PARA - NEO - PLASTIC SYNDROMES (PNSs)

Penchev, B. & Chaushev, B.
CONTENT

- What are PNSs?
- History & statistics
- Pathogenesis
- Classification
- PNS patterns
- Clinical approach to PNSs
- Conclusion
HISTORY OF PNSs

In the 1840s Trousseau taught that:

Cancerous patients often develop venous thrombosis (phlegmasia)

A. Trousseau (1801-1867)


http://qjmed.oxfordjournals.org/content/early/2011/03/02/qjmed.hcr018/F1.expansion.html
In 1865 Trousseau diagnosed himself with the same syndrome. “I am lost! Phlegmasia leaves me no doubt about the nature of my affliction, a visceral malignancy…”

The autopsy proved him correct; stomach cancer infiltrating pancreas
1940s-the term PNSs was established

1965 - 2010 - PUBMED PUBLISHED

9227 articles using the term PNSs

By August 2014 - 11590 articles

In the last 4 years → 2 articles / day
PNSs ← NEOPLASM
INCIDENCE

AVERAGE 8-23%
PATHOGENESIS OF PNSs

NEOPLASIA

INFLAMMATION

- Anti-Hu
- Anti-Yo
- Anti-Ri
- Anti-Ma2
WHICH NEOPLASMS CAN CAUSE PNSs?

ANY NEOPLASM, BUT MOSTLY THE MALIGNANT

MALIGNANT NEOPLASMS ARE OF TWO TYPES

Mesenchymal → **SARCOMA** (chondro-S, fibro-S, osteo-S, ...)

Epithelial → **CARCINOMA** (skin-Ca, bronchogenic-Ca, intestinal-Ca, ...)

PNSs


http://www.healthtalk.umn.edu/2013/06/03/new-research-identifies-genetic-variants-associated-with-osteosarcoma
CLASSIFICATION / PATTERNS

PNSs

- MUCO CUTANEOUS
- NEUROLOGICAL
- MUSCULO SKELETAL
- CARDIO VASCULAR
- GASTRO INTESTINAL
- URINARY
- HEMATOLOGICAL
- ENDOCRINE
- MIXED

http://www.globalpost.com/photo/5918348/143474115
MUCCO-CUTANEOUS PNSs

- Recurrent mucosa ulcerations
- Rash spreading to torso
- Ulcerations of mouth angles
- Depapilated red tongue

Pemphigus Vulgaris
http://www.dermrounds.com/photo/pemphigus-vulgaris-oral next?context=user

PNSs

Chelitis and glossitis

Necrolytic migratory erythema
http://www.dermaamin.com/site/atlas-of-dermatology/9-g/584-glucagonoma-syndrome-.html

Pancreatic endocrine neoplasm

http://www.med-ed.virginia.edu/courses/rad/gi/pancreas/nec03.html
MUUCO-CUTANEOUS PNSs

Thickening of palmar fascia

Carcinoma of urinary bladder

Tripe palm

PNS


http://www.learningradiology.com/archives05/CCW_20178-Bladder%20cancer/bladdercorrect.htm


http://fasciitis.co/paraneoplastic-fasciitis/

https://www.google.co.nz/search?ibm=isch&q=bladder+cancer&rc=0%3Bbladder%20cancer%20ultrasound%20images&imgdil=_&imgref=_
MUOC-CUTANEOUS PNSs

Dermatomyositis

- Red, scally skin lesions
- Muscle weakness
- Usually female

Can be linked to GIT carcinoma

Stomach carcinoma

http://e-radiography.net/ibase8/Git/slides/Git_applecore.htm

Gotton’s papules

http://www.aocd.org/?page=Dermatomyositis
NEUROLOGICAL PNSs
Paraneoplastic Cerebellar atrophy

- Female
- Nausea, vertigo
- Gait disturbances
- Wheel-chair bound 9 months after the first symptoms
- MRI 9 months after the first symptoms

http://www.eurorad.org/eurorad/case.php?id=1475
NEUROLOGICAL PNSs

- Mammography & mastectomy
- Antineuronal antibodies found
- Paraneoplastic cerebellar atrophy may appear with:
  - Breast ductal carcinoma
  - Ovarian carcinoma
  - Lung carcinoma

http://www.sciencealert.com/releases/2013/12/131204091411.htm

MUSCULO-SKELETAL PNSs

RHEUMATIC PNSs

Autoimmune syndromes
• Dermatomyositis & polymyositis
• RA-like syndromes

Osteoarthropathic syndromes
• Hypertrophic osteoarthropathy
• Carcinoma polyarthritis
• Oncogenic osteomalacia
• Gout
Polymyositis & dermatomyositis

- Skin alterations
- Muscle alterations: myalgia & muscle weakness

Foot drop

Combing difficulties

Prostate carcinoma

Lung carcinoma
MUSCULO-SKELETAL PNSs

Rheumatoid arthritis-like conditions

Juvenile idiopathic RA

Early idiopathic RA

63% increased risk for lung cancer

200% increased risk for lymphoma
MUSCULO-SKELETAL PNSs

Hypertrophic (pulmonary) osteoarthropathy

- Clubbing of distal phalanges
  - Hippocratic fingers

Shamroth’s sign

Lung carcinoma


MUSCULO-SKELETAL PNSs

Hypertrophic (pulmonary) osteoarthropathy

- Periostitis:
  - long bones
  - bilateral
  - symmetrical

Lung carcinoma


MUSCULO-SKELETAL PNSs

Hypertrophic (pulmonary) osteoarthropathy

- **Polyarthritis in multiple joints simultaneously:** MCP’s, PIP’s, carpal, elbows, knees and ankles
- **Bilaterally symmetrical**
MUSCULO-SKELETAL PNSs

Hypertrophic (pulmonary) osteoarthropathy

- Weight loss
- A 2-month history of swelling in knees, ankles, hands and feet!
- Fatigue
- No respiratory symptoms!

Mesothelioma

71-year-old woman
abrupt onset of RA symptoms

Physical examinations

X-ray, CT, MRI

Tc-99m HDP scan
(the most sensitive tool for detecting bone pathology)

All of the above suggested typical rheumatoid arthritis!
MUSCULO-SKELETAL PNSs
Carcinoma arthropathy

Consider cancer if:

- abrupt onset
- late age 1st onset
- no joint deformities
- no periarthritic nodules
- seronegative rheumatoid arthritis
- ineffective rheumatologic therapies

Pancreatic cancer with hepatic metastases
MUSCULO-SKELETAL PNSs

Oncogenic osteomalacia

- Mostly in lower limbs
- **In children:**
  - rickets-like
  - but normal Vit D
- **In adults** - Tolouse-Lautrec syndrome
  - musculo-skeletal pains
  - fatigue
  - recurrent fractures
- Differential diagnoses:
  - old #
  - pseudo #
  - pathological #
  - rickets
  - osteo-chondro-dysplasia

http://courses.washington.edu/bonephys/hypercalU/opmal2.html

http://radiopaedia.org/articles/pyknodyostosis
MUSCULO-SKELETAL PNSs

Oncogenic osteomalacia

- Subcutaneous nodule
- DWIBS-MRI “hot spot”
- Biopsy: mesenchymal phosphaturic neoplasm

renal phosphate wasting

compromised mineralisation
MUSCULO-SKELETAL PNSs

Oncogenic osteomalacia

- Young (22)
- Bone pain
- Muscle weakness
- Wheel-chair bound in a year

- Generalised osteopenia
- Multiple nontraumatic fractures

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3279070/
MUSCULO-SKELETAL PNSs

Oncogenic osteomalacia

- CT examination
  neoplasm in ethmoid and sphenoid sinuses

- Biopsy
  Phosphaturic mesenchymal

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3279070/figure/f4-ccmbm8_2p012/
Gout

Hyperuricemia contributes to cancerogenesis in:

- Skin
- Respiratory system
- Hemopoietic tissue
- Digestive tract
- Liver and pancreas
- Genitourinary systems

Consider cancer if: fulminant development of gout symptoms & signs!
CARDIOVASCULAR PNSs

Raynaud's disease / syndrome / phenomenon

A localised excessive vasospasm due to:
- emotional stress
- temperature drop, “allergy to cold”
- sympathetic tone & autoimmune CT disorders

Raynaud was a French doctor
CARDIOVASCULAR PNSs

Raynaud's syndrome

Hepatocellular carcinoma

Multiple myeloma
CARIOVASCULAR PNSs

Carney complex

- It comprises:
  - Lentiginous pigmentations
  - Skin mixomas
  - Papules

PNSs

Lentiginous pigmentations

Skin mixomas

Papules

http://www.familypracticenews.com/fileadmin/content_images/fpn/archive_image/vol37iss6/70374_fx1.jpg


CARDIOVASCULAR PNSs

- Carney complex includes heart myxoma
CARDIOVASCULAR PNSs

➢ Carney complex includes testicular carcinoma

http://www.med-ed.virginia.edu/courses/rad/petct/Lymphoma.html
CARDOVASCULAR PNSs

➢ Carney complex includes **Swanomas**

Acoustic Sw

Vagal Sw

SC Sw

Tibial nerve Sw

➢ Carney complex includes **thyroid carcinoma**
GASTROINTESTINAL PNSs

Chronic GI pseudo obstruction

- Chronic, delayed, GI tract emptying
- **Dry mouth**, orthostatic hypotension, urinary retention
- **Pupillary** abnormalities
- **Impotence**

Small cell lung carcinoma → Paraneoplastic encephalomyelitis → Autonomic nervous system involvement?

[Link to article: http://www.journalmc.org/index.php/JMC/article/view/961/513]
The “clinical masquerade“

- Hypertension - 40%
- Fatigue - 30%
- Hypercalcemia - 20%

- Liver failure-jaundice- 3 - 20%
  Stauffer’s syndrome

- Galactorrhea

- Cushing syndrome - 2%

- Bone & abdominal pain, nausea, disorientation
- Fever, weight loss, anaemia
- Vaculopathy, neuromyopathy, polycythemia
Renal cell carcinoma one of the greatest imitators
CLINICAL APPLICATIONS

STATISTICS-BASED

Acro-keratosis of Bazex

Acro-lentiginosis
Dermatomyositis

- Skin alterations - red, scaly, extensor surfaces
- Arthralgia, myalgia, weakness, weight loss, fever
- Calcinosiis in tendons and muscles

20 - 30% of patients with dermatomyositis have, or will develop a cancer of lung, stomach, breast, ovary, pancreas
CLINICAL APPLICATIONS

INVESTIGATION-BASED

18-FDG PET/CT

PNS + PNS ANTIBODIES

The best screening tool

Increased 18-FDG uptake

BIOPSY

Discitis

PNSs, PN-antibodies & “hot” spots malignant until proven otherwise!
“ALBATROSS” SYNDROME
PRESENT ???

CONSIDER MALIGNANCY
CONCLUSION

- First reported 190 years ago (Boillaud, 1823 / Trousseaux, 1840s)
- Not due to invasion or metastases
- Incidence 8% to 23%
- Mimicked by inflammation & antibodies
- Often precede a "visible" neoplasm
- May mask, or may indicate neoplasm
- "Albatross" pattern
- Have prognostic value
- Treatment successful
- Recurrence possible!