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Use of the QuantiFERON®-TB Gold Assay in Pregnant Patients

Bassem M.Chehab, M.D.[1], K. James Kallail, Ph.D.[2], Riad O. El Fakih, M.D.[3], Rosalee E. Zackula, M.A.[4], Garold O. Minns, M.D.[2]
[1]University of Kansas School of Medicine-Kansas City
Department of Internal Medicine, Division of Cardiovascular Diseases
[2]University of Kansas School of Medicine-Wichita
Department of Internal Medicine
[3]University of Oklahoma College of Medicine
Department of Internal Medicine
[4]University of Kansas School of Medicine-Wichita
Office of Research

Abstract

Background. The QuantiFERON®-TB Gold assay is a new test for latent tuberculosis infection. It is thought to be more reliable and have fewer false positives than the tuberculin skin test (TST). Both tests are dependent on a normal immune system for diagnostic accuracy. However, no comparisons of the two tests have assessed the accuracy in pregnant women. This investigation assessed the consistency of results between the two tests in both pregnant and non-pregnant women.

Methods. The study included 152 women presenting for care at the Sedgwick County Health Department. They were divided into two groups of pregnant and non-pregnant women. Both groups were assessed with the Quantiferon assay and the TST. Subjects were adults between the ages of 18 and 45. All had a pregnancy test and a negative HIV test. None had existing morbidities that would influence the test results.

Results. Concordant results between the tests were shown in 131 subjects (86.2%). Of the pregnant women, 91.2% had concordant results. Of the non-pregnant women, 76% had concordant results. Significantly more discordant results occurred in non-pregnant women ($p<.022$).

Conclusion. Current guidelines favor using either test in healthy individuals. Although more discordant results occurred in the non-pregnant women, both tests were effective in pregnant women. Thus, TST and Quantiferon are accurate to use in pregnant women. The decision to use either test in pregnant women should be based mainly on the compliance of the patient to return to have the TST read. *KJM 2010; 3(2):24-30.*

Introduction

Tuberculosis is a communicable disease caused by infection with *M. tuberculosis* complex organisms, which typically spreads to new hosts via airborne droplet nuclei from patients with respiratory tuberculosis disease.[1] A newly-infected individual can become ill from tuberculosis within weeks to months, but most infected individuals remain well. Latent tuberculosis infection (LTBI), a non-communicable asymptomatic condition, persists in some who might develop tuberculosis disease months or years later.[1,2]

Until recently, the tuberculin skin test (TST) was the only available method for diagnosing LTBI. Cutaneous sensitivity to tuberculin develops from 2 to 10 weeks after infection. This test uses a small amount of purified protein derivative (PPD) prepared from *M. tuberculosis,* placed intradermally

and measured 48 to 72 hours later to identify the delayed hypersensitivity response, indicating previous infection.[2] However, some infected individuals, including those with a wide range of conditions hindering immune functions, but also others without these conditions, do not respond to tuberculin. Conversely, some individuals who are unlikely to have *M. tuberculosis* infection exhibit sensitivity to tuberculin and have positive tuberculin skin test (TST) results after vaccination with bacilli Calmette-Guerin (BCG) infection with mycobacteria other than *M. tuberculosis* complex or undetermined other factors.[3-5]

LTBI must be distinguished from tuberculosis disease, a reportable condition which usually involves the lungs and lower respiratory tract, although other organ systems also may be affected. Tuberculosis disease is diagnosed from historical, physical, radiological, histological, and mycobacteriological findings.[1,5,6]

The QuantiFERON®-TB Gold test is a new test for cell mediated immune (CMI) responses to peptide antigens that simulate mycobacterial proteins.[4] These proteins, ESAT-6 and CFP-10, are absent from all BCG strains and from most non-tuberculosis mycobacteria with the exception of *M. kansasii*, *M. szulgai*, and *M. marinum.* It is thought to be more reliable and has fewer false positives than the TST. Individuals infected with *M. tuberculosis* complex organisms usually have lymphocytes in their blood that recognize these and other mycobacterial antigens. This recognition process involves the generation and secretion of the cytokine, IFN-γ. The detection and subsequent quantification of IFN-γ forms the basis of this test.[4,7-9]

Since the Quantiferon test is dependant on immune mediators and factors, like TST, it also is affected by changes in the immune system of the tested subjects.[10,11] Both tests are dependent on a normal immune system for diagnostic accuracy. Therefore, any condition that alters the immune system, especially that will depress this system, theoretically can cause false-negative results with this test.[12-16]

In the US Centers for Disease Control and Protection (CDC) guidelines of 2003, pregnancy was one of the conditions in which use of this test was not recommended, because pregnancy has the potential to decrease the immune response.[7] In the CDC guidelines of 2005, the spectrum to use QuantiFERON®-TB Gold was broadened and pregnancy no longer showed as one of the conditions for which it is not recommended.[17] However, no serious investigations have been done concerning the correlation of pregnancy with the accuracy of the Quantiferon assay, and the CDC arbitrarily included, then excluded, pregnancy in the contraindication category for that assay.

This investigation assessed the consistency of results between the the QuantiFERON®-TB Gold assay and the TST in both pregnant and non-pregnant women.

Methods

Study population. Subjects were women presenting for care at the Sedgwick County Health Department. Eligibility criteria included:

- Female patients
- Age between 18 and 45 years old
- HIV negative status
- No history of corticosteroids use, taking the equivalent of greater than 15 mg/day of prednisone for one month or more
- Non-diabetic patients
- Non-transplant patients
- No current treatment with immuno-suppressive drugs
- No renal failure

- No pre-existing hematologic problems (e.g., myeloproliferative disorders, leukemias, and lymphomas)
- No pre-existing malignancies (e.g., carcinoma of the head, neck, or lung)

Exclusion criteria included:

- Abortion prior to study completion
- Conversion to HIV positive during study participation
- Any diversion from the eligibility criteria
- Withdrawal of informed consent by the subject

Procedures. Approval of the Institutional Review Board at the University of Kansas School of Medicine-Wichita was obtained. Subjects were recruited by clinical personnel at the Sedgwick County Health Department. All pregnant subjects were recruited during visits to the prenatal clinic. Non-pregnant subjects were recruited from other Health Department clinics.

Each woman signed an informed consent in either Spanish or English, as appropriate. Each subject was given four clinical tests. Two tests determined eligibility for participation: a pregnancy test and an HIV test. Then, the two TB tests (Quantiferon and TST) were given when eligibility was established. Women who were pregnant received the TST as part of their usual care regardless of study participation.

Blood was drawn by clinical personnel at the Health Department to determine pregnancy (for the non-pregnant control group) and HIV status. Pregnant subjects did not receive an additional pregnancy test because they entered the study with a known pregnancy status from the prenatal clinic. Subjects were required to return to the Health Department two to three days after the TST to have the test results read by a trained person. Laboratory testing was performed according to standard Health Department policy and procedures.

Tuberculin Skin Testing. The TST was administered by the Mantoux method using 0.1 ml (5TU) of Tubersol (Connaught Laboratories Inc., Toronto, Ontario) and interpreted by trained clinical personnel according to American Thoracic Society (ATS)/CDC guidelines.[18] Transverse induration at the TST site was measured 48 to 78 hours after injection of purified protein derivative (PPD). TST results were interpreted using the risk-stratified interpretation of induration as recommended by the ATS/CDC guidelines.

QuantiFERON®-TB Gold Assay. The assay was performed and interpreted according to the manufacturer's instructions using previously described cut-points to identify infected persons.

Statistical measures. Statistical measures of agreement (*kappa*) were performed using MedCalc for Windows, version 10.1.3 (MedCalc Software, Mariakerke, Belgium). All other tests were conducted in StatXact, version 8.0.0, Cytel Studio.

Results

A total of 152 women (102 pregnant subjects and 50 non-pregnant controls) participated in the study. All met study criteria to participate. Group demographics according to pregnancy status are shown in Table 1. Pregnant subjects were younger, with greater representation of Caucasians and Hispanics. Non-pregnant subjects were older and more racially diverse, but with fewer Hispanics.

Table 2 shows concordant results between the two TB tests in 131 subjects (86.2%). A *kappa* statistic revealed fair agreement between the two tests (K=0.288).[19]

Table 3 shows the TB test results of the 102 pregnant women. A total of 93 (91.2%) had concordant results between both tests and nine had discordant results (8.8%). A *kappa* statistic revealed fair agreement

Table 1. Composition of the pregnant and non-pregnant subject groups.

	Pregnant Subjects n=102[#]	Non-Pregnant Subjects N=50[#]	*p*
Mean Age (sd)[*]	25.94 (5.25)	29.34 (7.25)	0.004
Race [§]			
Caucasian (%)	97 (.97)	37 (.79)	<0.001
African-American (%)	3 (.03)	6 (.13)	
Asian (%)	0 (.00)	4 (.08)	
Ethnicity[§]			
Hispanic (%)	87 (.87)	12 (.26)	<0.001
Non-Hispanic (%)	13 (.13)	35 (.74)	

[#] Race and ethnicity data were available for 47 of the 50 non-pregnant and 100 of 102 pregnant subjects.
[*] Two sample t-test with unequal variance.
[§] Pearson Chi-Square Test.

Table 2. Comparisons between the QuantiFERON®-TB Gold assay and TST results for all subjects.

		Quantiferon			
		Positive	Negative	Indeterminate	*kappa*
TST	Positive	5 (3.3%)	15 (9.9%)	1 (.7%)	0.288
	Negative	2 (1.3%)	126 (82.9%)	3 (2.0%)	

Table 3. Comparisons between the QuantiFERON®-TB Gold assay and TST results for pregnant subjects.

		Quantiferon			
		Positive	Negative	Indeterminate	*kappa*
TST	Positive	3 (3%)	7 (7%)	0 (0%)	0.358
	Negative	2 (2%)	90 (88%)	0 (0%)	

Table 4. Comparisons between the QuantiFERON®-TB Gold assay and TST results for all non-pregnant subjects.

		Quantiferon			
		Positive	Negative	Indeterminate	*kappa*
TST	Positive	2 (4%)	8 (16%)	1 (2%)	0.213
	Negative	0 (0%)	36 (72%)	3 (6%)	

Table 5. Level of concordance between the two TB tests in pregnant and non-pregnant subjects.

	Concordant	Discordant	*p*[*]
Pregnant	93 (91%)	9 (9%)	0.022
Non-Pregnant	38 (76%)	12 (24%)	

[*] Fisher's Exact Test.

between the tests for pregnant women (*K*=0.358).

Table 4 shows the TB test results of the 50 non-pregnant women. A total of 38 (76%) had concordant results between both tests and 12 (24%) had discordant results. A *kappa* statistic also revealed fair agreement between the tests for non-pregnant women (*K*=0.213).

Fisher's exact testing revealed that significantly more discordant results occurred in non-pregnant than pregnant women ($X^2 = 6.159$; $p<.022$; see Table 5).

Discussion

The increase in prevalence of tuberculosis and the emergence of multidrug-resistant strains have created a public health urgency for early identification of *M. tuberculosis*-infected individuals.[1,2] The gold standard for detecting exposure remains the TST and is one of the oldest tests still in clinical use. Despite the long history of clinical application, limitations and controversy with regard to placement and interpretation remain.[2-4]

The TST has several drawbacks including false-positive reactivity due to non-tuberculin strains, such as BCG, inter-observer variability in reading, false-negative results due to underlying immunosuppression, and variability with repeat testing. Due to changes in disease prevalence and demographics, a heightened need for early detection and better testing methodologies has emerged.[2-5]

The Quantiferon test and TST are dependant on immune mediators and factors, thus, affected by changes in the immune system of the tested subjects. Pregnancy certainly falls within that category. However, current guidelines favor using either test in healthy individuals.[9,20]

In this study, results between the two TB tests in all subjects (86.2%) showed fair agreement between the two tests with 91.2% of pregnant women and 76% of non-pregnant women having concordant results. Interestingly, concordance between test results in a population of university international students was only 59%.[21]

Although the groups in this study differed by age and race/ethnicity, it is doubtful whether these differences were clinically significant. No evidence is available that indicates that delayed type hypersensitivity reacts differently by race/ethnicity or in the relatively narrow age range of the reported subjects.

Even though more discordant results occurred in the non-pregnant women, both tests were effective in pregnant women. To our knowledge, this is the first study that compared both tests in pregnant individuals. In conclusion, the TST and Quantiferon tests can be used with pregnant women. The decision to use either test in pregnant women should be based mainly on the compliance of the patient to return to have the TST read.

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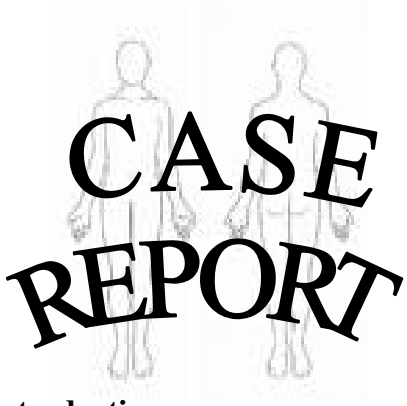

Metabolic Effect of Atypical Antipsychotics: How Bad It Can Be?

Rami Mortada, M.D.[1], Justin Moore, M.D.[1],
Jean M. Dostou, M.D.[2]
[1]University of Kansas School of Medicine - Wichita
Department of Internal Medicine
[2]University of North Carolina at Chapel Hill
Department of Medicine

Introduction

Metabolic syndrome has been associated with schizophrenia since long before the era of antipsychotic medications.[1] The introduction of atypical antipsychotics has been associated with worsened weight gain, hyperglycemia, and hypertriglyceridemia.[2] An American Diabetes Association/ American Psychiatric Association (ADA/ APA) consensus paper recognized that certain atypical antipsychotic medications are associated with greater metabolic dysfunction than others.[3]

A case of a young female patient with uncontrolled type 2 diabetes mellitus on atypical antipsychotics is presented. Her antipsychotic medications were discontinued due to pregnancy. The patient subsequently had significant weight loss and improvement in her glycemic control.

Case Report

A 35-year-old female was seen in the endocrinology clinic for type 2 diabetes mellitus complicated by gastroparesis, peripheral neuropathy, and nephropathy. Glycemic control had not been achieved on insulin glargine 40 units twice daily, insulin lispro 10 units before meals, pioglitazone 30 mg daily, and metformin 850 mg twice daily. Hemoglobin A_{1c} was thirteen percent.

Her past medical history was significant for resolved renal failure secondary to lithium toxicity, asthma, primary hypothyroidism, bipolar disorder, hyperlipidemia, hypertension, and schizophrenia. Other medications included quetiapine 500 mg daily in a divided dose, citalopram 40 mg daily, divalproex 2500 mg daily, aripiprazole 20 mg daily, levothyroxine 100 mcg daily, lisinopril, pravastatin, pantoprazole, docusate, aspirin, propranolol, odansetron, promethazine, metoclopramide, and trazodone.

Physical exam revealed a blood pressure of 113/69 mmHg, weight 99.5 kg, a body mass index (BMI) of 35 kg/m^2, mild acanthosis nigricans, and decreased sensation in both feet. Cushingoid features were not present. Urine free cortisol in a 24-hour collection was not elevated.

Metformin was discontinued because of diarrhea. The patient attended diabetic education sessions and attempted dosing insulin by carbohydrate counting without success. The pharmacy confirmed that her prescriptions were being filled and she was observed taking insulin in clinic with little demonstrable effect on her blood glucose.

She became pregnant and all medications were discontinued with the exception of insulin, levothyroxine, and citalopram. Acceptable glycemic control was achieved on insulin glargine 50 units once daily and insulin aspart 27 units three times daily.

Term delivery was complicated by failure to progress, resulting in a Cesarean section. The infant was not macrosomic. The patient experienced postpartum respiratory failure of uncertain etiology requiring brief mechanical ventilation. Marked hypoglycemia occurred post-partum

and insulin was discontinued.

She was seen in the endocrinology clinic seven weeks post-partum without diabetic or antipsychotic medications. Her hemoglobin A_{1c} was 6.5 percent and her weight had decreased to 81.87 kilograms. She was not breastfeeding. She was restarted on metformin 1 gram twice daily and later extended release glipizide 5 mg daily. Subsequent follow-up showed well controlled blood glucose and stable weight.

Discussion

Schizophrenia has a prevalence of 1%.[4] It is associated with a significant increase in mortality. A correlation between diabetes mellitus and schizophrenia has been observed for many years. In 1879, Sir Henry Maudsley wrote, "Diabetes is a disease which often shows in families in which insanity prevails."[5] The prevalence of type 2 diabetes mellitus in patients with schizophrenia is 9% versus 4.6% in the general population.[6]

The reasons that underlie the high prevalence abnormalities are much debated.[7] In spite of the increased risk of metabolic disturbances, patients with severe mental illness are less likely to receive treatment for hyperlipidemia, hypertension, or diabetes mellitus than patients without psychosis.[8]

Pharmacologic agents used in the treatment of schizophrenia, particularly second generation antipsychotics, have been linked to the metabolic syndrome. The US Food and Drug Administration has labeled this as a class effect, although there are major differences in risk associated with the various medications.[9]

Clozapine causes metabolic syndrome in more than 50% of long time users.[10] The risk of new-onset diabetes was equivalent for patients treated for one year with olanzapine, risperidone, or quetiapine, and significantly greater than in patients treated with haloperidol.[11] Atypical antipsychotics also have been associated with a small increase in risk of diabetic ketoacidosis.[12] In a case control study comparing patients treated with antipsychotic drugs to control patients without antipsychotic medication, the odds ratio for hyperlipidemia ranged from 1.82 for clozapine to 1.26 for first generation antipsychotics; aripiprazole was the only antipsychotic that did not increase the risk for hyperlipidemia significantly.[13]

Several mechanisms have been proposed to explain the effect of antipsychotic medications on the metabolic syndrome. Antipsychotics can disrupt energy balance, creating an imbalance between energy intake and expenditure, thus resulting in weight gain and obesity.[14] This can be explained partially by antagonism of histamine and possibly by serotonin inducing weight gain, which in turn leads to changes in glucose homeostasis.[15] Some antipsychotic drugs may have direct inhibitory effects on insulin release from pancreatic beta cells.[16] Other theories include a potential direct blockade of glucose accumulation at the level of the glucose transporter in cells derived from both peripheral and brain tissue,[17] perturbation in appetite regulation, and the release of counter regulatory hormones.[18]

Treatment. No adjunctive medication has been conclusively shown to reduce these metabolic effects.[19] Even among drugs showing positive effects for preventing weight gain, such as metformin, the metabolic effects have been modest. Patients who develop antipsychotic-induced metabolic disturbance should be switched, if clinically practical, to an agent with fewer propensities for this side effect, such as aripiprazole or ziprasidone. A consensus statement prepared by the American Psychiatric Association, the American Diabetes Association, and others recommended baseline assessment of weight, blood pressure, fasting plasma

glucose, and fasting lipid profile, and reassessment 12 weeks after initiation of the antipsychotic medication.[3] Patients with impaired fasting glucose should be tested for diabetes with a two-hour oral glucose tolerance test. Weight should be followed monthly for the first three months and quarterly thereafter.

Conclusion

The association between schizophrenia and the metabolic syndrome has long been recognized. Unfortunately, metabolic disturbances, including diabetes mellitus, hypertension, hyperlipidemia, and weight gain, appear to be caused or exacerbated by atypical antipsychotics. Several mechanisms have been proposed, mainly a perturbation of the body's ability to react, metabolize, and transport glucose causing weight gain and exacerbating insulin resistance. Patients requiring antipsychotic medications should be assessed for aspects of the metabolic syndrome before and during treatment. Switching to antipsychotic medications not related to metabolic disturbances or even discontinuing antipsychotic medications should be evaluated on an individual patient basis.

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Keywords: antipsychotic agents, diabetes mellitus, schizophrenia, metabolic syndrome

Ovarian Adenocarcinoma Presenting as Axillary Lymphadenopathy

Bridget Harrison, MS4[1], David J. Lerner, MS4[1], Patty L. Tenofsky, M.D.[1,2,4], Pavan S. Reddy, M.D.[1,3,5]
[1]University of Kansas School of Medicine - Wichita
[2]Department of Surgery
[3]Department of Internal Medicine
[4]Wichita Clinic, PA, Wichita, KS
[5]Cancer Center of Kansas, PA, Wichita, KS

Introduction

Ovarian adenocarcinoma is the fifth leading cause of death for women in the United States, with an estimated 15,520 deaths per year.[1] However, ovarian adenocarcinoma presenting as axillary lymphadenopathy is quite a rare occurrence. This case documents an ovarian adenocarcinoma presenting as axillary lymphadenopathy, with a focus on the importance of the surgeon differentiating the axillary mass from metastatic breast cancer.

Case Report

A 74-year-old female was referred for the evaluation of right axillary lymphadenopathy detected on a routine mammogram. She denied fever, fatigue, recent travel, axillary pain, or skin changes. Her age of menarche was 15, her first pregnancy was at the age of 23, and her age of menopause was 43. Her family history was significant for two sisters with breast cancer, one of whom was diagnosed in her forties and died within two years. Her other sister was diagnosed in her seventies and still living at that time. She also had multiple paternal aunts and cousins diagnosed with breast cancer. There was no family history of ovarian cancer.

The patient's past medical history included hypertension, ulcers, hyper-lipidemia, diverticulosis, hemorrhoids, and a myocardial infarction. Her past surgical history included removal of two benign growths from her left breast at the age of 28. Her last mammogram and breast exam performed one year previously were normal.

The physical exam at presentation revealed right axillary adenopathy with no observable primary mass. There was no erythema, pain with palpation, or swelling. Ultrasound of the axilla easily identified the enlarged nodes and was used to perform fine needle aspiration (FNA). FNA of the node revealed adenocarcinoma of undefined origin. A breast MRI did not reveal a primary mass. CT of the chest and a bone scan also were negative.

CT of the abdomen and pelvis revealed multiple lobulated peritoneal and omental masses, as well as intraabdominal masses in the region of the gall bladder and spleen, including a 16 X 41 mm mass in the right lower quadrant. Additionally, a complex cystic lesion was seen in the left adnexa. A core biopsy of right axillary lymph nodes, CA-125 level, and staining for estrogen, progesterone, HER2, Ki-67, and CA-125 were performed. Her CA-125 level was elevated to 900 ng/ml and the axillary core biopsy stained positive for CA-125 within the neoplastic cells. The positivity rate of the estrogen receptor was 1%, progesterone 90%, and HER2 2+, features which can be seen with ovarian or breast carcinoma. Ki-67 positivity was 90%, indicating a high

proliferative rate. The high CA-125 level along with the CT findings indicated metastatic ovarian cancer as the diagnosis.

A port-a-catheter was placed and the patient was started on six cycles of chemotherapy with paclitaxel and carboplatin. After completing her chemotherapy regimen, a diagnostic bilateral mammogram revealed improved right axillary adenopathy, while a sonogram of the right breast showed no abnormal lymphadenopathy. Her CA-125 levels normalized. At last follow-up, a CT of the abdomen and pelvis revealed no increase in number or size of nodes. The main post treatment side effect was grade three neuropathy.

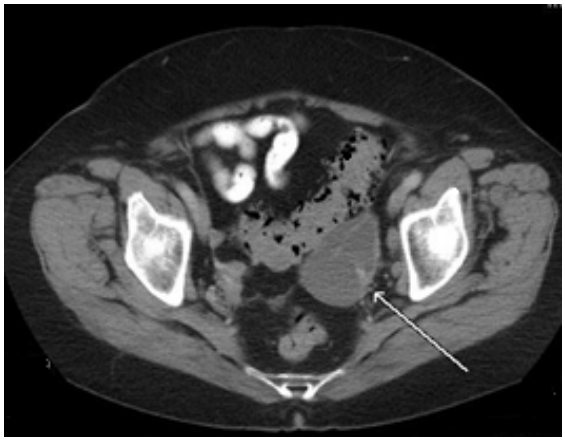

Figure 1. CT scan showing left ovarian mass.

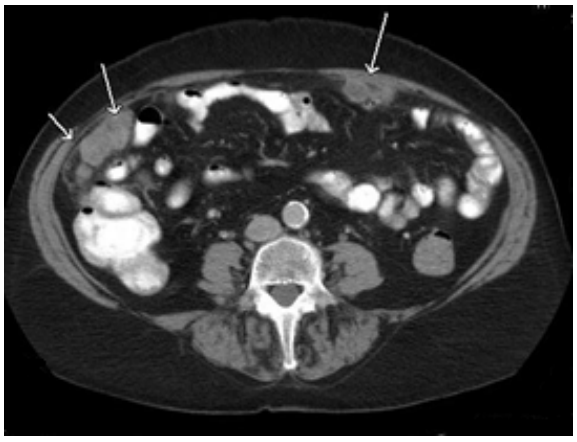

Figure 2. CT scan showing peritoneal metastases.

Discussion

Most ovarian cancers are epithelial in origin and result from malignant transformation of the ovarian epithelium, which is contiguous with the peritoneum.[2] At the time of staging, approximately 85% of ovarian cancer remains confined to the peritoneal cavity. Distant metastases at the time of presentation occurred in 8% of patients in one study and were most common in the liver, pleura, and lung.[3]

Ovarian cancer presenting as axillary lymphadenopathy is quite rare. The largest study to date on the topic of ovarian cancer presenting as extra-abdominal lymph-adenopathy involved a twenty-year review of cases.[4] In this twenty-year period, 35 extra-abdominal lymphadenopathic present-ations of ovarian, fallopian tube, or peritoneal carcinoma were found. Only two cases of peritoneal disease presented as axillary lymphadenopathy. A case presentation similar to that described here was reported in 1997 after a patient was erroneously treated for metastatic breast cancer.[5]

Breast cancer is a logical consideration in a patient with axillary lymphadenopathy, but alternative diagnoses must be entertained. Skin infections, cat-scratch disease, tularemia, sporotrichiosis, sarcoid-osis, syphilis, leprosy, brucellosis, melanoma, lymphoma and Kaposi's sarcoma can result in axillary lympha-denopathy.[6,7] Key aspects of the history include the presence of constitutional symptoms, recent travel, or high risk behaviors. Careful examination of other nodal sites also is required.

This patient's history of breast surgery for the removal of tumors coupled with a fine needle aspiration of adenocarcinoma suggested breast cancer, but the imaging studies, an MRI and CT, revealed no obvious site of a primary breast cancer. Breast MRI is highly sensitive in the

detection of occult breast cancer in patients with axillary lymphadenopathy.[8] Evidence of abdominal and adnexal masses are more convincing of a primary ovarian neoplasm.

The CA-125 level at presentation was 900 ng/ml and supported the diagnosis of metastatic ovarian adenocarcinoma. Although elevated CA-125 levels can be associated with other benign and malignant conditions, at levels above 320 ng/ml, there is a higher sensitivity and specificity for ovarian cancer (71% sensitivity, 84% specificity).[9] Additionally, above levels of 510 ng/ml, there is increased sensitivity and specificity for peritoneal implants outside of the pelvis as well as lymph node metastasis (67% sensitive, 80% specific).

Although a biopsy of the ovarian mass is usually required for complete confirmation of ovarian cancer, it was not performed in this case. The chemotherapy regimen would not have been altered by this diagnosis and the patient was already responding to chemotherapy. In addition, the patient's age and cardiac history raised concerns that she may not tolerate such a large operation. The CT image of an adnexal mass, a CA-125 level of 900 ng/ml, as well as the axillary node staining positive with CA-125, was sufficient for a diagnosis of primary ovarian cancer with axillary metastasis. The decrease of the CA-125 level to within normal limits after treatment with paclitaxel and carboplatin supported the diagnosis.

Axillary lymphadenopathy as an initial presentation of ovarian cancer is quite rare. Based on previous reports, our patient was the only one that did not receive surgical resection, only chemotherapy, and at last follow-up was performing well. For breast surgeons and referring providers, axillary lymphadenopathy in a female of older age, especially in the absence of an obvious breast lesion, potentially could represent metastasis from primary ovarian carcinoma. Recognition of this differential diagnosis could prevent unnecessary lumpectomy or mastectomy and lead to better outcomes with the appropriate treatment of the true primary cancer.

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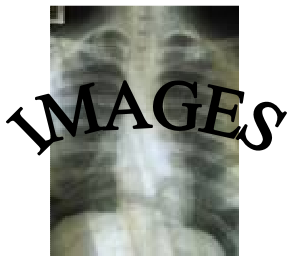
Keywords: carcinoma, ovarian neoplasms, axillary lymphadenopathy



Simultaneous Bilateral Subdural Hygromas, Arachnoid Cyst, and Empty Sella Syndrome in a 66 Year-Old Female

Nathan Tofteland, M.D.
Justin Moore, M.D.
University of Kansas School of Medicine-Wichita
Department of Internal Medicine

We present the only known case report of simultaneous bilateral subdural hygromas, arachnoid cyst, and empty sella syndrome.

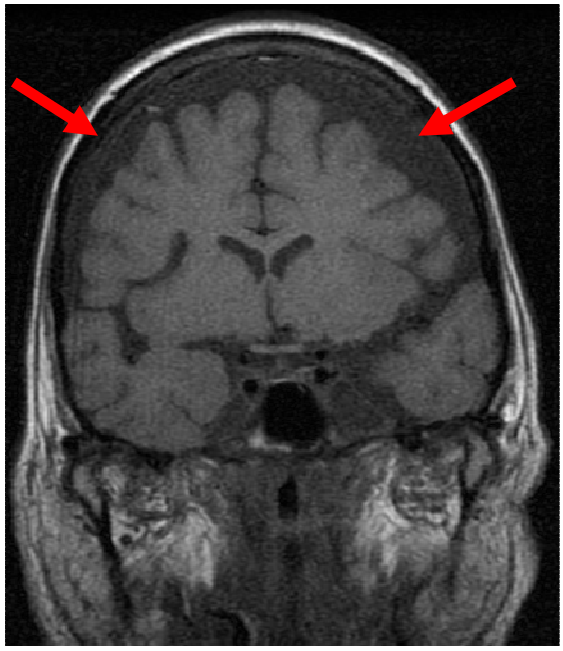


Figure 1. Bilateral subdural hygromas.

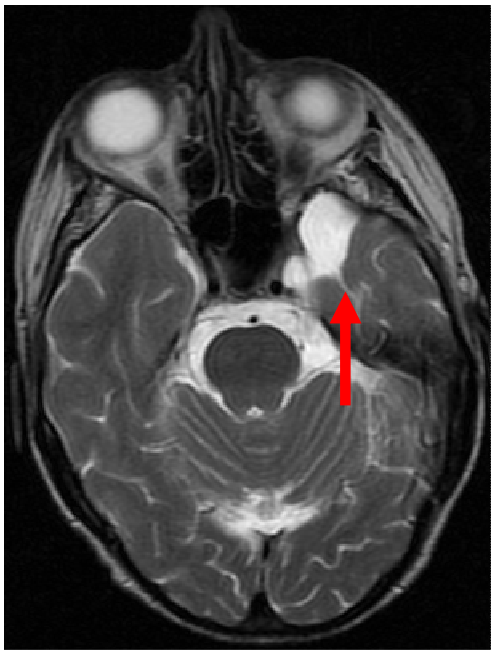


Figure 2. Left temporal lobe arachnoid cyst.

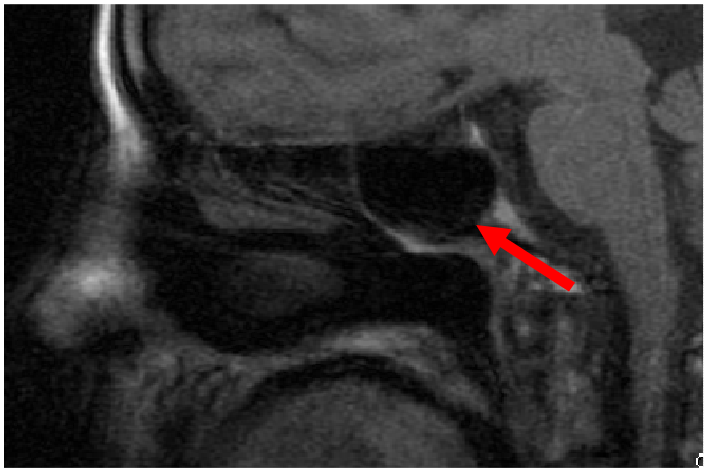


Figure 3. Empty sella turcica.

A 66-year-old female presented to the emergency department for evaluation of syncopal episodes and altered level of consciousness. Magnetic resonance imaging (MRI) of the brain revealed bilateral subdural hygromas (Figure 1), a left temporal lobe arachnoid cyst (Figure 2), and an empty sella turcica (Figure 3). The patient and family were unable to give any prior history of significant head trauma. An electroencephalogram was unremarkable and a neurology consultation did not reveal seizure activity.

Despite a relatively normal hormonal history, with normal menses until age 50 and only mild primary hypothyroidism prior to her hospitalization, laboratory evaluation revealed hypoglycemia, secondary adrenal insufficiency, probable secondary hypothyroidism (she was on thyroid hormone replacement), hypoprolactinemia, growth hormone deficiency, and secondary hypogonadism (characterized by a failure of the follicle-stimulating hormone level to rise appropriately in the postmenopausal state). Diabetes insipidus was not present. She was managed conservatively with fluids, glucocorticoid replacement, and thyroid hormone replacement. Cardiac monitoring was unremarkable and her hypoglycemia resolved with glucocorticoid replacement. She was discharged to home in her baseline state of health.

Arachnoid cysts are cerebrospinal fluid (CSF) filled collections between two arachnoid layers accounting for one percent of all intracranial space-occupying lesions. They are thought to be congenital and microscopically formed by mesothelial cells.[1] Subdural hygromas are collections of CSF in the subdural space. Rarely, subdural hygromas may be a consequence of ruptured arachnoid cysts.[2] Other etiologies are controversial, but most subdural hygromas are thought to be derived from chronic subdural hematomas. Other possible etiologies include a sudden decrease in pressure by ventricular shunting, severe brain atrophy, head trauma, dehydration in the elderly, lymphoma, and connective tissue diseases. Differentiation of subdural hygroma from subdural hematoma on imaging can be difficult and gadolinium-enhanced MRI is the imaging modality of choice.[3]

Empty sella syndrome is divided broadly into primary empty sella, a congenital defect caused by downward herniation of the sellar diaphragm, or secondary empty sella, in which the pituitary is displaced or destroyed by an acquired disease process, surgery, or radiation. Primary empty sella rarely is accompanied by hormonal dysfunction, although hyperprolactinemia may be present in 15% of cases. The majority of patients with secondary empty sella have endocrine disturbances.[4] This patient's normal menarche and regular menses until the normal age of menopause followed by profound endocrine disturbances make secondary empty sella much more likely than primary.

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Keywords: subdural hygroma, arachnoid cyst, empty sella syndrome, case report