اپروچ به هایپرتری‌گلیسریدمی در بیمار آقای 49 ساله در درمانگاه پزشکی خانواده

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Chief complaint

آقای ۴۹ ساله با تشخیص هایپرتریگلیسریدمی در چک‌آپ روتین

present illness

بیمار آقای ۴۹ ساله‌ای است که بدون هیچ گونه سابقه‌ی بیماری خاص، جهت چک‌آپ روتین مراجعه کرده و در آزمایشاتی که از وی گرفته شده، تری‌گلیسرید بالا داشته است. سابقه‌ی بیماری قلب و عروق ندارد و از علایمی همچون تنگی نفس، درد اپی‌گاستر و درد قفسه‌ی سینه شکایت ندارد. با قد ۱۷۲ و وزن ۱۱۵ دارای BMI حدود ۳۹ است. خستگی مزمن، خشکی پوست، اختلال خواب و ریزش مو را ذکر نمی‌کند.

PMHx: neg

PSHx: جراحی شکستگی ساق پای راست ۵ سال قبل به علت تصادف

DHx: neg

FHx: neg

AHx: neg

HHx: سیگار روزانه یک پاکت – الکل مصرف نمی‌کند

Physical examination

بیمار در معاینه هوشیار و اورینته است.

دارای ظاهری چاق است.

Pale و ایکتریک نیست.

در چین‌های کف دست، خطوط زردرنگ مشاهده نمی‌شود.

سمع قلب، فاقد سوفل و صدای اضافه و سمع ریه Clear است.

فشار خون ۱۳۲ روی ۷۶ دارد.

Lab data

FBS: 115

Cr: 1.08

Cholesterol: 186

Triglycerides: 416

HDL: 38

LDL: 120

ALT: 20

AST:24

ALK: 330

HbA1c: 5.6

Causes

- Hereditary

  Familial hypertriglyceridemia

  Familial combined hyperlipidemia

  Lipoprotein lipase deficiency

  Apolipoprotein C-II deficiency

  Type III dysbetalipoproteinemia

Causes

Acquired causes

A) Metabolic and endocrine

- Uncontrolled DM (especially type II)
- Hypothyroidism
- Nephrotic syndrome
- CKD
- Obesity and metabolic syndrome

Causes

Acquired causes

B)Medications

- Corticoseroids
- Estrogens and OCP
- Non-selective Betablockers (e.g., propranolol)
- Thiazide diuretics
- Protease inhibitors in HIV treatment
- Retinoids
- Antipsychotic drugs (e.g., olanzapine clozapine)

Causes

Acquired causes

C)Diet and lifestyle

- Excessive alcohol consumption
- High-carbohydrate and high-fat diet
- Sedentary lifestyle
- Prolonged fasting and malnutrition

Causes

Other related causes

- Acute pancreatitis (both cause and consequence)
- Pregnancy (hormones affecting lipid matebolism)

برای این بیمار، علل ژنتیکی به دلیل عدم وجود سابقه‌ی بیماری‌های ذکر شده در اعضای خانواده رد می‌شود. از بین علل اکتسابی با توجه به آزمایش‌ها، مواردی همچون دیابت، سندرم نفروتیک و CKD رد می‌شود اما هایپوتیرو‌ییدی و سندرم متابولیک محتمل هستند. به ویژه سندرم متابولیک چرا که مطابق کرایتریای ATP III که در ادامه ذکر خواهد شد، بیمار دارای دور شکم بزرگتر مساوی ۱۰۲ سانتی‌متر در کنار تری‌گلیسرید بزرگتری مساوی ۱۵۰ و همچنین قند ناشتای بزرگتر مساوی ۱۰۰ است.

Metabolic syndrome

1. **Prevalence**: Metabolic syndrome, defined by ATP III criteria, affected 22% of U.S. adults in NHANES III (1988–1994), with higher rates in older adults and Mexican Americans. Prevalence increased to 34.5% by NHANES 1999–2002, particularly among women.
2. **Risk Factors**:
    1. **Weight**: Obesity is a major risk factor, with 60% of obese individuals having metabolic syndrome compared to 5% of normal-weight individuals.
    2. **Waist Circumference**: A large waist circumference predicts metabolic syndrome development.
    3. **Other Factors**: Age, race, postmenopausal status, smoking, low income, high-carb diets, physical inactivity, and genetic factors contribute to risk. Soft drink consumption and atypical antipsychotic medications (e.g., clozapine) also increase risk.
    4. **Genetics**: Genetic variants linked to insulin resistance and reduced subcutaneous fat may explain metabolic syndrome in some normal-weight individuals.
3. **Trends**: The prevalence of metabolic syndrome is rising, driven by increasing obesity rates. Prevention efforts focusing on weight management and physical activity are critical.
4. **Unique Cases**: Some normal-weight individuals exhibit metabolic syndrome traits, possibly due to genetic factors affecting fat distribution.

- In summary, metabolic syndrome is a growing public health concern, influenced by obesity, lifestyle, genetics, and other factors, with significant implications for diabetes and cardiovascular disease risk.

Criteria:

Current ATP III criteria define the metabolic syndrome as the presence of any **three** of the following five traits:

- Abdominal obesity, defined as a waist circumference in men ≥102 cm (40 in) and in women ≥88 cm (35 in)
- Serum triglycerides ≥150 mg/dL (1.7 mmol/L) or drug treatment for elevated triglycerides
- Serum high-density lipoprotein (HDL) cholesterol <40 mg/dL (1 mmol/L) in men and <50 mg/dL (1.3 mmol/L) in women or drug treatment for low HDL cholesterol
- Blood pressure ≥130/85 mmHg or drug treatment for elevated blood pressure
- Fasting plasma glucose (FPG) ≥100 mg/dL (5.6 mmol/L) or drug treatment for elevated blood glucose

1. **Clinical Implications**:
    1. Metabolic syndrome is a significant risk factor for type 2 diabetes and CVD.
    2. Aggressive lifestyle changes, such as **weight loss** and **increased physical activity**, are critical for managing the syndrome.
    3. Regular screening for metabolic risk factors (e.g., blood pressure, waist circumference, fasting glucose, and lipid profile) is recommended.
2. **Risk of Type 2 Diabetes**:
    1. Metabolic syndrome strongly predicts the development of type 2 diabetes, with risk increasing with the number of syndrome components.
    2. Insulin resistance plays a key role in this progression.
3. **Risk of CVD**:
    1. Metabolic syndrome increases the risk of CVD and all-cause mortality, particularly in individuals with insulin resistance or subclinical CVD.
    2. Obesity alone is not as significant a risk factor as obesity combined with metabolic syndrome.
4. **Other Associations**:
    1. Metabolic syndrome is linked to conditions like **fatty liver disease**, **chronic kidney disease**, **polycystic ovary syndrome**, **sleep apnea**, and **cognitive decline**.

1. **Therapy**:
    1. **Lifestyle modification** (diet, exercise, weight loss) is the primary treatment.
    2. Diets like the **Mediterranean diet** and **DASH diet** are beneficial.
    3. Exercise improves insulin sensitivity and reduces abdominal fat.
    4. Medications like **metformin** and **thiazolidinediones** may help but are not as effective as lifestyle changes.
2. **Prevention of Type 2 Diabetes**:
    1. Lifestyle interventions are more effective than medications in preventing diabetes.
    2. Metformin may be considered for high-risk individuals.
3. **Cardiovascular Risk Reduction**:
    1. Managing hypertension, cholesterol, and smoking cessation is crucial.
    2. Statins are effective in reducing CVD risk in patients with metabolic syndrome.

Hypertriglyceridemia in adults:
approach to evaluation

- **Introduction:**
  Hypertriglyceridemia, a common condition identified during cardiovascular risk assessments, is linked to adverse cardiovascular events and disorders of triglyceride (TG) metabolism. This review covers its relationship with cardiovascular disease, underlying mechanisms, and management strategies.
- **Classification:**
- **Normal:** <150 mg/dL (<1.7 mmol/L)
- **Moderate:** 150-499 mg/dL (1.7-5.6 mmol/L)
- **Moderate to Severe:** 500-999 mg/dL (5.65-11.3 mmol/L)
- **Severe:** >1000 mg/dL (>11.3 mmol/L)
- Severe hypertriglyceridemia often involves chylomicrons and very low-density lipoprotein (VLDL) increases.

- **Prevalence:**

  Hypertriglyceridemia is common, with 24.7% of adults having TG levels >150 mg/dL. Severe cases (>1000 mg/dL) are rare (<1 in 5000 individuals). Prevalence varies by race, ethnicity, and cardiovascular disease status.

- **Etiology:**

  Hypertriglyceridemia results from genetic and acquired factors:

- **Genetic:** Polygenic determinants or monogenic disorders (e.g., LPL deficiency).
- **Acquired:** Conditions like diabetes, obesity, alcohol abuse, hypothyroidism, and medications (e.g., thiazides, glucocorticoids).

- **Clinical Manifestations:**
- **Symptoms:** Often asymptomatic, but severe cases may cause pancreatitis, xanthomas, or chylomicronemia syndrome.
- **Lipid Profile:** Elevated TG levels are often accompanied by low HDL-C and small, dense LDL particles, increasing cardiovascular risk.
- **Clinical Syndromes:**
- **Moderate Hypertriglyceridemia:** Polygenic causes, often with environmental influences.
- **Severe Hypertriglyceridemia:** Polygenic or monogenic (e.g., familial chylomicronemia due to LPL deficiency).
- **Dysbetalipoproteinemia:** Rare, associated with premature cardiovascular disease.
- **Associated Conditions:**
- **Pancreatitis:** Risk increases with TG levels >500 mg/dL, especially in recurrent cases.
- **Atherosclerotic Cardiovascular Disease (ASCVD):** Elevated TG levels are associated with ASCVD, but causality is not firmly established. TG-rich lipoprotein remnants may contribute to atherosclerosis.

- **Diagnosis and Evaluation:**
- **Indications for Testing:** Screening for lipid disorders, evaluating pancreatitis, or monitoring treatment.
- **Diagnostic Criteria:** Fasting TG >150 mg/dL (1.7 mmol/L) is diagnostic. Repeat testing is recommended to confirm.
- **Evaluation:** Identify secondary causes (e.g., diabetes, hypothyroidism) and assess complications like pancreatitis or ASCVD risk. Genetic testing is reserved for suspected monogenic cases.

- **Conclusion:**

  Hypertriglyceridemia is a multifactorial condition with significant implications for cardiovascular health and pancreatitis risk. Management involves addressing both genetic and acquired factors, with a focus on reducing cardiovascular risk and preventing complications.

Hypertriglyceridemia in adults: Management

- **Introduction**
- Hypertriglyceridemia is commonly identified during cardiovascular risk assessments.
- Management focuses on reducing the risk of pancreatitis and ASCVD, though evidence on the efficacy of TG-lowering is limited.
- **Treatment Goals**
- **Primary Goals**: Lower the risk of pancreatitis and ASCVD.
- **Pancreatitis Risk**: TG levels >500 mg/dL significantly increase pancreatitis risk, and lowering TG levels is crucial for prevention.

ASCVD Risk: TG-lowering's role in reducing ASCVD risk is less clear compared to LDL-C lowering.

- **General Management**

1. **Lifestyle Modifications**:
    1. Weight loss, regular aerobic exercise, and dietary changes (reducing simple carbohydrates, added sugars, and alcohol).
    2. Dietary fat restriction is critical for severe hypertriglyceridemia.
2. **LDL-C Management**:
    1. Statins are the cornerstone for lowering LDL-C and reducing ASCVD risk.

       High-intensity statins can also lower TG levels significantly.

- **Additional Therapy Based on TG Levels**
- **Moderate Hypertriglyceridemia (150-499 mg/dL)**:
  - Focus on lifestyle changes and LDL-C management.
  - For high ASCVD risk patients, consider adding marine omega-3 fatty acids (icosapent ethyl preferred).
- **Moderate to Severe Hypertriglyceridemia (500-999 mg/dL)**:
  - Add fibrates or omega-3 fatty acids (icosapent ethyl) for high ASCVD risk patients.
  - For those without high ASCVD risk, fibrates are the initial choice, with omega-3 fatty acids added if TG levels remain high.
- **Severe Hypertriglyceridemia (≥1000 mg/dL)**:
  - Immediate dietary fat restriction and alcohol abstinence.
  - Defer TG-lowering drugs until TG levels are <1000 mg/dL, except in acute pancreatitis cases where fibrates are used.

- **Specific Agents**
- **Statins**: Primarily for LDL-C lowering but also have mild to moderate TG-lowering effects.
- **Fibrates**: Effective in reducing TG levels but limited evidence for reducing pancreatitis or ASCVD risk.
- **Marine Omega-3 Fatty Acids**: Icosapent ethyl has shown cardiovascular benefits, particularly in high ASCVD risk patients.
- **Niacin**: Not routinely used due to limited benefits and adverse effects.
- **Monitoring Therapy**
- Frequent monitoring of TG levels, especially in severe cases, to guide therapy adjustments.
- **Emerging Therapies**
- **APOC3 Inhibitors**: Reduce TG levels but are not widely approved.
- **ANGPTL3 Inhibitors**: Under investigation for severe hypertriglyceridemia.

Gene Therapy: Previously approved in Europe but no longer available.

levels of prevention

- Primordial
- Primary
- Secondary
- Tertiary
- qaternary

- **Primordial Prevention**
- **Goal**: Prevent the development of risk factors for hypertriglyceridemia.
- **Actions**:
  - Promote healthy lifestyle habits from an early age.
  - Encourage a balanced diet low in refined sugars, saturated fats, and trans fats.
  - Advocate for regular physical activity and weight management.
  - Educate about the risks of smoking and excessive alcohol consumption.

- **Primary Prevention**
- **Goal**: Prevent the onset of hypertriglyceridemia in individuals at risk.
- **Actions**:
  - Screen for lipid levels in high-risk individuals (e.g., those with obesity, diabetes, or a family history of dyslipidemia).
  - Encourage a heart-healthy diet rich in fiber, omega-3 fatty acids, and unsaturated fats.
  - Promote regular exercise (e.g., 150 minutes of moderate-intensity activity per week).
  - Limit alcohol intake and avoid sugary beverages.

- **Secondary Prevention**
- **Goal**: Early detection and management of hypertriglyceridemia to prevent complications.
- **Actions**:
  - Regular monitoring of lipid profiles in individuals with borderline or elevated triglycerides.
  - Initiate lifestyle modifications (diet, exercise, weight loss) to lower triglyceride levels.
  - Consider medications (e.g., fibrates, omega-3 fatty acids, statins) if lifestyle changes are insufficient.
  - Manage underlying conditions (e.g., diabetes, hypothyroidism) that contribute to elevated triglycerides.

- **Tertiary Prevention**
- **Goal**: Reduce complications and improve quality of life in individuals with established hypertriglyceridemia.
- **Actions**:
  - Intensify lifestyle and pharmacological interventions to prevent pancreatitis or cardiovascular events.
  - Monitor and manage comorbidities (e.g., metabolic syndrome, atherosclerosis).
  - Provide patient education and support for adherence to treatment plans.

- **Quaternary Prevention**
- **Goal**: Avoid overmedicalization and harm from unnecessary interventions.
- **Actions**:
  - Ensure that treatment plans are evidence-based and tailored to individual risk profiles.
  - Avoid excessive use of medications in low-risk individuals.
  - Focus on patient-centered care and shared decision-making.