Paraneoplastik Sendromlar

Dr. Deniz Tural
Bakırköy Dr. Sadi Konuk Eğitim ve Araştırma Hastanesi
Tıbbi Onkoloji

Ders Planı

- Paraneoplastik endokrin sendromlar
- Paraneoplastik nörolojik sendromlar
- Paraneoplastik dermatolojik ve romatolojik sendromlar
- Paraneoplastik hematolojik sendromlar
- Paraneoplastik renal sendromlar
- Diğer paraneoplastik sendromlar

Paraneoplastik Sendromların Ortaya Çıkması

Paraneoplastik Sendromların Ortaya Çıkması

- Hormon ve benzeri ürünler
- Sitokin ve benzeri ürünler
- Çapraz reaksiyonlar ile immünolojik mekanizma

Kanser Hastalarında Paraneoplastik Sendromların Görülme Oranı

- Paraneoplastik sendromlar, kanser hastalarında %4-8 oranında görülebilir
- Kanser türü, evresine göre ve yaşam beklentisinin uzamasına göre bu oran değişir
- Tedavisi semptoma göre ve primer hastalığını türüne göre yapılır

Montserrat Miret at al, PLoS ONE 2017

Paraneoplastik Endokrin Sendromlar

SENDROM GRUBU	SENDROM	SIK NEDEN OLAN KANSERLER	MEKANİZMA
ENDOKRİN	Cushing sendromu	•Küçük hücreli AC Ca •Pankreas Ca •Nöral tümörler •Timoma	Ektopik ACTH ve ACTH-like maddeler
	UADHS	•Küçük hücreli AC Ca •CNS malignansiler	Antidiuretik hormon
	Hiperkalsemi	•AC Ca (yassı hücreli) •Meme Ca •Renal hücreli Ca •Multiple myelom •Adult T hücreli leukemia/lenfoma •Over Ca	PTHrP (Parathyroid hormone-related protein), TGF-α, TNF, IL-1
	Hipoglisemi	•Fibrosarkoma •Diğer mezankimal sarkomlar •Hepatoselüller Ca	Insulin, insulin-benzeri madde veya IGF-II
	Karsinoid sendrom	•Nöroendokrin tümörler	Serotonin, bradakinin

Paraneoplastik Endokrin Sendromlar

Cushing Sendromu

- **Increased levels of ACTH may be detectable in up to 50% of patients with lung cancer**
- **Cushing syndrome has been described in 1 to 5% of patients with SCLC**
- **Most commonly, Cushing syndrome occurred in patients with pulmonary carcinoid (35 of 90)**

Hiraki A et al, Lung Cancer

Paraneoplastik Endokrin Sendromlar
Cushing Sendromu

- Iatrogenic Cushing's syndrome

- Ectopic ACTH syndrome

  About **1 -7%** of patients with small-cell lung cancer have ectopic ACTH syndrome small-cell lung carcinoma causes half of all cases of the syndrome.

- Cushing's disease

  Pituitary ACTH-dependent Cushing's syndrome

  ACTH-independent macronodular adrenal hyperplasia or primary pigmented nodular adrenocortical disease.

UpToDate 2023

Paraneoplastik Endokrin Sendromlar

Cushing Sendromu

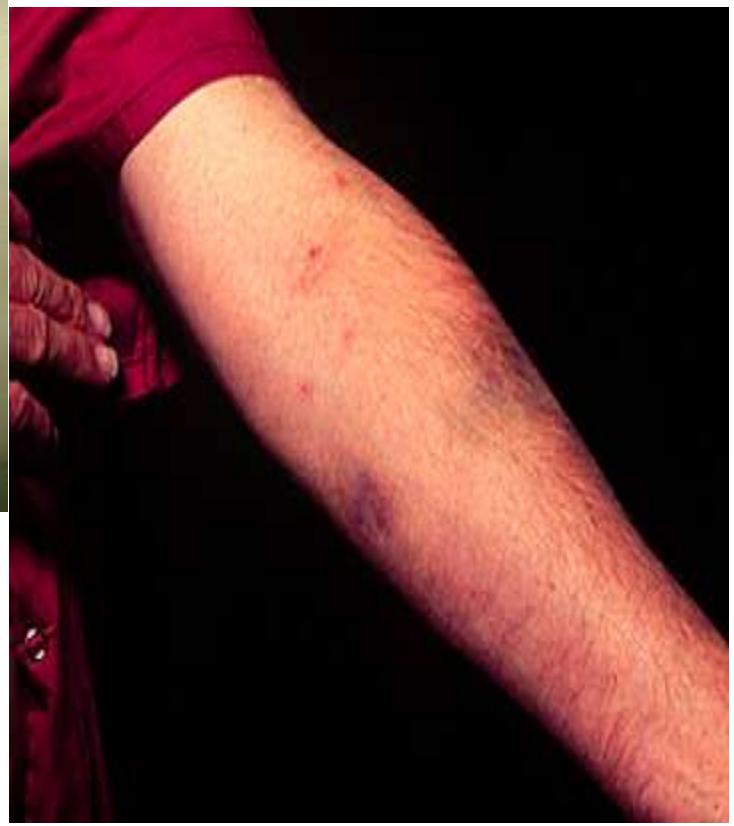
- Belirti ve bulgular
  - Sentripedal obezite
  - Pleatorik yüz
  - Glukoz intoleransı
  - Halsizlik, proksimal
  - Myopati
  - Hipertansiyon
  - Psikolojik değişiklik
  - Kolay çürük oluşumu
  - Hirsutizm
  - Oligo-amenore
  - İmpotans
  - Akne, yağlı deri
  - Abdominal stria
  - Bacak ödemi
  - Sırt ağrısı, vertebral
  - Kollaps, kırık
  - Polidipsi, poliüri
  - Böbrek taşı
  - Hiperpigmentasyon
  - Başağrısı
  - Eksoftalmus

HİPERGLİSEMİ, HİPOKALEMİ ve LENFOPENİ

Cushing Sendromu Semptomları ve Bulguları

Symptom or sign	Reported incidence, percent
Centripetal obesity	79 to 97
Facial plethora	50 to 94
Glucose intolerance	39 to 90
Weakness, proximal myopathy	29 to 90
Hypertension	74 to 87
Psychological changes	31 to 86
Easy bruisability	23 to 84
Hirsutism	64 to 81
Oligomenorrhea or amenorrhea	55 to 80
Impotence	55 to 80
Acne, oily skin	26 to 80
Abdominal striae	51 to 71
Ankle edema	28 to 60
Backache, vertebral collapse, fracture	40 to 50
Polydipsia, polyuria	25 to 44
Renal calculi	15 to 19
Hyperpigmentation	4 to 16
Headache	0 to 47
Exophthalmos	0 to 33
Tinea versicolor infection	0 to 30
Abdominal pain	0 to 21

Cushing Sendromu



Striae in Cushing's disease

Axillary and lower abdominal striae in a 21-year-old man with Cushing's disease. Abdominal obesity is also present.

Courtesy of David N Orth, MD.

Paraneoplastik Cushing Sendromu Prognozu Kötüdür

- SCLC associated with the ectopic ACTH syndrome is more resistant to chemotherapy and severe hypercortisolism is responsible for a high rate of life-threatening
- Median survival was only 3.57 months

Hiraki A et al, Lung Cancer, 2004

Paraneoplastik Endokrin Sendromlar Tedavi

KHAK tedavisinde;

Cushing Sendromu tedavisi derhal başlamalıdır

1. Tümör yükünün azaltılması
   - Kemoterapi
   - Radyoterapi
   - Cerrahi
2. Medikal ya da cerrahi endokrin tedaviler
   - Ketakanazol, mitotan, aminoglutetimid, metirapon, etomidat, mifepriston
   - Adrenalektomi

Paraneoplastik Endokrin Sendromlar
Uygunsuz ADH Sendromu

Check for full text availability | PubMed

The syndrome of inappropriate secretion of antidiuretic hormone (SIADH) in small-cell lung cancer.

List AF, Hainsworth JD, Davis BW, Hande KR, Greco FA, Johnson DH

J Clin Oncol. 1986;4(8):1191.

Review of clinical data from 350 patients with small-cell lung cancer (SCLC) revealed hyponatremia (sodium less than 130 mEq/L) attributable to the syndrome of inappropriate secretion of antidiuretic hormone (SIADH) in 40 patients (11%). Although hyponatremia was severe in most instances (median, sodium 117 mEq/L), symptoms attributable to water intoxication were identified in only 27% of hyponatremic episodes. Development of SIADH showed no correlation with clinical stage, distribution of metastatic sites, sex, or histologic subtype of small-cell carcinoma. SIADH occurred most often with initial presentation (33 of 40), and resolved promptly (less than 3 weeks) with initiation of combination chemotherapy in 80% of evaluable patients. The presence of SIADH did not influence response to chemotherapy or overall survival as an independent variable. However, in five patients profound hyponatremia developed immediately following primary cytotoxic therapy (range, one to five days). Despite initial control of SIADH, dilutional hyponatremia recurred in 70% of patients with tumor progression. Our findings suggest that development of clinically demonstrable SIADH in patients with SCLC is dependent on functional properties of the neoplastic cells, rather than tumor burden or metastatic site. The potential for development of clinically significant hyponatremia early in the course of cytotoxic therapy emphasizes the need to closely monitor patients, particularly those receiving chemotherapy, vs. giving prophylactic intravenous hydration.

3016206

Uygunsuz ADH Sendromun %75 SCLC(Küçük hücreli akciğer kanseri) ilişkili, ve SCLC yaklaşık %10 oranında görülür.

Check for full text availability | PubMed

The occurrence of hyponatremia in SCLC and the influence on prognosis: a retrospective study of 453 patients treated in a single institution in a 10-year period.

Hansen O, Sorensen P, Hansen H

Lung Cancer. 2010;67(1):

Hyponatremia is often seen in SCLC and is thought to be caused by the paraneoplastic syndrome SIADH. Variable results of the prognostic significance of low P-sodium (P-Na) have been reported. This study was performed to investigate the prognostic value of hyponatremia in SCLC. [illegible] was obtained from [illegible] patients diagnosed with SCLC and treated at Odense University Hospital from 1995 to 2005 in which data on P-sodium was available. The standard chemotherapy was six cycles of carboplatin-etoposide. P-Na was<125 mEq/L in 47 patients (7%), [illegible] 265 patients (44%), and 255 patients (56%) showed normal values. The median survival was 11.2 months in patients with normal P-Na, and 7.1 months in patients with subnormal values (p=0.0001). In a Cox multivariate analysis of the 402 patients treated with carboplatin-etoposide, hyponatremia was associated with poorer prognosis. Other independent prognostic factors included LDH, gender, age, performance status, stage, and low value of albumin. Treatment prior to year 2000 was of border line significance, while insignificant factors included hemoglobin level, WBC and alkaline phosphatase. In 61 patients with P-Na<130 mEq/L receiving two or more cycles of chemotherapy, only 15 of the 61 patients (25%) normalized the value of P-Na to 136 mEq/L or above at the time of the second cycleof chemotherapy. The patients who did not fully regain normal values of P-Na, had poorer survival compared with the patients who did in a univariate analysis (p=0.027), and in a Cox multivariate analysis. In conclusion, hyponatremia was a significant prognostic factor associated with poor prognosis and so was failure to normalize P-Na within the first two cycles of chemotherapy.

Department of Oncology, R, Odense University Hospital, DK-5000 Odense C, Denmark. olfred@dadlnet.dk

19535164

Paraneoplastik Endokrin Sendromlar
Uygunsuz ADH Sendromu

Check for full text availability | PubMed

Postoperative hyponatremic encephalopathy in menstruant women.

Ayus JC, Wheeler JM, Arieff AI

Ann Intern Med. 1992;117(11):891.

OBJECTIVES: To determine factors associated with the development of encephalopathy and with its clinical course in patients with postoperative hyponatremia.

SETTING: Consultation and referral services of two university medical centers and community hospitals.

DESIGN: Case-control study (risk factors for encephalopathy) and cohort study (clinical course among patients with encephalopathy).

PATIENTS: Case patients included 65 adults with postoperative hyponatremic encephalopathy; controls included 674 adult patients who had postoperative hyponatremia without encephalopathy and who were selected from 76,678 consecutive adult surgical inpatients.

MEASUREMENTS: Age, gender, menstrual status, neurologic symptoms, time to development and degree of hyponatremia, arterial blood gas determinations, serum chemistries, morbidity and mortality.

RESULTS: Case patients included 40 women (62%) and 25 men (38%) (P>0.05); controls included 367 women (54%) and 307 men (46%) (P>0.1). Of the 34 case patients who developed permanent brain damage or died, 33 (97%) were women (P<0.001). Among the women with brain damage, 25 (76%) were menstruant (P<0.001). The relative risk for death or permanent brain damage from hyponatremic encephalopathy in women compared with men was 26 (95% CI, 5 to 141) and in menstruant women compared with postmenopausal women, 26 (CI, 11 to 62). Arterial PO2 at diagnosis was significantly lower in female than in male case patients (34 +/- 5 compared with 91 +/- 3 mm Hg; P<0.001). Further, of the 38 case patients who had respiratory arrest before the diagnosis of hyponatremic encephalopathy, 36 (95%) were women. Extent of or time to development of hyponatremia did not correlate with subsequent brain damage (P>0.1).

CONCLUSIONS: Women and men are equally likely to develop hyponatremia and hyponatremic encephalopathy after surgery. However, when hyponatremic encephalopathy develops, menstruant women are about 25 times more likely to die or have permanent brain damage compared with either men or postmenopausal women.

Baylor College of Medicine, Houston, Texas.

1443949

Check for full text availability | PubMed

Thiazide-induced hyponatremia associated with death or neurologic damage in outpatients.

Ashraf N, Locksley R, Arieff AI

Am J Med. 1981;70(6):1163.

7224890

Check for full text availability | PubMed

Severe hyponatraemia: complications and treatment.

Ellis SJ

QJM. 1995;88(12):905.

To observe the incidence of complications in severely hyponatraemic hospitalized patients and relate outcome to rate of correction, all patients admitted to a tertiary referral hospital in New York City, USA or a group of hospitals in Oxford, UK with a sodium=<or = 120 mmol/l were studied. Review of the notes and prospective evaluation were used to ascertain cause of hyponatraemia, method of management and outcome. There were 64 episodes in New York and 160 in Oxford, over 9.5 months and one year, respectively; 79% had chronic hyponatraemia (>3 days duration). During hyponatraemia, 76% of patients had clouding of consciousness with 11% in coma. Other hyponatraemic complications included long track signs (including hemiparesis) (6.0%), seizures (3.3%), hallucinations (0.5%), tremor (1.0%), intellectual impairment without clouding of consciousness (0.5%), and acute psychosis (0.5%). 4.3% died as a direct result of their electrolyte disturbance. After correction, central pontine myelinolysis (0.3%), post-correction seizures (1.0%), intellectual impairment (2.2%), tremor (0.5%), paraesthesiae (0.5%), and striatal syndrome (0.5%) were observed. Correction of hyponatraemia was started in 156 patients, and the mean maximum rate of correction in 24 h was 8.4 mmol/l (SD 5.6, range 2-42). The maximum rate of correction was higher in those who developed neurological sequelae (12.1 mmol/l/24 h vs. 8.2 mmol/l/24 h; p = 0.0125, t-test, separate variance, two-tail). Neurological sequelae were associated with faster rates of correction, and correction of chronic severe hyponatraemia should be<=10 mmol/l in 24 h.

Department of Neurology, University of Keele, North Staffordshire Royal Infirmary, Stoke-on-Trent, UK.

Nausea and malaise, which are the earliest findings, may be seen when the serum sodium concentration falls below 125 to 130 .Headache, lethargy, obtundation and eventually seizures, coma, and respiratory arrest can occur if the serum sodium concentration falls below 115 to 120 Noncardiogenic pulmonary edema has also been described.

Paraneoplastik Endokrin Sendromlar
Uygunsuz ADH Sendromu

TANI

- Plazma Na< 135 meq/l
- Plazma ozmolarite <280 mosm/kg
- İdrar Na >20 meq/l

Paraneoplastik Endokrin Sendromlar
Uygunsuz ADH Sendromu

TEDAVİ

- **Altta yatan malignite tedavisi**

- **Akut tedavi(Na <120)**

  Hipertonik NaCl

  - **IV Furosemid 1mg/kg +elektrolit replasmanı**
  - **24 saat Na artışı 10-12mmol /L geçmemeli**
  - **Aksi takdirde nörolojik hasar: santral pontin myelinoliziz**

- **Kronik tedavi**
  - **Su kısıtlaması günde 500-1000ml**
  - **Demeklosiklin 300-600mg/gün**
  - **Vasopresin reseptör antagonisti (conivaptan)**

Paraneoplastik Endokrin Sendromlar
Uygunsuz ADH Sendromu

- Elevated levels of antidiuretic hormone (ADH) and impaired water handling can be observed in 30 to 70% of lung cancer patients
- However, excessproduction of ADH does not always produce symptoms
- Only 1 to 5% of all patients with lung cancer have symptoms attributable to the syndrome of inappropriate antidiuretic hormone secretion.
- SIDAH is frequently caused by SCLC. In a study by List and co-workers approximately 10% of patients with SCLC had SIADH
- SIADH did not correlate with clinical stage or metastatic sites.
- SIADH occurred most often with initial presentation and promptly resolved with initiation of combined chemotherapy in 80% of the patients.
- Response to chemotherapy and survival was not influenced by the presence of SIADH
- Recurrence of SIADH was associated with tumour progression.

Hiraki A et al, Lung Cancer, 2004

Hiperkalsemi Nedenleri

- Paratiroid ile ilişkili → % 90
- Maligniteler ile ilişkili
- D vitamini ile ilişkili
- Artmış kemik dönüşümü
- Renal yetersizliğe bağlı

Hiperkalsemi Semptomları

- Yorgunluk, halsizlik
- Kilo kaybı, zayıflama
- Bulantı, kusma
- Konstipasyon
- Poliüri
- Mental konfüzyon, şuur kaybı
- Kardiak aritmi

Paraneoplastik Hiperkalsemi

- Semptomlar daha belirgin
- Akut olarak ortaya çıkabilir
- Acil tedavi gereksinimi fazla
- Kanser tanısından önce ortaya çıkabilir
- Kötü bir prognostik faktördür

Paraneoplastik Hiperkalsemi

- Akciğer kanseri (%35)
- Meme kanseri (% 25)
- Hematolojik maligniteler (miyelom+lenfoma) (%14)
- Genitouriner tümörler (% 6)
- Diğer (% 20)

Paraneoplastik Hiperkalsemi

- Hiraki and colleagues examined 1149 patients with **lung cancer** and found **6%** to have hypercalcemia
- Among those with hypercalcemia, **51% had squamous cel** carcinoma, **22% had adenocarcinoma**, and **15% had SCLC**.
- **Most of those patients** had **advanced disease (stage III or IV).**
- **Median survival was only 3.8 months**.

Hiraki A et al, Lung Cancer, 2004

Paraneoplastik Hiperkalsemi

- Solid tümörlerde görülen hiperkalseminin % 70’ i humoral
- PTHrP (parathormone related peptide) salınımına bağlı
- PTH ile % 70 benzerlik var

Paraneoplastik Hiperkalsemi

Malignancies associated with hypercalcemia

Osteolytic metastases:
Breast cancer
Multiple myeloma
Lymphoma
Leukemia
Humoral hypercalcemia (PTHrP):
Squamous cell carcinomas
Renal carcinomas
Bladder carcinoma
Breast cancer
Ovarian carcinoma
Non-Hodgkin lymphoma
CML
Leukemia
Lymphoma
1,25-dihydroxyvitamin D:
Lymphoma (Non-Hodgkin, Hodgkin, lymphomatosis/granulomatosis)
Ovarian dysgerminomas
Ectopic PTH sectretion:
Ovarian carcinoma
Lung carcinomas
Neuroectodermal tumor
Thyroid papillary carcinoma
Rhabdomyosarcoma
Pancreatic cancer

Graphic 74189 Version 2.0

Osteolytic metastases with local release of cytokines (including osteoclast activating factors); tumor secretion of parathyroid hormone-related protein (PTHrP); and tumor production of 1,25-dihydroxyvitamin D (calcitriol)

Osteolytic metastases account for approximately 20 percent of cases of hypercalcemia of malignancy

Hiperkalsemi Düzeyi

- Ca + = 11.5 – 12 mg / dl semptomsuz
- Ca + > 12 mg / dl semptomatik
- Ca + > 13 mg / dl acil müdahale
- Ca + > 15 mg / dl koma ve kardiak arest
- **Düzeltilmiş Ca = Ölçülen Ca + 0.8 x (4 – alb)**

TEDAVİ

- Hidrasyon
- Diüretik
- Bifosfonatlar(zoledronik asit)
- RANKL(Receptor activator of nuclear factor kappa-B ligand) inhibitörleri(Denosumab)
- Kalsitonin
- Steroid

BİSFOSFONATLAR

- Etkileri 48 saatten sonra başlar
- Uzun dönem kontrol sağlar
- Nefrotoksisiteye dikkat etmek gerekir
- Böbrek yetmezliğinde doz ayarlaması gerekir

Kalsitonin

- Osteoklastik kemik resorbsiyonunu önler
- Böbreklerden Ca+ atılımını arttırır
- Akut etkisi önemli
- Taşiflaksi gelişebilir
- Steroidlerle birlikte kullanımı önerilmekte
- 2-4 saat içinde akut etkili
- 4 – 8 U/kg i.m /s.c 12 saatte bir

Paraneoplastik Endokrin Sendromlar

Hipoglisemi

- İnsülinoma
- İnsülinoma dışı tümör hipoglisemisi
  - Fibrosarkom
  - Diğer mezenkimal tümörler
  - Hepatosellüler Ca
  - Mezotelyoma
  - AC Ca

Paraneoplastik Endokrin Sendromlar

Hipoglisemi

- İnsülinoma dışı tümör hipoglisemisi
  - İnsulin, insulin-like madde veya IGF-II'ye bağlı ortaya çıkar
  - Yaşlı hastalara
  - İleri evre hastalar
  - Ara sıra malignite tanısından önce ortaya çıkabilir
  - Tekrarlayıcı veya sürekli özelliktedir
  - İnsülin,C-peptit,Büyüme hormon düzeyleri düşük bulunur

Paraneoplastik Nörolojik Sendromlar

SENDROM GRUBU	SENDROM	SIK NEDEN OLAN KANSERLER	MEKANİZMA
NÖROLOJİK	Lambert-Eaton miyastenik sendromu (LEMS)	• Küçük hücreli AC Ca	İmmunolojik
	Paraneoplastik serebellar degenerasyon	• AC Ca • Over Ca • Meme Ca	
	Ensefalomiyelitis		
	Limbik ensephalitis	• Küçük hücreli AC Ca	
	Brainstem ensephalitis		
	Opsoklonus -miyoklonus		
	Anti-NMDA reseptor ensephalitis	• Teratoma	

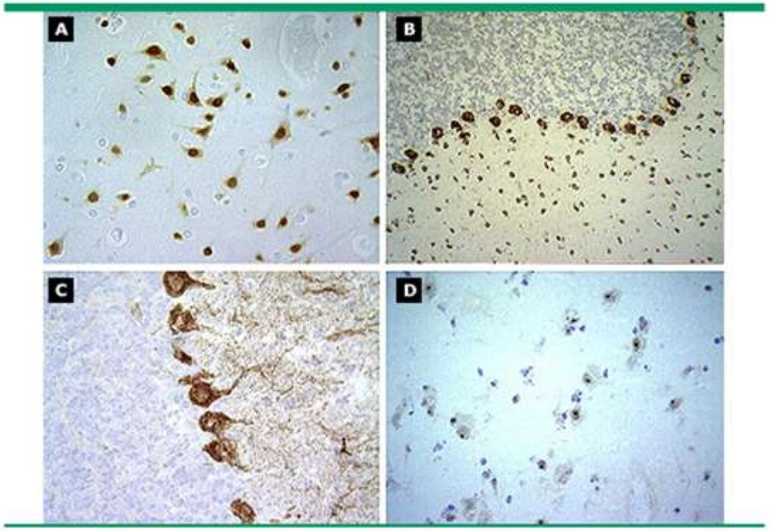
Paraneoplastik Nörolojik Sendromlar

Paraneoplastic syndromes of the central nervous system
Encephalomyelitis*
Myelitis*
Limbic encephalitis*
Brainstem encephalitis*
Cerebellar degeneration*
Opsoclonus myoclonus ataxia*
Visual syndromes
Cancer associated retinopathy*
Melanoma associated retinopathy*
Optic neuritis
Necrotizing myelopathy
Motor neuron syndrome
Subacute motor neuronopathy
Other syndromes
Stiff-person syndrome*
Subacute sensory neuronopathy*
Paraneoplastic syndromes of the peripheral nervous system
Chronic sensorimotor neuropathy
Association with plasma cell dyscrasias
Acute sensorimotor neuropathy
Guillain-Barré syndrome
Plexitis (eg, brachial neuritis)
Autonomic neuropathy*
Vasculitis of nerve and muscle
Paraneoplastic syndromes of the neuromuscular junction and muscle
Myasthenia gravis*
Lambert-Eaton myasthenic syndrome*
Dermatomyositis/polymyositis
Neuromyotonia*
Acute necrotizing myopathy
Cachectic myopathy

* Syndromes in which specific paraneoplastic markers have been identified in more than three patients. However, the absence of antibodies does not exclude a paraneoplastic etiology.

Paraneoplastik Nörolojik Sendromlar

Reactivity of paraneoplastic antineuronal antibodies



Reactivity of different paraneoplastic antibodies with the nervous system. Panel A: Reactivity of anti-Hu antibodies with human cerebral cortex. There is predominant staining of the nuclei of the neurons (with sparing of the nucleoli), and milder staining of the cytoplasm. Glial cells are not immunoreactive. Panel B: Reactivity of anti-Yo antibodies with rat cerebellum. There is intense immunolabeling of the cytoplasm of the Purkinje cells and of neurons of the molecular layer. Panel C: Reactivity of anti-Tr antibodies with rat cerebellum. There is a characteristic dot-like immunolabeling of the cytoplasm of Purkinje cells and the neuropil of the molecular layer of cerebellum. Panel D: Reactivity of anti-Ma2 (Ta) antibodies with human cerebral cortex. This antibody reacts with the nucleoli of the neurons, and shows mild immunolabeling of the cytoplasm; glial cells are not immunoreactive.

Courtesy of Josep Dalmau, MD, PhD.

Paraneoplastik Nörolojik Sendromlar

- PNS sinir sisteminin herhangi bir parçasını tutabilir
  - Yalnız bir alan (limbik ensefalit)
  - Yalnız bir hücre grubu (beyincikte Purkinje hücreleri)
  - Bir çok odak tutulumu (ensefelamiyeloradikülitis)

- Patolojik bulgular değişkendir
  - Paraneoplastik serebellar degenerasyon
    - Purkinje hücreleri tutulur
    - Nöronlar sağlam
  - Paraneoplastik ensefelomiyelitis
    - Nöron ve purkinje hücreleri tutulmuş
  - Opsoklonus–miyoklonus sendromun
    - Patolojik bulgu gözlenmeyebilir

Paraneoplastik Nörolojik Sendromlar

- Semptom ve bulgular değişken ve farklıdır
- Sıklıkla (%80) kanser tanısından önce ortaya çıkar
  - Aylar, yıllar sonra
  - Başlangıçta kanser araştırması sonuç vermeyebilir
  - PET/CT maligniteyi saptamak için en iyi seçim olabilir
- Malignite yavaş seyir göstermesine rağmen nörolojik hastalık hızlı seyir gösterebilir
  - Nörolojik tablo birkaç gün-ay içinde ortaya çıkabilir
  - Şiddetli, sakat bırakıcı ve bazen öldürücü olabilir
  - Kanserin tedavisi nörolojik hasarı düzeltemeyebilir

Paraneoplastik Nörolojik Sendromlar

Antibody	Syndrome	Associated cancers
Well characterized paraneoplastic antibodies*		
Anti-Hu (ANNA-1)	Encephalomyelitis including cortical, limbic, brainstem encephalitis, cerebellar degeneration, myelitis, sensory neuronopathy, and/or autonomic dysfunction	SCLC, other
Anti-Yo (PCA-1)	Cerebellar degeneration	Gynecological, breast
Anti-Ri (ANNA-2)	Cerebellar degeneration, brainstem encephalitis, opsoclonus-myoclonus	Breast, gynecological, SCLC
Anti-Tr	Cerebellar degeneration	Hodgkin's lymphoma
Anti-CV2/CRMP5	Encephalomyelitis, cerebellar degeneration, chorea, peripheral neuropathy	SCLC, thymoma, other
Anti-Ma proteins• (Ma1, Ma2)	Limbic, hypothalamic, brainstem encephalitis (infrequently cerebellar degeneration)	Germ-cell tumors of testis, lung cancer, other solid tumors
Anti-amphiphysin	Stiff-person syndrome, encephalomyelitis	Breast, lung cancer
Anti-recoverinΔ	Cancer-associated retinopathy (CAR)	SCLC
Partially-characterized paraneoplastic antibodies*		
Anti-Zic 4	Cerebellar degeneration	SCLC
mGluR1	Cerebellar degeneration	No tumor or Hodgkin's lymphoma
ANNA-3	Sensory neuronopathy, encephalomyelitis	SCLC
PCA2	Encephalomyelitis, cerebellar degeneration	SCLC
Anti-bipolar cells of the retina	Melanoma-associated retinopathy (MAR)	Melanoma
Antibodies that occur with and without cancer association		
Anti-VGCC	Lambert-Eaton myasthenic syndrome, cerebellar dysfunction	SCLC
Anti-AChR	Myasthenia gravis	Thymoma
Anti-NMDAR	Multistage syndrome with memory and behavioral disturbances, psychosis, seizures, dyskinesias, and autonomic dysfunction	Teratoma
Anti-AMPAR	Limbic encephalitis, psychiatric disturbances	Variable solid tumors
Anti-GABA(B) receptor	Seizures, limbic encephalitis	SCLC
Anti-LGI1 (previously attributed to VGKC)	Limbic encephalitis, seizures	Thymoma, SCLC
Anti-CASPR2 (previously attributed to VGKC)	Morvan's syndrome and some patients with neuromyotonia	Thymoma and variable solid tumors
Anti-nAChR	Subacute pandysautonomia	SCLC, others
GlyR	Encephalomyelitis with muscle spasms, rigidity, myoclonus, hyperekplexia	Often without cancer

PCA: Purkinje cell antibody; ANNA: antineuronal-nuclear antibody; VGCC: voltage-gated calcium channel; VGKC: voltage-gated potassium channel; nAChR: neuronal acetyl-choline receptor.

* Well-characterized antibodies are those directed against antigens whose molecular identity is known, or that have been identified by several investigators. (Graus F, et al. J Neurol Neurosurg Psychiatry 2004; 75:1135.)

• Antibodies to Ma2: younger than 45 years, usually men with testicular germ-cell tumors; older than 45, men or women with lung cancer and less frequently other tumors. Ma1 antibodies often associated with tumors other than germ-cell neoplasms and confers a worse prognosis, with more prominent brainstem and cerebellar dysfunction.

Δ Other antibodies reported in a few or isolated cases include antibodies to tubby-like protein and the photoreceptor-specific nuclear receptor.

Paraneoplastik Nörolojik Semptomla Ortaya Çıkan Malignitelerin Seyri Daha İyidir

Check for full text availability | PubMed

Anti-Hu antibodies in patients with small-cell lung cancer: association with complete response to therapy and improved survival.

Graus F, Dalmou J, ReñéR, Tora M, Malats N, Verschuuren JJ, Cardenal F, Viñolas N, Garcia del Muro J, Vadell C, Mason WP, Rosell R, Posner JB, Real FX

J Clin Oncol. 1997;15(8):2866.

PURPOSE: Anti-Hu antibodies (HuAb) recognize antigens expressed by neurons and small-cell lung cancer (SCLC). High titers of HuAb were initially reported in serum from patients with paraneoplastic encephalomyelitis/sensory neuropathy (PEM/SN) and SCLC. Preliminary studies have indicated that some SCLC patients without PEM/SN harbor low titer of HuAb in their serum, and that the SCLC of these patients may grow more indolently. Based on these observations, we conducted a multicenter prospective study of SCLC patients without PEM/SN to determine the incidence and prognostic implications of HuAb.

METHODS: Serum samples were collected at diagnosis of SCLC in 196 patients without PEM/SN. HuAb were determined by immunoblot of purified recombinant HuD antigen.

RESULTS: HuAb were detected in 32 (16%) of the 196 patients. Of the 170 patients who received treatment for the tumor, 27 (16%) were HuAb positive. HuAb was associated with limited disease stage (59.3% v 38.6%; P = .047), complete response to therapy (55.6% v 19.6%; P< 001), and longer survival (14.9 v 10.2 months; P = .018). In a logistic regression analysis, HuAb status was an independent predictor of complete response induction. The probability of achieving a complete response was more than five times higher in HuAb-positive than in HuAb-negative patients (odds ratio, 5.4; 95% confidence interval, 1.71 to 16.89; P = .004). Cox multivariate analysis indicated that HuAb status was not independently associated with survival.

CONCLUSION: The presence of HuAb at diagnosis of SCLC is a strong and independent predictor of complete response to treatment. This feature accounts for the association between HuAb and longer survival.

Service of Neurology, Hospital Clínic i Provincial, Barcelona, Spain. graus@medicine.ub.es

9256130

Check for full text availability | PubMed

Favourable prognosis in Lambert-Eaton myasthenic syndrome and small-cell lung carcinoma.

Maddison P, Newsom-Davis J, Mills KR, Souhami RL

Lancet. 1999;353(9147):117.

10023900

Check for full text availability | PubMed

P/Q-type calcium channel antibodies, Lambert-Eaton myasthenic syndrome and survival in small cell lung cancer.

Wirtz PW, Lang B, Graus F, van den Maagdenberg AM, Saiz A, de Koning Gans PA, Twijnstra A, Verschuuren JJ

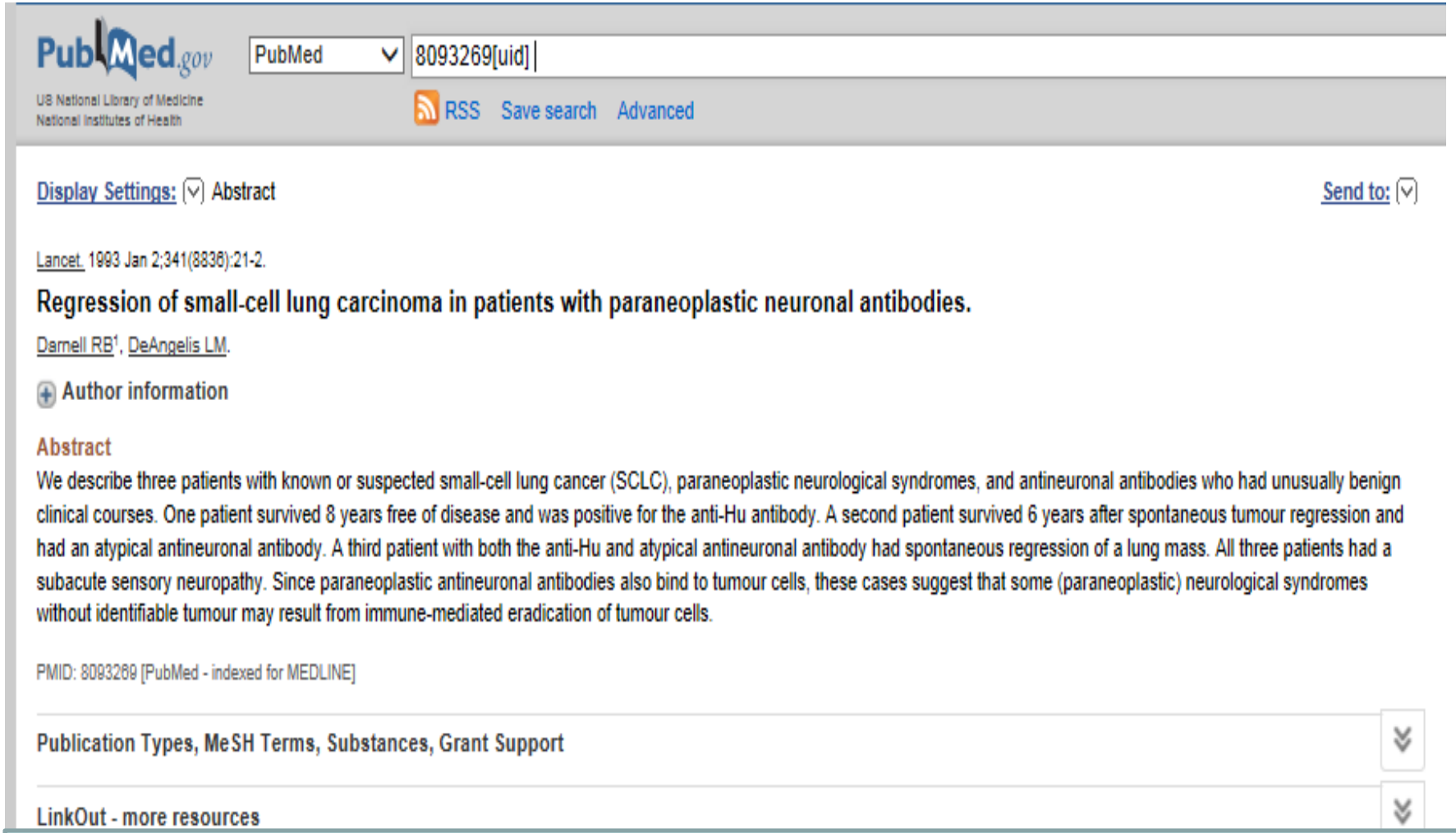
J Neuroimmunol. 2005;164(1-2):161.

To assess the survival impact of the presence of P/Q-type calcium channel antibodies in patients with small cell lung carcinoma (SCLC), we examined the frequency of the antibodies and Lambert-Eaton myasthenic syndrome (LEMS) in 148 consecutive patients with SCLC, and in 30 patients with paraneoplastic cerebellar degeneration and SCLC, and studied their relation with survival. In both series, only patients with LEMS had a remarkably long survival, whereas presence of the antibodies without LEMS did not result in a better prognosis.

Department of Neurology, Leiden University Medical Center, P.O. Box 9600, 2300 RC Leiden, The Netherlands. pwwirtz@lumc.nl

15904978

Paraneoplastik Nörolojik Sendromlar



PubMed.gov
US National Library of Medicine
National Institutes of Health

PubMed | 8093269[uid]

RSS Save search Advanced

Display Settings: Abstract

Send to:

Lancet. 1993 Jan 2;341(8836):21-2.

Regression of small-cell lung carcinoma in patients with paraneoplastic neuronal antibodies.

Darnell RB[1], DeAngelis LM.

Author information

Abstract

We describe three patients with known or suspected small-cell lung cancer (SCLC), paraneoplastic neurological syndromes, and antineuronal antibodies who had unusually benign clinical courses. One patient survived 8 years free of disease and was positive for the anti-Hu antibody. A second patient survived 6 years after spontaneous tumour regression and had an atypical antineuronal antibody. A third patient with both the anti-Hu and atypical antineuronal antibody had spontaneous regression of a lung mass. All three patients had a subacute sensory neuropathy. Since paraneoplastic antineuronal antibodies also bind to tumour cells, these cases suggest that some (paraneoplastic) neurological syndromes without identifiable tumour may result from immune-mediated eradication of tumour cells.

PMID: 8093269 [PubMed - indexed for MEDLINE]

Publication Types, MeSH Terms, Substances, Grant Support

LinkOut - more resources

Anti-Hu pozitif spontan hastalık regresyonu görülen
3 küçük hücreli akciğer vakası

Paraneoplastik Nörolojik Semptomlar

PARANEOPLASTIC SYNDROMES OF THE SPINAL CORD, NERVE, AND MUSCLE

STACY A. RUDNICKI, MD,[1] and JOSEP DALMAU, MD, PhD[1,2]

[1] Department of Neurology, University of Arkansas for Medical Sciences, 4301 West Markham, Slot 500, Little Rock, Arkansas 72205, USA
[2] Arkansas Cancer Research Center, University of Arkansas for Medical Sciences, Little Rock, Arkansas, USA

Accepted 13 June 2000

In patients with cancer, the development of peripheral nervous system dysfunction usually represents the side effects of therapy, the infiltration of nerves or spinal roots by the tumor, or metabolic and nutritional deficits. The etiology of the neurologic disorder is defined as paraneoplastic when none of the aforementioned causes are detected or when specific cancer-related immunologic mechanisms are involved. During the last 20 years, many studies on paraneoplastic neurologic syndromes have focused on a group of disorders that often develop before the tumor is diagnosed. These disorders have a subacute and debilitating course and are associated with antibodies that are markers of paraneoplasia (Table 1). These disorders, however, are extremely rare (less than 1% of all cancer patients), with the exception of Lambert–Eaton myasthenic syndrome (LEMS) that affects 3% of patients with small-cell lung cancer (SCLC)[65] and myasthenia gravis (MG), which develops in one-third of thymoma patients.[164] Most paraneoplastic disorders of the peripheral nervous system are not associated with marker antibodies. Furthermore, a significant number of patients with cancer develop symptoms of paraneoplastic neuropathy or myopathy. These syndromes are usually less debilitating than those that precede tumor diagnosis and are not associated with identifiable immune-mediated mechanisms. The frequency of these disorders depends on the extent of the clinical and electrophysiologic examinations used to detect them, and varies from 5 to 40%.[188,228]

Identification of a neurologic disorder as paraneoplastic is important because it may lead to the detection of the tumor and avoid unnecessary studies to determine the cause of complications of the cancer. For some paraneoplastic syndromes, treatment of the tumor or immune modulation may result in neurologic improvement. This review focuses on paraneoplastic syndromes of the spinal cord, peripheral nerve, and muscle (Table 2).

Abbreviations: ALS, amyotrophic lateral sclerosis; CMAP, compound muscle action potential; CT, computed tomography; CSF, cerebrospinal fluid; EMG, electromyography; GAD, glutamic acid decarboxylase; GBS, Guillain–Barré syndrome; Ig, immunoglobulin; IL, interleukin; INF, interferon; IVIg, intravenous immunoglobulin; LEMS, Lambert–Eaton myasthenic syndrome; M protein, monoclonal protein; MAG, myelin-associated glycoprotein; MG, myasthenia gravis; MGUS, monoclonal gammopathy of undetermined significance; MND, motor neuron disease; MRI, magnetic resonance imaging; PEM, paraneoplastic encephalomyelitis; PET, positron emission tomography; POEMS, polyneuropathy, organomegaly, endocrinopathy, M component, and skin changes; PSN, paraneoplastic sensory neuronopathy; SCLC, small-cell lung cancer; TNF, tumor necrosis factor; VGCC, voltage-gated calcium channel; VGKC, voltage-gated potassium channel

Key words: myelopathy; myopathy; neuropathy; paraneoplastic

Correspondence to: J. Dalmau; e-mail: dalmaujosepo@exchange.uams.edu

Paraneoplastic disorders (PND) are more frequent than previously considered, with an incidence that varies with the neurologic syndrome and type of tumor. The more common syndromes are Lambert-Eaton myasthenic syndrome (LEMS), which affects approximately 3 percent of patients with small-cell lung cancer (SCLC), and myasthenia gravis, which affects 15 percent of all patients with thymoma. For other solid tumors, the incidence of paraneoplastic neurologic syndromes is far less than 1 percent in most tumors

Paraneoplastik Nörolojik Semptomlar
Lambert Eaton Sendromu

- Nöromusküler bileşkenin presinaptik bölgesini etkileyen otoimmün bir hastalık
  - KHAK'li hastaların %2-3'ünde (Tüm PNS LEMS'ların %60)
  - Sendrom sıklıkla tümör tanısından önce ortaya çıkar.
  - Daha çok erkeklerde
  - Timoma ve lenfomalarda da görülebilmektedir.
- Belirtiler
  - Pelvik ve uyluk kaslarında yorgunluk, miyalji
  - Ağız kuruluğu,
  - Disartri,
  - Disfaji,
  - Pitozis,
  - Okuler kas güçsüzlüğü, görme bozukluğu
  - Derin tendon reflekslerinin azalması ve/veya kaybolması

Paraneoplastik Nörolojik Semptomlar Ayrıcı Tanı

Kanser tanısı ile takip edilen bir hastada

- Beyin metastazları
- Leptomeningeal hastalık
- Spinal kord ve sinir kökü basısı
- RT ve KT (platinler,taksanlar ve vinka alkaloidleri) 'yi de içeren tedavilerin yan etkileri
- İnfeksiyonlar ile tablo nörolohik semptom yada bulgular açıklanamıyorsa NPNS akla gelmelidir

Paraneoplastik Nörolojik Semptomlar Ayrıcı Tanı

J Neurol Neurosurg Psychiatry. 2010 Jan;81(1):42-5. doi: 10.1136/jnnp.2008.159483. Epub 2009 Mar 25.

Cerebrospinal fluid study in paraneoplastic syndromes.

Psimaras D[1], Carpentier AF, Rossi C; PNS Euronetwork

Author information

Abstract

OBJECTIVE: Paraneoplastic neurological syndromes (PNS) probably result from an immune reaction against antigens shared by the nervous system and tumour cells. To characterise CSF alterations in these syndromes, we studied a large series of paraneoplastic patients.

METHODS: Using the PNS European database which includes patients diagnosed with PNS in Europe, we reviewed the clinical data of all patients included between 2000 and 2007 for which information on CSF was available. Patients were studied if they met the following inclusions criteria: (1) definite paraneoplastic disease with anti-Hu, anti-Yo, anti-CV2, anti-Ri anti-Ma/Ta and anti-Tr antibodies; (2) clinical information available; and (3) at least one CSF study.

RESULTS: 295 patients met the inclusion criteria. Abnormal CSF (pleiocytosis and/or high protein level and/or oligoclonal bands) was found in 93% of patients. Pleiocytosis, but not hyperproteinorachia, was more frequently seen in patients in whom the CSF study was done early in the evolution. In 24 patients, oligoclonal bands were the only abnormality found in the CSF (10%). Elevated numbers of cells were found in 47% of patients before the third month compared with 28% after the third month ($p<0.01$). This evolution might suggest a subacute inflammation phase within the nervous system, followed by a non-inflammatory phase. The inflammation profile was similar in all antibody types, cancers or neurological syndromes of the PNS. Surprisingly, anti-Hu patients with high pleiocytosis at the time of diagnostic had a better survival in this study than those without pleiocytosis (572 days vs 365 days; $p = 0.05$).

CONCLUSION: CSF inflammation is a common finding in PNS patients and can be a helpful tool for diagnosis, especially if this analysis is done within 3 months after neurological onset.

Comment in

Cerebral spinal fluid abnormalities in patients with paraneoplastic syndromes of the nervous system. [J Neurol Neurosurg Psychiatry. 2010]

The combination of negative cytology for malignant cells and the absence of meningeal enhancement on MRI can reasonably exclude leptomeningeal carcinomatosis.

Inflammatory changes (eg, pleocytosis, intrathecal synthesis of IgG, oligoclonal bands) can support the presence of an inflammatory or immune-mediated neurologic disorder

.

Paraneoplastik Nörolojik Semptomlar
Ayrıcı Tanı

NCBI Resources How To

PubMed.gov US National Library of Medicine National Institutes of Health

PubMed 24360484[uid]

RSS Save search Advanced

Display Settings: Abstract Send to:

Lancet Neurol. 2014 Feb;13(2):167-77. doi: 10.1016/S1474-4422(13)70282-5. Epub 2013 Dec 18.

Antibody titres at diagnosis and during follow-up of anti-NMDA receptor encephalitis: a retrospective study.

Gresa-Arribas N[1], Titulaer MJ[2], Torrents A[3], Aguilar E[1], McCracken L[4], Leypoldt F[1], Gleichman AJ[5], Balice-Gordon R[6], Rosenfeld MR[7], Lynch D[8], Graus F[1], Dalmau J[9].

Author information

Erratum in
Lancet Neurol. 2014 Feb;13(2):135.

Abstract

BACKGROUND: Anti-N-methyl-d-aspartate (NMDA) receptor encephalitis is a severe but treatable autoimmune disorder which diagnosis depends on sensitive and specific antibody testing. We aimed to assess the sensitivity and specificity of serum and CSF antibody testing in patients with anti-NMDA receptor encephalitis, and the relation between titres, relapses, outcome, and epitope repertoire.

METHODS: In this observational study, we used rat brain immunohistochemistry and cell-based assays (CBA) with fixed or live NMDA receptor-expressing cells to determine the sensitivity and specificity of antibody testing in paired serum and CSF samples. Samples were obtained at diagnosis from patients with anti-NMDA receptor encephalitis and from control participants worldwide. We deemed a patient to be antibody positive if their serum, their CSF, or both tested positive with both immunohistochemistry and CBA techniques; we determined titres with serial sample dilution using brain immunohistochemistry. We examined samples from 45 patients (25 with good outcome [modified Rankin Scale, mRS 0-2], ten with poor outcome [mRS 3-6], and ten with relapses) at three or more timepoints. We determined the epitope repertoire in the samples of 23 patients with CBA expressing GluN1-NMDA receptor mutants.

FINDINGS: We analysed samples from 250 patients with anti-NMDA receptor encephalitis and 100 control participants. All 250 patients had NMDA receptor antibodies in CSF but only 214 had antibodies in serum (sensitivity 100·0% [98·5-1000%] vs 85·6% [80·7-89·4%], p<0·0001). Serum immunohistochemistry testing was more often in agreement with CBA with fixed cells (77 [71%] of 108) than with CBA with live cells (63 [58%] of 108, p=0·0056). In multivariable analysis, CSF and serum titres were higher in patients with poor outcome than in those with good outcome (CSF dilution 340 vs 129, difference 211, [95% CI 1·421], p=0·049; serum dilution 7370 vs 1243, difference 6127 [2369-9885], p=0·0025), and in patients with teratoma than in those without teratoma (CSF 395 vs 110, difference 285 [134-437], p=0·0079; serum 5515 vs 1644, difference 3870 [548-7193], p=0·024). Over time there was a decrease of antibody titres in the 35 patients with good or poor outcome and samples followed at three timepoints regardless of outcome (from diagnosis to last follow-up: CSF 614 to 76, difference 538 [288-788]; serum 5460 to 1564, difference 3896 [2428-5362]; both p<0·0001). Relapses were associated with a change in titre more often in CSF than in serum (14 of 19 vs seven of 16, p=0·037). After recovery, 24 of 28 CSF samples and 17 of 23 serum samples from patients remained antibody positive. Patients' antibodies targeted a main epitope region at GluN1 aminoacid 369; the epitope repertoire did not differ between patients with different outcomes, and did not change during relapses.

INTERPRETATION: The sensitivity of NMDA receptor antibody testing is higher in CSF than in serum. Antibody titres in CSF and serum were higher in patients with poor outcome or teratoma than in patients with good outcome or no tumour. The titre change in CSF was more closely related with relapses than was that in serum. These findings emphasise the importance of including CSF in antibody studies, and that antibody titres can complement clinical assessments.

FUNDING: Dutch Cancer Society, National Institutes of Health, McKnight Neuroscience of Brain Disorders award, the Fondo de Investigaciones Sanitarias, ErasmusMC fellowship, and Fundació la Marató de TV3.

Santaral sinir sistemi sıvıda antikor saptanması tanı için daha spesifik, yüksek antikor düzeyi kötü prognoz ile ilişkili

Paraneoplastik Dermatolojik ve Romatolojik Sendromlar

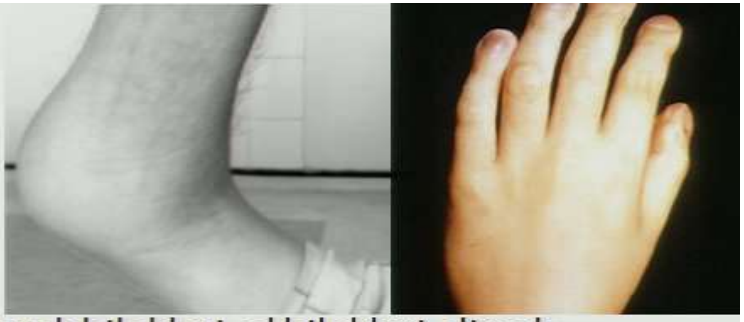
SENDROM GRUBU	SENDROM	SIK NEDEN OLAN KANSERLER	MEKANİZMA
DERMATOLOJİK ROMATOLOJİK	**Akantosis nigrikans**	Abdominal organların adeno Ca (en sık mide)	Immunologjik EGF sekresyonu
	Piyoderma gangrenozum	Hematolojik maligniteler	Immunologjik
	Pemfigus	Lenfoma, Timoma, Sarkomlar Hematolojik maligniteler	Immunologjik
	Sweet sendromu	AML ve hematolojik maligniteler Meme Ca GİS tümörleri Üriner sistem tümörleri	Immunologjik
	Dermatomiyositis	Prostat Ca Meme Ca Over Ca Akciğer Ca	Immunologjik
	Lökositoklastik vaskülit	Hematolojik maligniteler, Akciğer Ca GİS tümörleri Üriner sistem tümörleri	Immunologjik
	Hipertrofik Osteoartropati	Akciğer Ca Mezotelyoma	VEGF PDGF PGE2

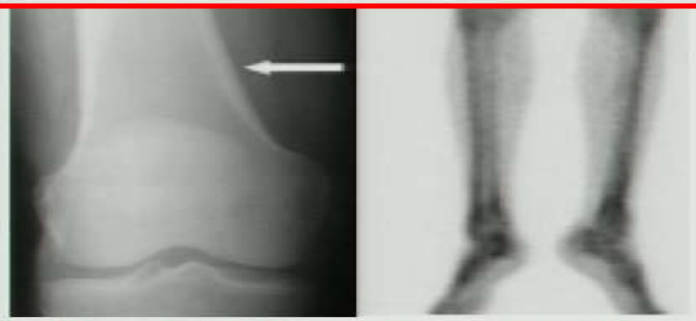
Paraneoplastik Dermatolojik ve Romatolojik Sendromlar

Hipertrofik Osteoartropati

Oligo veya poliartrit,
El ve ayak parmaklarında çomaklaşlma, } Klinik triad
Uzun kemiklerde periostit

Yaklaşık olarak %90 sebep paraneoplastiktir.
Sıklıkla akciğer ve plevral malignitelerde görülür.
AC Ca'ların %10, en sık adeno ca

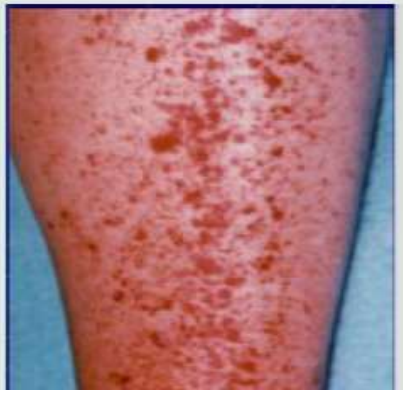




Artrit dizler, ayak bilekleri, el bilekleri, dirsek, metakarpofalangeal ve proksimal interfalangeal eklemleri tutar.
Çoğunlukla simetrik ve ağrılıdır
Komşu uzun kemiklerde hassasiyet ve periostitte bağlı şiddetli ağrılar olabilir
Tedavi altta yatan tümörün tedavisi, NSAE'lar, Bifosfonatlar, opioid analjezikler, lokalize palyatif RT

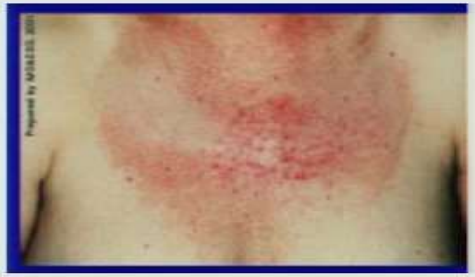
Lökositoklastik vaskülit

Alt ekstremitelerde ağrı,yanma ve kaşıntının eşlik ettiği palpable purpura
Nadiren GİS ve renal tutulum
Dolaşımdaki tümör ilişkili antijenler suçlanmaktadır.
Kanser tanısından önce ortaya çıkabilir
Tedavide tümör tedavisiyele gerileme olur
Hematolojik maligniteler, akciğer, GİS ve üriner sistem tümörleri

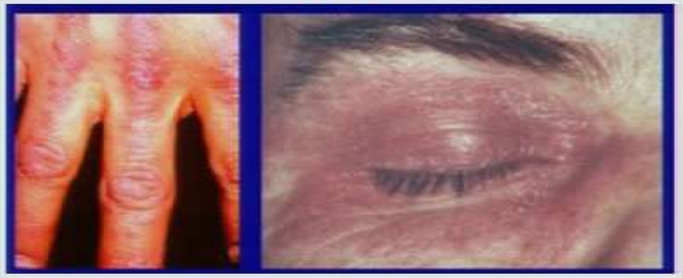


Paraneoplastik Dermatolojik ve Romatolojik Sendromlar

Dermatomyozit



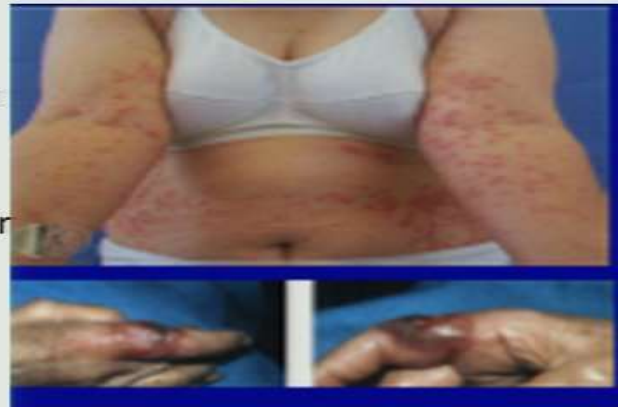
Çok sayıda deri değişikleri (heliotrop raş, boyunda V işaret, gottron papülleri) ile birlikte görülen inflamatuvar miyopati
İlerleyici simetrik proksimal kas güçsüzlüğü
Kas enzimleri artar.Anti-Mi2 ve Anti-SRP pozitifliği
Vakaların %10-25 'i paraneoplastik
Meme, over, akciğer, prostat kanseri



Konstitüsyonel semptomları varsa!
Miyosit çok ani başlangıçlıysa!
ESR yüksek ise (48 vs 25 mm/saat)!
CK seviyesi çok yüksek ise (2550 vs 1250U/ml)!
Reynoud fenomeni eşlik etmiyorsa!
Polimyozit nadiren malignite ile ilişkili.

Sweet sendromu

Yüz, gövde ve ekstremitelerde, ani başlangıçlı, ağrılı, eritematöz plak, papül ve nodüller, nötrofili ve ateş ile karakterizedir.
Sweet sendromlu hastaların yaklaşık %20'sinin altında kanser vardır.Altta yatan tümörün tedavisi nadiren semptomları iyileştir
Çoğunlukla AML ve diğer hematolojik maligniteler
Solid tümörlerden meme, gentoüriner ve GİS kanserleri



Paraneoplastik Dermatomiyozit ve Polimiyozit

Display Settings: Abstract Send to:

Ann Intern Med. 1976 Jan;84(1):68-76.

Dermatomyositis and malignancy. A review of the literature.

Barnes BE, Mawr B.

Abstract

Although there appears to be an increased incidence of malignancy among patients with dermatomyositis, demonstration of definitive statistical significance is precluded by the lack of large, controlled series. Patients with the two diseases tend to be older than the general dermatomyositis population and younger than those with cancer alone; and there is a preponderance of female patients. Tumors of the ovary and stomach are more frequently observed than in the general population, while colorectal malignancies are underrepresented. Most reported cases show development of the diseases within a year of one another, and, in some patients, the course of the myopathy follows that of the tumor. No definitive cause for the myopathy in these patients has been established.

PMID: 1106291 [PubMed - indexed for MEDLINE]

İleri yaş, kadın cinsiyeti, mide ve over ca ile ilişkili

Paraneoplastik Dermatomiyozit ve Polimiyozit

N Engl J Med. 1992 Feb 6;326(6):363-7.

Risk of cancer in patients with dermatomyositis or polymyositis. A population-based study.

Sigurgeirsson B[1], Lindelof B, Edhag O, Allander E

Author information

Abstract

BACKGROUND: An association between polymyositis and cancer was first proposed in 1916, but the existence of the association has been disputed. An association between dermatomyositis and cancer is better accepted, but its magnitude is not known.

METHODS: We undertook a study to provide accurate estimates of the risk of cancer in patients with dermatomyositis or polymyositis. We studied the incidence of cancer and the rate of mortality from cancer in a population-based cohort of 788 patients with dermatomyositis or polymyositis in Sweden from 1963 through 1983. The results were compared with those for the general population.

RESULTS: Among the 396 patients with polymyositis, 42 cancers were diagnosed at the same time or after polymyositis was diagnosed in 37 patients (9 percent). The relative risk of cancer was 1.8 (95 percent confidence interval, 1.1 to 2.7) in the male patients and 1.7 (95 percent confidence interval, 1.0 to 2.5) in the female patients. Eighty-four males and 85 females died, and in 24 of these cases (14 percent) cancer was the principal cause of death. The mortality ratio (the rate of mortality from cancer in these patients as compared with that in the general population) was 0.90 (95 percent confidence interval, 0.6 to 1.4). Among the 392 patients with dermatomyositis, 61 cancers were diagnosed at the same time or after dermatomyositis was diagnosed in 59 patients (15 percent). The relative risk of cancer was 2.4 (95 percent confidence interval, 1.6 to 3.6) in the male patients and 3.4 (95 percent confidence interval, 2.4 to 4.7) in the female patients. Fifty-seven males and 110 females died, and in 67 of these cases (40 percent) cancer was the principal cause of death (mortality ratio, 3.8; 95 percent confidence interval, 2.9 to 4.8).

CONCLUSIONS: The risk of cancer is increased in patients with polymyositis or dermatomyositis. In patients with dermatomyositis there is also a higher rate of mortality from cancer.

PMID: 1729618 [PubMed - indexed for MEDLINE] Free full text

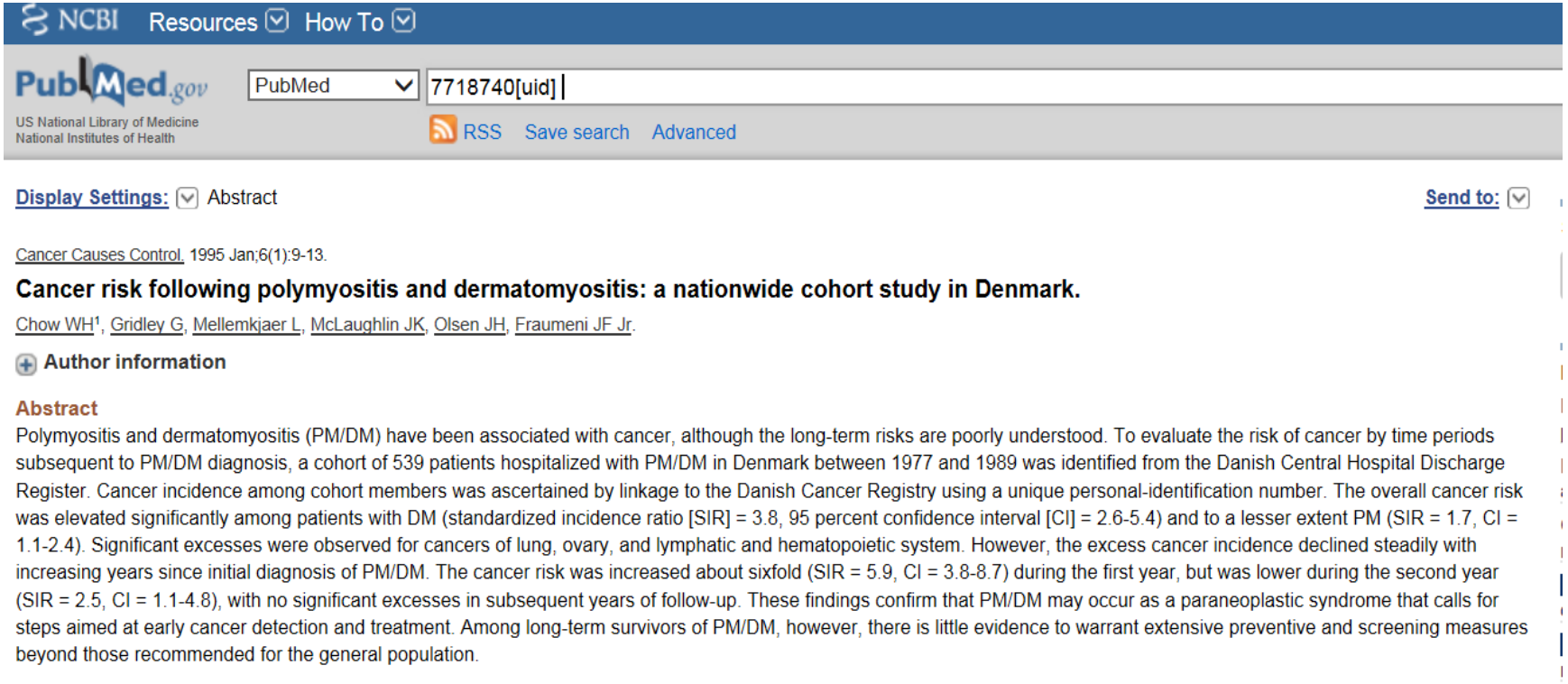
MeSH Terms

LinkOut - more resources

The relative risk of cancer among patients with DM was 2.4 for males and 3.4 for females. The relative risk of cancer among patients with PM was 1.8 for males and 1.7 for females.

DM and PM, was not associated with an increased risk of cancer mortality compared with the general population.

Paraneoplastik Dermatomiyozit ve Polimiyozit



NCBI Resources How To

PubMed.gov
US National Library of Medicine
National Institutes of Health

PubMed 7718740[uid]

RSS Save search Advanced

Display Settings: Abstract Send to:

Cancer Causes Control. 1995 Jan;6(1):9-13.

Cancer risk following polymyositis and dermatomyositis: a nationwide cohort study in Denmark.

Chow WH[1], Gridley G, Mellemkjaer L, McLaughlin JK, Olsen JH, Fraumeni JF Jr.

Author information

Abstract

Polymyositis and dermatomyositis (PM/DM) have been associated with cancer, although the long-term risks are poorly understood. To evaluate the risk of cancer by time periods subsequent to PM/DM diagnosis, a cohort of 539 patients hospitalized with PM/DM in Denmark between 1977 and 1989 was identified from the Danish Central Hospital Discharge Register. Cancer incidence among cohort members was ascertained by linkage to the Danish Cancer Registry using a unique personal-identification number. The overall cancer risk was elevated significantly among patients with DM (standardized incidence ratio [SIR] = 3.8, 95 percent confidence interval [CI] = 2.6-5.4) and to a lesser extent PM (SIR = 1.7, CI = 1.1-2.4). Significant excesses were observed for cancers of lung, ovary, and lymphatic and hematopoietic system. However, the excess cancer incidence declined steadily with increasing years since initial diagnosis of PM/DM. The cancer risk was increased about sixfold (SIR = 5.9, CI = 3.8-8.7) during the first year, but was lower during the second year (SIR = 2.5, CI = 1.1-4.8), with no significant excesses in subsequent years of follow-up. These findings confirm that PM/DM may occur as a paraneoplastic syndrome that calls for steps aimed at early cancer detection and treatment. Among long-term survivors of PM/DM, however, there is little evidence to warrant extensive preventive and screening measures beyond those recommended for the general population.

DM ve PM tanısından sonra ilk 2 yıl içinde malignite riski var, sonraki yıllarda normal popülasyondan fark yok

Paraneoplastik Dermatomiyozit ve Polimiyozit

Display Settings: Abstract Send to:

Ann Intern Med. 2001 Jun 19;134(12):1087-95.

Incidence of malignant disease in biopsy-proven inflammatory myopathy. A population-based cohort study.

Buchbinder R[1], Forbes A, Hall S, Dennett X, Giles G.

Author information

Abstract

BACKGROUND: The validity and magnitude of an association between myositis and malignant disease continue to be debated. Such issues as the legitimacy of a myositis diagnosis and distinction among myositis subgroups in previous population-based studies remain unresolved.

OBJECTIVE: To determine the risk for malignant disease in patients with biopsy-proven inflammatory myopathies.

DESIGN: Population-based, retrospective cohort study.

SETTING: Victoria, Australia.

PATIENTS: 537 patients in whom a biopsy-positive idiopathic inflammatory myopathy was first diagnosed from 1981 through 1995.

MEASUREMENTS: Standardized incidence ratios were calculated to compare the incidence of malignant disease in patients with inflammatory myopathy and the general population.

RESULTS: A total of 116 cases of malignant disease were found in 104 patients. Seventy-four cases were identified concurrently with (within 7 days) or after diagnosis of myositis. The highest risk for malignant disease was associated with dermatomyositis (standardized incidence ratio, 6.2 [95% CI, 3.9 to 10.0]). The risk was also increased in polymyositis (standardized incidence ratio, 2.0 [CI, 1.4 to 2.7]), although the relative risk for malignant disease in dermatomyositis compared with polymyositis was 2.4 (CI, 1.3 to 4.2). An increased risk for malignant disease was also found in inclusion-body myositis (standardized incidence ratio, 2.4 [CI, 1.2 to 4.9]). The excess risk for malignant disease diminished with time (standardized incidence ratio, 4.4 [CI, 2.7 to 7.1] in the first year; 3.4 [CI, 2.3 to 5.1] between 1 and 3 years; 2.2 [CI, 1.3 to 3.9] between 3 and 5 years; and 1.6 [CI, 1.0 to 2.6] beyond 5 years [P for trend, 0.002]).

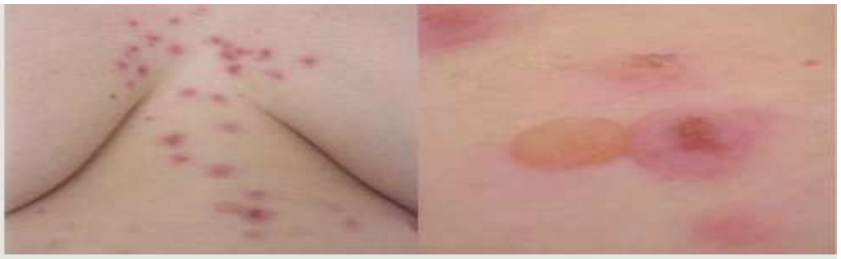
CONCLUSION: The risk for malignant disease is increased in biopsy-proven dermatomyositis and polymyositis and also appears to be increased in inclusion-body myositis.

PMID: 11412048 [PubMed - indexed for MEDLINE]

Paraneoplastik Dermatomiyositis ve Polimiyositis ilk 3 yılda malignite risk artmış, 5 yıl sonrası belirgin gerilemiş.

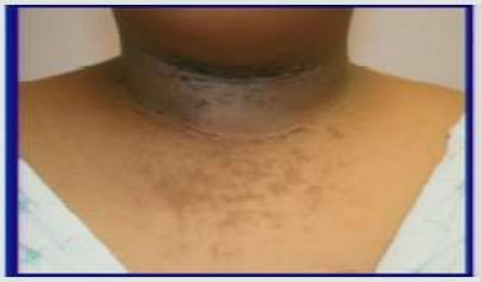
Paraneoplastik Dermatolojik, Romatolojik Sendromlar

Paraneoplastik pemfigus



Deri ve müköz membranları etkiler.
Tümör antijenlerine karşı gelişen antikorların epidermal proteinlerle immün çapraz reaksiyonu sonucu oluşur. Tedavide İmmünmodülatörler(KS'ler ve rituksimab) ve kansere yönelik tedavi

Lenfoma, timoma, sarkomlar ve hematolojik maligniteler



Akantozis Nigrikans

Aksilla, boyun ve kasıkta hiperpigmente plaklar
Histoloji: hiperkeratozis ve papillomatozisi gösterir.
Hastaların maligniteleri %90 abdominal organların adenokanseridir (en sık mide)
Avuç içlerinde akantosis nigrikansı olan hastaların %90'ı kanser ilişkili tespit edilmiştir.

Akantozis Nigrikans

Paraneoplastik AN daha agresif seyreder
Hastaların%50'den fazlasında mukazal tutulum da vardır.
Etyolojide Transforming growth faktör alfa ve epidermal growth faktör
Tedavi topikal kortikosteroidler

Paraneoplastik Hematolojik Sendromlar

SENDROM GRUBU	SENDROM	SIK NEDEN OLAN KANSERLER	MEKANİZMA
HEMATOLOJİK	**Granulositoz**	İleri evre kanserler	G-CSF
	Polisitemi	• Renal hücreli Ca • Serebellar hemangioma • Hepatosellular karsinoma	Erythropoietin
	Tomboembositoz	İleri evre kanserler	Trombopoetin ve IL6
	Nonbakteriel trombotik endocarditis	İleri evre kanserler	Hiperkoagulabilite
	Anemi	• Timik neoplazmlar	Bilinmiyor

Solid Tümör-Anemi Tedavisi

Comparison of risks and benefits of erythropoiesis-stimulating agents (ESAs) versus red blood cell (RBC) transfusion for chemotherapy-related anemia in patients with solid tumors

	ESAs	RBC transfusion
Risks	Thrombotic events*	Transfusion reactions*
	Potentially decreased survival*	Circulatory overload
		Viral infection•
		Iron overload
		Development of multiple alloantibodies
Benefits	Gradual improvement in hemoglobin/hematocrit	Rapid improvement in hemoglobin/hematocrit
	Gradual clinical improvement	Rapid clinical improvement
	Avoidance of RBC transfusions in some patients	
	Net reduction in transfusion requirements‡	

* Febrile nonhemolytic reactions (1:100); hemolytic reactions (1:19,000); transfusion-related acute lung injury (1:1000-1:5000).

• Hepatitis B, Hepatitis C, HIV.

† In trials where target hemoglobin was >12 g/dL.

‡ Average 1 unit per person.

Adjuvan tedavi alan kür şansı ve uzun yaşam beklentisi olan hastalarda kan transfüzyonu ön planda düşünülmelidir

Paraneoplastik Lökositoz

Check for full text availability | PubMed

Leukocytosis and large cell lung cancer. A frequent association.

Ascensao JL, Okeon MM, Ewing SL, Goldberg RJ, Kaplan ME.

Cancer. 1987;60(4):903.

In a retrospective study of 105 patients with non-small cell lung cancer during a 5-year period, 43 had leukocytosis. In 19 of the 43 patients, no clear cut etiology for the leukocytosis was apparent and it was attributed to the tumor itself. In these 19 patients, absolute neutrophilia was detected in 13, eosinophilia was present in three, and eleven exhibited concomitant thrombocytosis. Tumor-associated leukocytosis occurred predominantly, and eosinophilia exclusively, in patients with large cell pulmonary neoplasms. These results suggest an unusual myeloproliferative stimulus in this type of cancer. It may result from tumor cell production of hemopoietic growth factors such as granulocyte-macrophage colony-stimulating activity; however, additional studies are needed to elucidate the underlying mechanism(s), and to determine whether this is a peculiar characteristic of the cells that comprise large cell undifferentiated carcinoma of the lung.

3036338

Check for full text availability | PubMed

Leukocytosis in non hematological malignancies--a possible tumor-associated marker.

Shoenfeld Y, Tal A, Berliner S, Pinkhas J.

J Cancer Res Clin Oncol. 1986;111(1):54.

Leukocytosis (WBC counts 10,000/mm3) was detected in 77 out of 252 patients (30%) with ten different types of nonhematological malignancy (NHM) at the time of diagnosis. A full search including serological and bacteriological screening was performed to exclude other possible causes of leukocytosis. Among the different tumors, carcinomas of the lung and colorectum were the most prevalently associated with leukocytosis. Absolute monocytosis was found in 25% of the patients and absolute eosinophilia in only 4.8%. The leukocytosis was attributed mainly to an increase in the mature polymorphonuclears, suggesting a release mechanism of WBC from storage pools by factors secreted or induced by the tumor. Neither the age nor the sex of the patients affected the incidence or magnitude of leukocytosis. However, the presence of metastases was associated with a significantly higher incidence of leukocytosis (p less than 0.05). The associated leukocytosis may be regarded as a poor prognostic sign, and was associated with a significantly (p less than 0.007) shorter survival time. In contrast, absolute lymphocytosis may have a positive effect on the survival time (p = 0.01). Tumor-associated leukocytosis may be an additional tumor-associated marker, of value in assessing and monitoring patients with NHMs.

3949651

Check for full text availability | PubMed

Primary squamous cell carcinoma of the thyroid associated with leukocytosis and hypercalcemia.

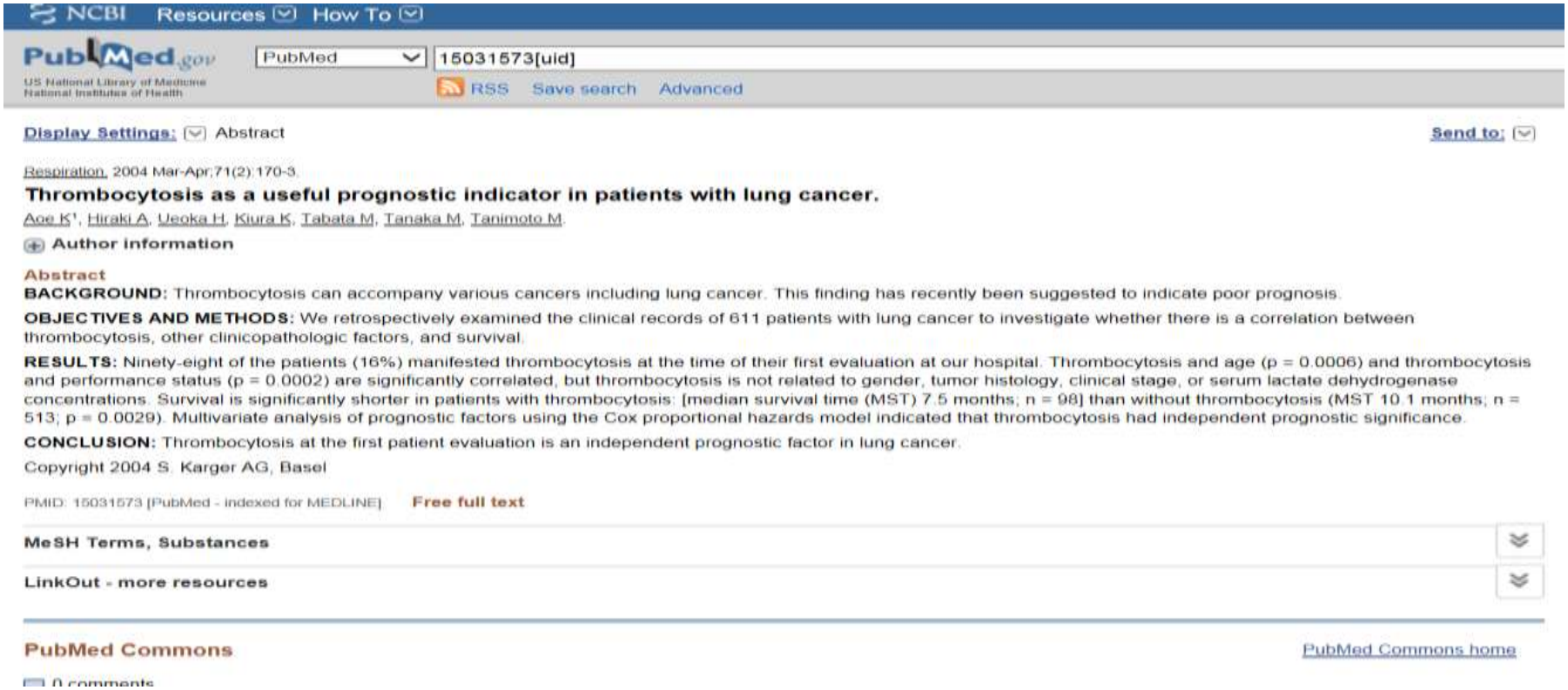
Riddle PE, Dincsoy HP.

Arch Pathol Lab Med. 1987;111(4):373.

Primary squamous cell carcinoma of the thyroid is an extremely rare, aggressive neoplasm with a uniformly poor prognosis. Described herein is a case of a 66-year-old man with primary squamous cell carcinoma of the thyroid associated with hypercalcemia (13 mg/dl, [3.24 mmol/L]) and unexplained leukocytosis (20,400/mm3 [20.4 X 10(9)/L]). The histogenesis of squamous cell carcinoma of the thyroid remains controversial. The associated hypercalcemia and leukocytosis most likely represent a form of paraneoplastic syndrome; possible mechanisms will be discussed in the light of recent studies on tumor-derived mediators.

Paraneoplastik lökositoz, myeloproliferatif sitimülan faktörlere bağlı gelişir ve kötü prognoz ile ilişkilidir..

Paraneoplastik Trombositoz



NCBI Resources How To

PubMed.gov US National Library of Medicine National Institutes of Health

PubMed 15031573[uid]

RSS Save search Advanced

Display Settings: Abstract Send to:

Respiration. 2004 Mar-Apr;71(2):170-3.

Thrombocytosis as a useful prognostic indicator in patients with lung cancer.

Aoe K[1], Hiraki A, Ueoka H, Kiura K, Tabata M, Tanaka M, Tanimoto M.

Author information

Abstract

BACKGROUND: Thrombocytosis can accompany various cancers including lung cancer. This finding has recently been suggested to indicate poor prognosis.

OBJECTIVES AND METHODS: We retrospectively examined the clinical records of 611 patients with lung cancer to investigate whether there is a correlation between thrombocytosis, other clinicopathologic factors, and survival.

RESULTS: Ninety-eight of the patients (16%) manifested thrombocytosis at the time of their first evaluation at our hospital. Thrombocytosis and age ($p = 0.0006$) and thrombocytosis and performance status ($p = 0.0002$) are significantly correlated, but thrombocytosis is not related to gender, tumor histology, clinical stage, or serum lactate dehydrogenase concentrations. Survival is significantly shorter in patients with thrombocytosis: [median survival time (MST) 7.5 months; n = 98] than without thrombocytosis (MST 10.1 months; n = 513; $p = 0.0029$). Multivariate analysis of prognostic factors using the Cox proportional hazards model indicated that thrombocytosis had independent prognostic significance.

CONCLUSION: Thrombocytosis at the first patient evaluation is an independent prognostic factor in lung cancer.

Copyright 2004 S. Karger AG, Basel

PMID: 15031573 [PubMed - indexed for MEDLINE] Free full text

MeSH Terms, Substances

LinkOut - more resources

PubMed Commons PubMed Commons home

0 comments

Thrombocytosis at presentation has been identified as an independent predictor of shortened survival. Thrombocytosis is not related clinical stage

Paraneoplastik Renal Sendromlar

SENDROM GRUBU	SENDROM	SIK NEDEN OLAN KANSERLER	MEKANİZMA
RENAL	Membranöz nefropati	Akciğer Ca, Kolon Ca Mide CA Diğer bir çok	İmmunolojik
	Membranoproliferatif glomerülonefrit	•KLL •Burkit lenfoma •Melamom •Hair cell lösemi	İmmunolojik
	Minimal değişiklik hastalığı	Hodgkin lenfoma Pankreas CA Kolon Ca Akciğer Ca, Renal hücreli Ca	VGEF
	Fokal ve segmental glomeroskleroz	Hematolojik maligniteler	IL13?
	Ig A nefropatisi	Akciğer Ca, Baş-boyun Renal hücreli Ca	İmmunolojik

Paraneoplastik Renal Sendromlar

- Genelde kanser tanısı konulduktan sonra ortaya çıkarlar.
- Kanser tanısından sonra 1 yıl içinde orta çıkmaktadırlar
- 50 yaş üstü nedeni açıklanamayan glomerulonefritli hastalar kanser taramasına adaydır
- En sık membranöz glomerulonefrit görülür

Paraneoplastik Renal Sendromlar

Membranöz glomerulonefrit

- Membranöz glomerulonefritlerin %10 maligniteye bağlı gelişir
- Hastaların tamamında aktif kanser saptanmasına rağmen malignitelerin yarısı asemptomatiktir
- Tam remisyon ancak kanserin küratif tedavisi edilen hastaların yarısında mümkün olmaktadır
- 65 yaş üstü ve 20 yıl/paket sigara içmiş membranöz glomerulonefritli hastalarda malignite riski daha yüksektir

Paraneoplastik Renal Sendromlar

- Tam idrar tetkikinde
  - Proteinüri
  - Dismorfik hematüri
- Kan biyokimyası
  - Hipoalbuminemi

Paraneoplastik glomerulonefrit akla gelmelidir

Tedavi malignitenin tedavisi ve glomerulonefrit için uygulanan tedaviler şeklinde yapılır

Paraneoplastik Kaşeksi

- Cancer cachexia is perhaps the most common manifestation of advanced malignant disease (50%)
- Symptoms of cachexia include anorexia, weight loss, muscle loss, anemia, and alterations in carbohydrate, lipid and protein metabolism.
- Cortisol and glucagon, tryptophan, TNF, IL-1, IL-6, IFN-a,
- Corticosteroids, Medroxyprogesteron, Ibuprofen,

Hiraki A et al, Lung Cancer, 2004

Paraneoplastik Bitkinlik-Yorgunluk Sendromu

- Cancer-related fatigue is also extremely common. Up to 90% of cancer patients report fatigue symptoms while in most studies prevalence rates are 60%
- Plasma levels of free tryptophan
- An increase in brain serotonin (5-HT) levels and/or upregulation of a population of 5-HT receptors, may lead to reduced somatomotor drive, modified hypothalamicpituitary-adrenal (HPA) axis function, and a sensation of reduced capacity to perform physical work.
- Treatment of cancer-related fatigue should be individualized according to the underlying pathology when a specific cause has been identified. In addition to older therapies, such as hematopoietics, antidepressants, corticosteroids, and psychostimulants

Hiraki A et al, Lung Cancer, 2004