liver failure; tachyarrhythmia.

Case report

A 34-year-old male, resident of New Delhi, carpenter by occupation, presented to the medical emergency with symptoms of fever and jaundice for 3 weeks, and epigastric pain and vomiting for 7 days. He was apparently well 3 weeks back when he developed progressive jaundice, epigastric pain, fever and vomiting. There was no history of alcohol intake or recent travel. There was no past history of jaundice or blood transfusion also. On examination, he was conscious and oriented. Icterus was present. Abdominal examination revealed hepatomegaly (2 cm below costal margin) but spleen was not palpable and there was no free fluid on percussion. Respiratory, cardiovascular and nervous system examination was unremarkable. Initial investigations revealed leucopenia, thrombocytopenia and deranged liver function tests. Viral markers, serologies for infection and autoimmume profile were negative. All the investigations have been summarised in Tables I and II. On further inquiry, later in the course of hospital stay, his relatives gave a history of consumption of large amount of Ayurvedic medications (containing *Solanium nigrum* and *Senna occidentalis*) for atleast 3 weeks prior to his illness (Fig. 1). He was taking this to promote better digestion.

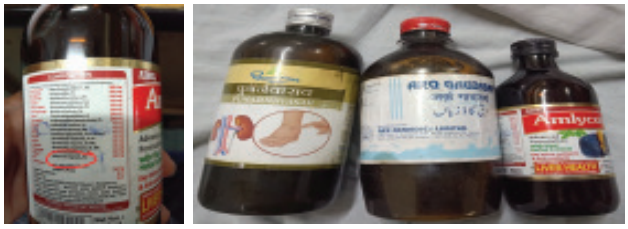

Fig. 1: *Bottles showing the contents of the Ayurvedic preparations being consumed by the patient.*

Even with supportive management, the patient's liver and kidney functions gradually deteriorated. He had an episode of ventricular tachycardia on day 7 of hospital admission and despite best efforts, succumbed to his illness.

Table I: Routine investigations of the patient.

Parameters	Day 1	Day 3	Day 5	Day 7
Haemoglobin (gm/dl)	11.2	9.4	9.3	9.7
Total leukocyte count (per ul)	2,700	2,170	1,290	1,400
Platelet count (per mm^3)	56,000	70,000	68,000	89,000
Blood urea (mg/dl)	73	48	48	89
Serum creatinine (mg/dl)	1.1	0.4	1.1	2.0
Sodium (Na^+) (meq/l)	136	134	132	131
Potassium (K^+) (meq/l)	4.1	4.2	3.8	4.2
Total bilirubin (mg/dl)	6.5	9.4	12.3	15.7
Direct bilirubin (mg/dl)	2.7	6.0	7.2	6.6
SGOT (U/L)	552	166	445	800
SGPT (U/L)	212	266	510	853
ALP (U/L)	173	55	215	108
Total protein (gm/dl)	6.1	–	–	5.3
Serum albumin (gm/dl)	2.3	–	–	2.2
INR	1.6	1.5	1.2	1.3

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