

FIBROZELE PULMONARE INTERSTITIALE

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DEFINITIE

- FPI=boli variate, care afecteaza septuri alveolare +tesutperialveolar
 - cronice
 - nonmaligne
 - noninfectioase
 - +/- afect.cai aeriene mici:BOOP
- MP:-inflamatie+fibroza+distorsiune parench.pulm → UIP
 - alte aspecte:DIP(exsud alv:MFage,putina fibroza),NSIP
- Imagistica:RX valoare redusa;ideal-CT:rezolutie inalta/spiral

CLASIFICARE ETIOLOGICA

- Greu; multe (cca 150); unele cu cauza cunoscuta, altele necunoscuta
- Clasificare practica:
 - cauza cunoscuta/necunoscuta
 - granulomatoase/negrulomatoase

FPI NONGRANULOMATOASE

- Cauza cunoscuta:
azbest/fum,gaze/medicamente/rx/aspiratie/rezidual post ARDS
- Cauza necunoscuta:
FPI idiopatic/colagenoze:LES,PAR,SPA,sclerodermii,Sjogren,PM-DM/hemoragii pulm:Goodpasture,hemosideroza pulm idiop/proteinoza pulm alv/pneumonii interst cu limfocite/PI cu eozinofile/limfangioleiomiomatoza*/amiloidoza/boli mostenite:scleroza tuberoasa,neurofibromatoza,Niemann Pick,Gaucher,Hermansky Pudlak/boli gastro:IBD,CBI,hep cr activa/GVHD

*cuvant de scrabble

FPI GRANULOMATOASE

- Etiologie cunoscuta
 - pneumonii de hipersensibilizare
 - pulberi anorg:Be,SiO₂
- Etiologie necunoscuta
 - Sarcoidoza/gran.cel.Langerhans/vasculite
 - gr(Wegener,Churg Strauss)/gr
 - bronhocentrica

FPI IDIOPATICA

- Entitate bine definita, nu “cos de gunoi”
- Immunopatogenie:
- Reminder-boala afecteaza: pneumocite tip I (scuamoase)/tip II (→ surfactant)/suport interst: fblasti mioFB, Mo-Ma, Lf/capilar alv/bronhiole respiratorii
- LBA-normal: MF-80%, Lf-10% (70% LT), PMNN-1-3%, Eoz-1%
 - CD4/CD8 N=1,5
- Stadii histol ale alveolitei:
 - 1) edem alv+membr hialine
 - 2) exsudat intraalv
 - 3) fibroza

FPI IDIOP PATOGENIE

- Elem central=MF:
- 1) via IL8,LTB4,TNF Alfa → apel PMN,Eoz(LBA:PMN>20%,Eoz2-4%)
- 2)stimuleaza cel mezench:MF stimulat de IFN gama → PDGF/TGF beta → prolifer/secr FBlasti → fibroza

TABLOU CLINIC FPI IDIOP

- Debut-varsta medie:dispnee,astenie,tuse uscata
 - *anamneza:?cauze profesionale
- Ex fizic:-initial N
 - crackles/cianoza/clubbing/cord pulmonar

PARACLINIC(FPI IDIOP)

- RX-sticla mata → ret-nod fin → ret nod grosier → fagure/Schweizer
- CT:spiral/HRCT-optim
- Laborator:VSH/CIC/Ig
- Spirometrie:pattern restrictiv:reducere:CPT, CV, Vrez, IPB
N
- Gaze:scad paO₂,scad paCO₂,creste grad alv capil la efort
- T CO scazut(scade si in emfizem!)
- Bronhoscopie:biopsii(4-6);LBA:PMNN 20%,Eoz 2-4%
- Biopsie chirurgicala(open lung)

DIAGNOSTIC(FPI IDIOP)

- Context:FPI(dispnee,crackles,aspect RX,scad T CO)
- Anamneza:excludere:agenti profesionali/ag de mediu/medicamente/aspiratie/infectii respir recente
- Bronhoscopie:
 - excludere:infectii,neoplasme
 - biopsie
 - LBA
- Scinti Ga* Hcaptare in std active

TRATAMENT

- Corticoterapie:PDN 1mg/kg 8 sapt scazut treptat +/-puls solu medrol
- CFA (daca nu raspunde la PDN):-po 1 mg/kg;se poate creste cu 50 mg saptamanal →NLx1/2
 - inject 500mg x2/sapt
- Imuran in loc de CFA
- Altele:Dpenicilamina,ciclosporina,colchicina
- Noutati:pirfenidona-scade sinteza+prolif FBlasti
 - IFN beta,gama-fara rezultat convingator
- Adjuvante:fumatul/O2/diuretice/vaccin:gripa,pneumococ/transplant(1 plaman)

FORME PARTICULARE DE FPI

- LES:det.pulm:pleurita/pleurezie/pneumonita acuta/(mai rar)FPI progresiva-alveolita limf./shrinking lung
- PAR:pleurezie/FPI/nod.reum./BOOP
*iatrogen:FPI:MTX,Au
BOOP:DPA
- SPA:fibr bilat LS(boala fibrocavitara);posibile:hemoptizii,Aspergiloza,confuzie cu TB
- Sclerodermie:FPI ca atare+aspiratie+sd restrictiv(daca sunt modif cutanate severe torace)
- Sjogren:infiltr Lf interst→veritabil limfom;posibil BOOP
- PM/DM:Ac antisintetaza-ma antiJo1
aspiratia

FORME PARTICULARE FPI(2)

- FPI cu hragii pulm:
 - LES/Behcet/Wegener/Churg-Strauss/Henoch-Schonlein/crioglob/Goodpasture/hemosider.pulm. idiop.(HPI)
 - *renopulm:LES/Goodpasture/Wegener/Henoch Schonlein
 - *Goodpasture:autoac. Anti MB glom si anti MB alv → clinic:hptizii+glom.nefrita
 - *HPI:hragie alv/fara afect alt organ/fara cauza imunologica evidenta(dg. excludere)

FORME PARTICULARE FPI(3)

- Proteinoze alveolare pulmonare(PAP):
 - clinic&RX-FPI
 - HP:in alveole:material PAS+*;FARA INFLAMATIE septala(nu-i FPI stricto sensu)
 - exista PAP
 - “secundare”:pneumoconioze/tumori/infectii
- *compoz:surfactant,LDH,Ig

FORME PARTICULARE FPI(4)

- Pneumoniile interstittiale cu limfocite(PIL):
 - infiltr. Interst.:lf,plasmoc
 - benign/caract de limfom cu malignitate joasa
 - asocieri:Sjogren/HIV
- *din acelasi spectru:lf.adenop.
Angioimunoblastica/granulomatoza limfomatoida

FORME PARTICULARE FPI(5)

- Pneumonii interst cu eozinofile(PIE):
 - infiltrat is cu eoz;+-eoz.filie sanguina
 - spectru larg
- *Clasificare:
 - cauza cunoscuta:
 - micozeBP
 - alergice(aspergillus/penicillium/candida/curvularia)
 -
 - paraziti:ascaris/ancylostoma/toxocara/strongyloides/wuchereria/
 - medicam:nitrofurantoin/sulfamide/peniciline
 - sd eozinofilie-mialgie(L-triptofan)

PIE DE CAUZA NECUNOSCUITA

- SD. Loffler-pneumonie acuta cu eozinofile, cu infiltrate migratoare si simptome minime
- Pneumonia acuta cu eozinofile
- Pneumonia cronica cu eozinofile
- Sd Churg Strauss
- Sd. hipereozinofilic (>1500 eoz/mm³)-6 luni.
*semne multisistemice: afect cardiaca (tricusp, cm restrictiva), pulm, splenica, hepatica, cutanata, SN.

PIE

- Caracteres generale RX ale infiltratului eozinofilic:
 - periferic,fara topografie lobara,cruta zona centrala:aspect de “negativ EPA “
 - regresie&reaparitie in aceleasi locuri
 - extrema corticosensibilitate

adri: 414

phil: 327

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LIMFANGIOLEIOMIOMATOZA

- Proliferare CMN imature
- Rol estrogeni?-apare la femei de varsta fertila
- Prezentare: dispnee/hemoptizie/pneumotorax/pleurezie chiloasa
- Terapie-manipulari hormonale:
 - progesteron-eficient
 - tamoxifen,ovarectomie-ineficient

Alte fpi negranulom.:amiloidoza,boli congenitale,boli digestive,GVHD

- Boli congenit:
 - facomatoze(hamartoame):scleroza tuber.,neurofibromatoza
 - b stocaj lizoz:Niemann Pick,Gaucher
 - Hermansky Pudlak:FPI/colita gran./albinism/disfctii plachetare
- Boli intest:IBD(m.a. Crohn)/ciroza biliara I/hepatite cronice
- GVHD:FPI+bronsiolita obliteranta

FPI GRANULOMATOASE

- Cauza cunoscuta: pulberi organice (pneumonii de hipersensibilizare), pulberi anorganice (unele pneumoconioze - ex: silicoza)
- Cauza necunoscuta: gr. cu cel. Langerhans / vasc gran / gran limfomatoida / gran bronhocentrica / sarcoidoza

GRANULOMATOZA CU CELULE LANGERHANS(HISTIOCITOZA X)

- Prolifereaza celula DENDRITICA LH
 - princ.cel.prez. Ag
 - markeri:IHC-CD1A;ME-gran. Birbeck(corpi X)
- * forme:granulom eozinofil,Hand Schuller Christian, Letterer Siewe
 - mai frecv la fumatori
- Tratament:fumatul/?DPA/iradiere os/transplant pulm//cortizon=inutil

ALTE FPI GRANULOMATOASE

- Vasculite
granulomatoase: Wegener/Churg-Strauss
- Granulomatoza limfomatoida-
afecteaza: pulmon/piele/SN/rinichi
- *50% → limfom
- Granulomatoza bronhocentrica
- Sarcoidoza

PNEUMONIILE DE HIPERSENSIBILIZARE (PHS)

- Determinate de pulberi organice(exceptie:tiocianati)
- Agentul:-actinomicete/proteine din excrete animale/tiocianati
- Patogenie:HS tip IV
- Clinic:tablou acut/subacut/cronic
- LBA-alv limf.-dc. Expunere f recenta:CD4,mai tarziu(sit c.m.comuna):CD8

PHS (2)

- Biopsie-tes granulomatos;1/2-bronsiolita
- Anticorpi precipitanti;valoare limitata-alte teste imunologice:test cutanate,TTL
- Dg +:-FPI
 - anamneza-expunerea
 - Ac precipitanti
- Tratament:-evitarea expunerii
 - f acute se pot vindeca si fara GC
 - f subacute si cronic-prednison 1 mg/kg

PNEUMOCONIOZE

- Azbest:FPI/mezoteliom pleural sau peritoneal/carcinom pulmonar
- Silicoza:-fibroza+noduli+adenop. Hilare calcificate(coaja ou)
 - asocieri
 - posibile:TBC,sclerodermie
- Antracoza:dat pulbere carbune ca atare silicoza concomitenta
- Berilioza~sarcoidoza

SARCOIDOZA

- Definitie: boala multisistemica/acumulare: cel T(m.a.CD4), MF, epiteloide, cel gigante → granuloame fara cazeificare, care distorsioneaza arhitectura + functia normale ale organelor respective
- Etiologie: -cauza necunoscuta
 - agenti infectiosi (nedovediti)
 - raspuns imun exagerat (tip HS IV) la anumiti Ag persistenti/autoAg

SARCOIDOZA

- Epidemiologie:
 - rel frecv;la orice:sex,varsta,rasa,localizare geografica
 - Barbati~femei;debut-20-40 ani;descrisa la gemeni monozigoti;fara corel HLA
- *Mai frecv la NEfumatori

SARCOIDOZA(2)

- Patogenie:
 - Caracteristic-granulomul,format din:lf CD4,Mo-Ma,epiteloide,cel gigante
 - Mec HS IV:activare CD4→citokine→atrag Mo/Ma
 - Caracteristic:compartimentalizarea raspunsului imun:lf CD4 din organele afectate elibereaza IL2 si prolifereaza intens;cele din alte organe “stau linistite”
 - Cel CD4 activate recruteaza Mo/Fblasti

SARCOIDOZA(3)

- Clinic:
 - c.m.frecv.=simpt respir.(posibil asimpt)
 - *Debut acut(20-40%)
 - simpt sistemice:febra,anorexie,scad G
 - sd Lofgren:AP hilare,eritem nodos,artrite
 - sd Heerfordt:febra,uveita ant,parotidita,pareza n facial
 - *Debut insidios-simpt exclusiv respiratorii

SARCOIDOZA(4)

Afectari de organ:

-pulmon:FPI

-AP:cervical,axilar,supraepitrochl,inghinal

-piele:eritem

nodos,placi,macule,papule,noduli,lupus pernio.

* EN nu este infiltrat cutanat sarcoid,ci vasculita
de hipersens indusa de~

ochi;:uveite ant,post;conjunctivite

Cai resp sup:amigdale,laringe

SARCOIDOZA(5)

- Hematologic:pancitopenie,splenomegalie,hipersplenism
- -hepatic:colestaza biochimica,asimptomatica
- rinichi:NEFROCALCINOZA>>infiltr.sarcoid
- -SN toate componentele pot fi afectate:pareza n VII,nevrita optica,edem papilar,hipoacuzie,afect HF,meningita,form tum cerebrale,leziuni multiple SM-like,PNP
- -locomotor:lez chistice osoase/artrite/rar miozita
- -Cardiac-tulb ritm,cond;endocr-diabet insipid;gl exocrine-parotidita ,sd sicca

SARCOIDOZA(6)

- Paraclinic:
 - analize:RFA,limfopenie,eozinofilie,hipergama
 - Angiotensinconvertaza serica(ACS)
 - Hipercalcemie,Hcalciurie
- RX pulm:std I-AP;std II-AP+FPI;std III-FPI
- Scinti Ga*
- LBA-alveolita cu cel CD4
- IDR PPD clasic NEGATIV
- IDR Kveim Silzbach

SARCOIDOZA(7)

- Diagnostic:-tipic-adult tanar cu:EN,AP hilar bilat simetrice mari cu st gen buna,+ -tulb vizuale
 - confirm:LBA,ACS,biopsii
- =/=TBC,funghi,limfoame
- Prognostic:adesea-bun(c.m. multi vindecare fara sechele-ma cei cu debut acut);1/2 disfctii de organ blande;15%-boala ramane activa/recurenta;10%-mortala

SARCOIDOZA(8)

Tratament:

- corticoizi:merita totdeauna tratata?!(daca nu-s afectari severe,unii recomanda expectativa 2-3 luni si abia atunci cortizon)
- altele:AINS, hidroxiclorochin, MTX, CFA, cicl osporina A

FPI MEDICAMENTOASE

- Amiodarone causing pleuropulmonary toxicity - 6%
- Vinca alkaloid (mitomycin–vinca alkaloid combination therapy) causing acute respiratory distress syndrome (ARDS) - 3-6%
- Transfusion-related acute lung injury (TRALI) - 1 in 5000 transfusions or 1 in 2000 patients who are transfused
- Aspirin-induced asthma - 10-20%
- Vinorelbine (vinca alkaloid) causing bronchospasm - 5%
- Angiotensin-converting enzyme inhibitor (ACE-I) causing cough - 10%
- Sodium morrhuate (esophageal sclerosant) causing pleural effusions - 40-50%
- Absolute alcohol (esophageal sclerosant) causing pleural effusions - 19%
- Methysergide causing pleuropulmonary complications - Less than 1%
- Bromocriptine causing pleural thickening and effusions - 6%
- Bleomycin causing pleuropulmonary reactions - 6-10%
- Methotrexate-induced pleuropulmonary disease - 3-4%
- Nitrofurantoin causing acute pleuropulmonary effects - 5-25%
- Interleukin 2 causing pleuropulmonary abnormalities - 75%
- Hydralazine-induced lupus causing pleuropulmonary disease - 30% (isolated parenchymal disease in <5

PARTICULARITATI CLINICE

- BOLI PULM INTERST CLASICE:
- Pneum HSens:
 - med:MTX/Au/CFA/nitrofur./antidepresive
 - caract:alveolita limfocitara
 - evol fav:stop adm/cortizon
- Pneumonia cu eozinofile:
 - med:mtx/sulfasal/minociclina/PAS/nitrofur./AINS
 - caract:alv.eoz/rash/febra/RX-infiltrate eoz
 - evol fav:stop adm/cortizon

PARTIC.CLINICE(2)

- BPI CLASICE(2):
- Pneumonita indusa de amiodarona:
 - caract:opacitati RX asim.,nesegmentale
- Fibroza pulm:
 - medicam:amiodarona/citostatice
 - caract:pneumonie interst fibrotica nespecifica
 - prognostic RAU
- DIP:
 - medicam:mtx/interferon/etanercept
 - prognostic bun

PARTIC.CLINICE(3)

- BPI CU INSUF. RESP. AC:
- ”plamanul de metotrexat”(mtx,Au)
- Pneumonia ac cu eozinofile(minociclina)
- Plamanul de chemoterapie(bleomicina,busulfan,carmustina,mitomicina)
- Edem pulm:ara-C,sange,narcotice,diuretice
- Hemoragie alveolara:AVK,fibrinolitice,antiplachetare

CLASIFICARE MED. → BPI

- Citotoxice: bleomicina, mtx, carmustin, busulfan, cfa, vinca
- Cardiovasculare: amiodarona (6% din bn. tratati!)
- Antibiotice: nitrofur., amfotericina B, sulfamide, sulfasalazina, minociclina
- Illicite: talcoza, EPA (cocaina, heroina)
- AINS: ARDS-like ← toxicitate salicilati
- Etc: alcool, moruat, bromocriptina, metisergid