Neuropathies périphériques
Et Vascularites

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Questions que se pose un neurologue ?

- Quelles différences cliniques, évolutives , réponses aux traitement, lésions ana path entre **NSVN (restreinte nerf périphérique)** d'une part et **Vascularite systémique** d'autre part , en particulier liée aux ANCA (PAM) ?

- Différences de la neuropathie périphérique entre vascularite systémique **primitive (PAN, PAM, GEPA, GPA) et secondaire** ?

- Différences en terme clinique, Immuno, évolution, réponse aux traitements entre les patients qui ont critères de vascularite **définie** sur la biopsie et ceux seulement **probable** ?

- Corolaire de ce point : révision des critères ana path de lésions de vascularite, quid de la nécrose ou **dommage pariétal** ? de la **taille des vaisseaux** ? **du type d'infiltrats** , du rendement muscle ou nerf ?

- Extension du concept : problème des diagnostiques différentiels (Lymphome, Hansen, Sarcoïdose etc..), de l'extension nerf-muscle à cutané ? des formes frontières (Parsonage Turner-Plexite-diabète ..)

- Quel type de vascularite ?
- Comment la rechercher ?
- La préciser ?

1

2

3

Panel 1: **Classification of vasculitides associated with neuropathy**

I Primary systemic vasculitides (mostly nerve large arteriole)
1 Predominantly small vessel vasculitis
- a Microscopic polyangiitis*
- b Churg-Strauss syndrome (eosinophilic granulomatosis with polyangiitis)*
- c Wegener's granulomatosis (granulomatosis with polyangiitis)*
- d Essential mixed cryoglobulinaemic (non-HCV)
- e Henoch-Schönlein purpura (IgA vasculitis)

2 Predominantly medium vessel vasculitis
- a Polyarteritis nodosa

3 Predominantly large vessel vasculitis
- a Giant cell arteritis

II Secondary systemic vasculitides associated with one of the following (mostly nerve large arteriole)
1 Connective tissue diseases
- a Rheumatoid arthritis
- b Systemic lupus erythematosus
- c Sjögren's syndrome
- d Systemic sclerosis
- e Dermatomyositis
- f Mixed connective tissue disease

2 Sarcoidosis
3 Behçet's disease
4 Infection (such as HBV, HCV, HIV, CMV, leprosy, Lyme disease, HTLV-I)
5 Drugs
6 Malignancy
7 Inflammatory bowel disease
8 Hypocomplementemic urticarial vasculitis syndrome

III Non-systemic or localised vasculitides (mostly nerve microvasculitides)
1 Non-systemic vasculitic neuropathy (includes non-diabetic radiculoplexus neuropathy and some cases of Wartenberg's migrant sensory neuritis)
2 Diabetic radiculoplexus neuropathy
- a Diabetic lumbosacral radiculoplexus neuropathy
- b Diabetic cervical radiculoplexus neuropathy
- c Diabetic thoracic radiculopathy
- d Painless diabetic motor neuropathy

3 Localised cutaneous or neuropathic vasculitis
- a Cutaneous polyarteritis nodosa
- b Others

Jusqu'où aller dans l'extension

Des

Neuropathies et « vascularite » ?

Box 1 | Classification of vasculitides associated with neuropathy

The classification is modified from the Peripheral Nerve Society guideline in accordance with the Chapel Hill Consensus Conference in 2012[4].

Primary systemic vasculitides

- Predominantly small-vessel vasculitis
  - Microscopic polyangiitis*
  - Eosinophilic granulomatosis with polyangiitis (Churg–Strauss syndrome)*
  - Granulomatosis with polyangiitis (Wegener granulomatosis)*
  - Essential mixed cryoglobulinaemia (non-HCV)
  - IgA vasculitis (Henoch–Schönlein purpura)
  - Hypocomplementemic urticarial vasculitis
- Predominantly medium-vessel vasculitis
  - Polyarteritis nodosa
- Predominantly large-vessel vasculitis
  - Giant cell arteritis

Vasculitides associated with systemic diseases

- Connective tissue diseases
  - Rheumatoid arthritis
  - Systemic lupus erythematosus
  - Sjögren syndrome
  - Systemic sclerosis
  - Mixed connective tissue disease
- Dermatomyositis
- Sarcoidosis
- Behçet disease
- Inflammatory bowel disease

Vasculitides associated with probable aetiologies

- Infection (such as hepatitis B virus, hepatitis C virus, HIV, cytomegalovirus, leprosy, Lyme disease, human T cell-lymphotropic virus-I, parvovirus B19)
- Drugs
- Malignancy
- Vaccinations

Single-organ vasculitides of the peripheral nervous system

- Nonsystemic vasculitic neuropathy, including but not limited to the following subtypes
  - Wartenberg migratory sensory neuropathy (non-mechanical cases)
  - Postsurgical inflammatory neuropathy
- Neuralgic amyotrophy (probably)
- Painful diabetic radiculoplexus neuropathy
  - Predominantly lumbosacral
  - Predominantly thoracic (thoracic radiculoneuropathy)
  - Predominantly cervical
- Painless diabetic radiculoplexus neuropathy
- Nonsystemic skin/nerve vasculitis
  - Cutaneous polyarteritis nodosa
  - Other

	Histopathology	Vessels affected	Other organs clinically involved (%)	Laboratory studies (%)	PNS, CNS changes
Polyarteritis nodosa	Necrotising vasculitis; mixed infiltrate; sparse immune deposits	Small and medium arteries	Skin (55–60%), joints (~50%), kidneys (40–50%), GI (~30%), testes (2–29%), heart (10–15%), ENT (rare), lungs (rare)	↑ESR (~85%), ↑WBC (~70%), ↓haemoglobin (~60%), ↑platelets (~60%), RF (~30%), Hep B (20–30%), ↓comp (~25%), ANA (~15%), Hep C (5–10%), ANCA (<10%), angio (angiogram abnormal in 70%, evidence of aneurysm)	PNS (65–67%), CrN (<5%), CNS (~5%)
Microscopic polyangiitis	Necrotising vasculitis; mixed infiltrate; sparse immune deposits; LCV in skin	Arterioles, capillaries, venules, veins affected more than small and medium arteries	Kidney (75–90%), joints (40–60%), skin (30–60%), lungs (35–50%), GI (30–40%), ENT (20–30%), heart (10–20%), testes (rare)	↑ESR (>90%), ANCA (75–85%; MPO>PR3), RF (25–50%), ANA 20–30%), ↓comp (rare), Hep B/C negative, angio (rare)	PNS (40–50%), CNS (10–15%)
Eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome)	Necrotising vasculitis; mixed infiltrate with eosinophils; granulomas; sparse immune deposits; LCV in skin	Small and medium arteries, arterioles, capillaries, venules, veins	Lungs (100%, asthma; 40–75%, infiltrates); ENT (sinusitis, rhinitis; 60–80%), skin (50–70%), GI (35–50%), joints (30–50%), heart (30–50%; 60% by MRI), kidney (15–30%)	↑Eosinophils (100%), ↑ESR (~85%), ↑IgE (~75%), ANCA (30–40%; MPO>PR3), RF (40–50%), ANA (~10%), ↓comp (rare), Hep B/C negative, angio (angiogram abnormal in 30%)	PNS (65%), CrN (<5%), CNS (10–15%)
Granulomatosis with polyangiitis (Wegener's granulomatosis)	Necrotising vasculitis; granulomas; collagen necrosis; sparse immune deposits; LCV in skin	Small and medium arteries, arterioles, capillaries, venules, veins	ENT (90–95%), lungs (65–85%), kidney (60–75%), eyes (50–60%), skin (25–50%), joints (65–75%), heart (5–20%), GI (5–10%)	ANCA (80–90%; PR3>MPO), ↑ESR (~85%), ↓haemoglobin (~75%), ↑platelets (55%), RF (50–60%), ↑WBC (~35%), ANA (~25%)	PNS (20–25%), CNS (5–10%), CrN (15%)
IgA vasculitis (Henoch-Schönlein purpura)	LCV in skin; IgA vascular deposits	Arterioles, capillaries, venules	Skin (100%), joints (65–70%), GI (~60%), GN (~40% children; ~70% adults), testes (~15%), lungs (rare)	↑ESR (50–60%), ↑IgA (~50%), ↑WBC (~50%), ↑ASO (20–50%), cryoglobulins (20–25%), ↓comp (10–20%), ↓haemoglobin (5–15%), RF (~5%), ANA (~5%), ANCA (<5%)	PNS (rare), CNS (rare)
Cryoglobulinaemic vasculitis	Necrotising vasculitis; microangiopathy; non-IgA immune deposits; LCV in skin	Small arteries, arterioles, capillaries, venules	Skin (~95%), joints (70–90%), GN (~30%), salivary glands (sicca; ~30%), Raynaud's (25–50%), GI (pain; 10–20%)	Hep C (80–90%), ↓comp (70–90%), RF (70–90%), ↑ESR (~70%), ↓haemoglobin (~70%), ANA (~55%), Hep B (~5%), ANCA (<5%), angio (infrequent)	PNS (~65%), CNS (rare)
Giant cell arteritis	Necrotising vasculitis; mononuclear infiltrate; granulomas and giant cells (~50%)	Medium–large arteries	PMR (~50%), liver (~30%; abnormal LFTs), subclavian-axillary-brachial (6–8%), aorta (15–20%), superficial femoral-popliteal (2–7%), kidney (GN) (~10%)	↑CRP (98–100%), ↑ESR (85–100%), ↓haemoglobin (55–60%), ↑WBC (20–30%), ANCA (rare), RF negative, ANA negative, angio (infrequent)	Otological (60–90%), optic nerve (15–20%), PNS (~5%), CNS (~5%)
Non-systemic vasculitic neuropathy	Necrotising and non-necrotising vasculitis in epineurium and perineurium much more than endoneurium; mononuclear infiltrate; immune deposits	Small arteries, arterioles, capillaries, venules	Muscle (25%)	↑ESR (~50%), ANA (~25%), ↓haemoglobin (~20%), ↑WBC (~15%), RF (~10%), ↓comp (~5%)	PNS (100%), CNS (0%)

Reproduced from reference 47, by permission of Elsevier. PNS=peripheral nervous system. GI=gastrointestinal involvement. ENT=upper respiratory tract involvement. ESR=erythrocyte sedimentation rate. WBC=white blood cell count. RF=rheumatoid factor. Hep B=hepatitis B surface antigenaemia. comp=circulating complement factors. ANA=antinuclear antibody. Hep C=hepatitis C antibodies or RNA. ANCA=antineutrophil cytoplasmic antibodies. angio=abdominal angiographically shown microaneurysms. CrN=cranial nerve involvement. LCV=leucocytoclastic vasculitis. MPO=myeloperoxidase. PR3=proteinase 3. GN=glomerulonephritis. ASO=antistreptolysin O. PMR=polymyalgia rheumatic. LFTs=liver function tests.

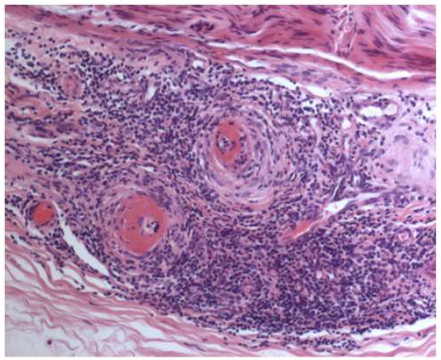
Table: **Clinical and pathological features of primary vasculitides associated with neuropathy**

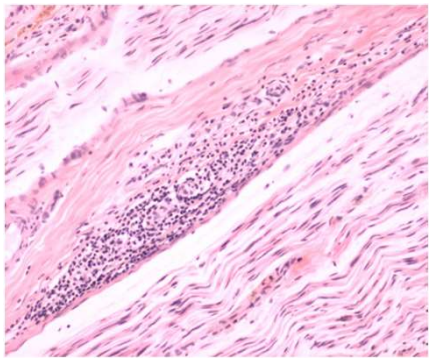
Vascularite secondaire systémique

Prédominance petits vaisseaux
Infiltrats Lymphocytaire
« vasculite Lymphocytaire »

Dommage pariétale, nécrose possible

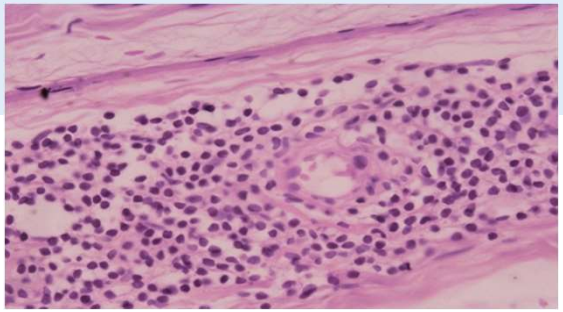
- Polyarthrite Rhumatoïde
- Lupus systémique
- **Cryoglobulinémie** (VHC ou autre cause)

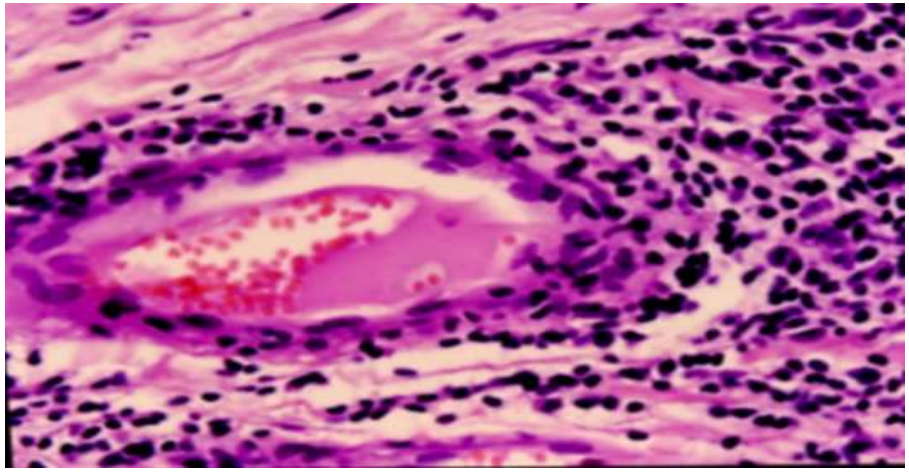




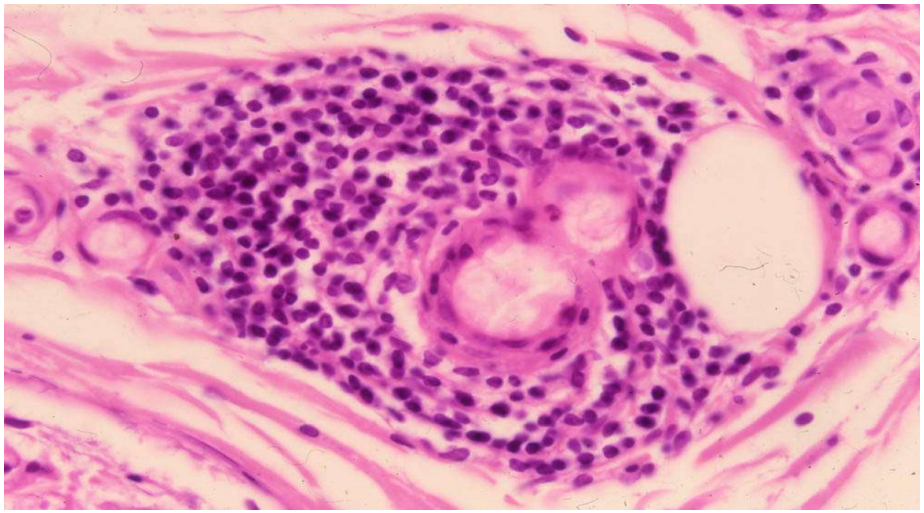
Dommage pariétale , nécrose rare

- Sjögren
- Sclérodermie, Connectivite mixte
- Lyme, VIH, Parvovirus B19
- Hansen (Lèpre)
- Cancer, Lymphome
- Diabète
- Sarcoïdose
- « Hypersensibilité » post toxique, drogue, vaccin

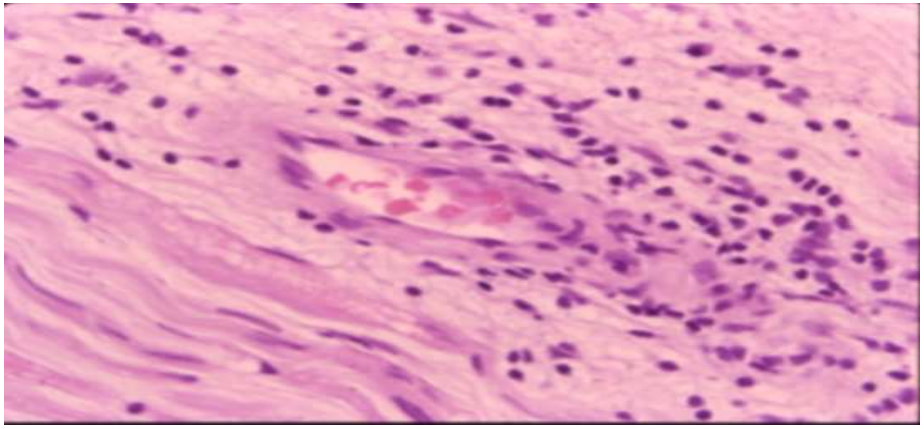




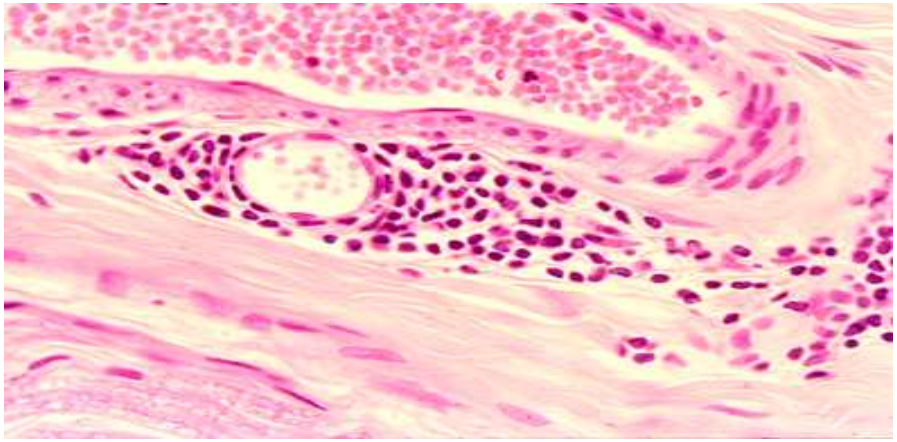
HIV



Hépatite C-Cryoglobulinémie



Lyme



Sjögren

Travail rétrospectif sur 7 ans (2014-2020) Ensemble des Neuropathies vascularitiques

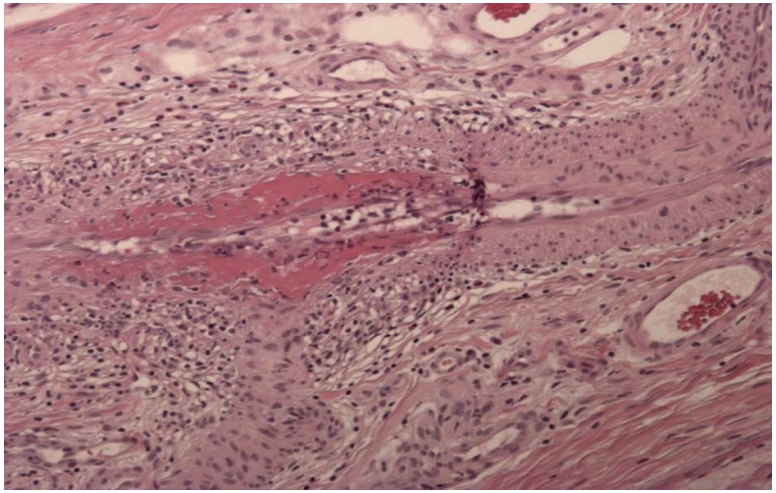
- **Multicentrique**
- Bicêtre (Andoni Echaniz-Laguna, Clovis Adam, Céline Labeyrie, Edouard Berling): N = 29 cas
- Limoges (Laurent Magy, Mathilde Duchesne) N =29 cas
- Pitié-Salpêtrière (Thierry Maisonobe) : N = 114 cas

- 30 à 40 % de formes restreintes nerf périphériques (NSVN)
- Pas de différence de sévérité de la neuropathie et des lésions et du pronostic
- Forte corrélation entre lésions de vascularites musculaires et caractère systémique et surtout présence d'ANCA +++
- Travail sur de nouveaux critères pour parler de vascularite définie ou probable ana-path dans le nerf

Vignette clinique

- Patiente de 48 ans, journaliste à Epernay (Dr Vaunaize)
- **Sportive , jogging, sans atcd particulier,**
- **Bon état général**
- après un vaccin grippe Revaxis ° , présente une sensation d'engourdissement des 2 pieds symétriques, puis progressivement sensation de rétraction des 2 pieds plus désagréable. Supporte difficilement les chaussures
- Hypoesthésie en petites chaussettes, aréflexie achilléenne, pas de déficit moteur, pas d'ataxie, continue de courir..Pas de limitation du périmètre de marche
- Aggravation progressive sur 2 ans, sensitive, douloureuse
- Aucun signe exra neuro , petite eruption sur le pieds, très froid « livedoide »
- EMG initilal sensitifs limites aux MI, 1 an et emi plus tard, abolition des sensitifs aux MI, reste peu altéré
- Bilan large Bio/immuno,PL, Scanner TAP, BGSA, TTR : normal ou négatif

Biopsie neuro-musculaire



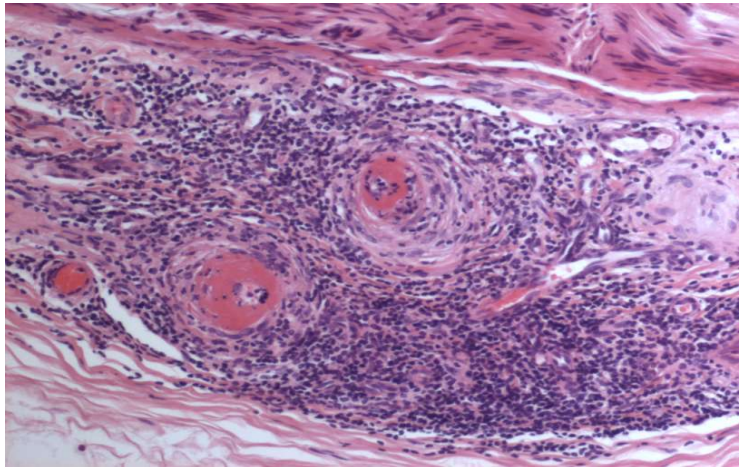
Vascularite nécrosante avec nécrose fibrinoïde floride

Vascularite restreinte au SNP (NSVN)

exemple Journaliste d'Epernay, joggeuse

- Nouvelles notions :

- Age jeune possible
- Notions de poussées spontanément réversible ou très stable
- Intervalle libre de plusieurs années
- > 2 ans
- Sensitif prédominant parfois S>>M
- ENMG plus sévère que clinique
- Évolutivité
- **Biopsie nerf** >>Muscle



SPECIAL ARTICLE

AMERICAN ACADEMY OF NEUROLOGY

Practice Parameter: Evaluation of distal symmetric polyneuropathy: Role of autonomic testing, nerve biopsy, and skin biopsy (an evidence-based review)

Report of the American Academy of Neurology, American Association of Neuromuscular and Electrodiagnostic Medicine, and American Academy of Physical Medicine and Rehabilitation

J.D. England, MD

ABSTRACT

Janv 2009

Role of nerve biopsy in the evaluation of polyneuropathy. Nerve biopsy is generally accepted as useful in the diagnosis of inflammatory diseases of nerve such as vasculitis, sarcoidosis, CIDP, infectious diseases such as leprosy, or infiltrative disorders such as tumor or amyloidosis.[3] Nerve biopsy is most valuable in mononeuropathy multiplex or suspected vasculitic neuropathy. There are no studies regarding the role of nerve biopsy in the evaluation of DSP although on occasion the above noted diseases may present in that fashion.

What is the usefulness of nerve biopsy in determining the etiology of distal symmetric polyneuropathy? Out of 50 articles judged to be relevant, no article attained a grade greater than Class IV. Most of the articles discussed the nerve biopsy findings in specific diseases, the clinical suspicion of which had prompted the biopsy.[23-34] No article provided guidance regarding when to perform a nerve biopsy in the evaluation of DSP.

Conclusions. There is no evidence to support or refute a conclusion regarding the role of nerve biopsy in the evaluation of DSP (Class IV).

Recommendations. No recommendations can be made regarding the role of nerve biopsy in determining the etiology of DSP (Level U).

Quand aller plus loin ?

Quand demander une biospie Neuro-Musculaire ?

Quelles étiologies à rechercher Surtout ?

Biopsie Neuro Musculaire

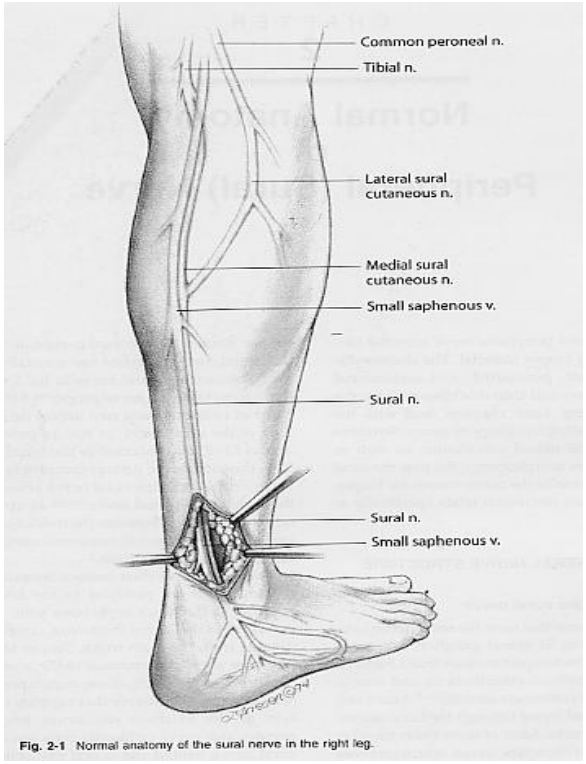
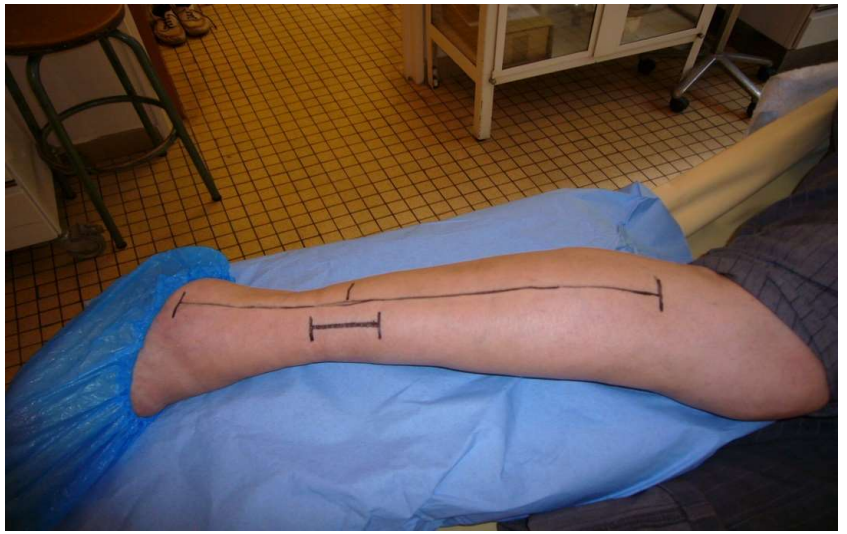
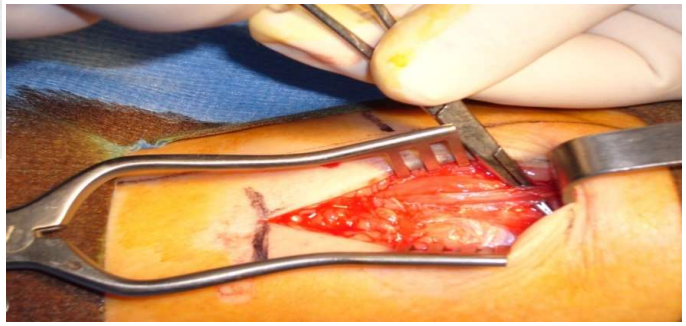
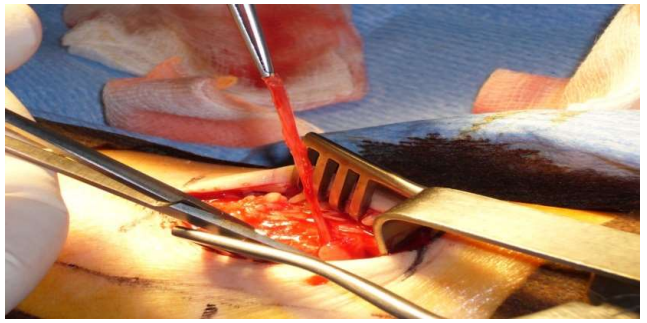


Fig. 2-1 Normal anatomy of the sural nerve in the right leg.

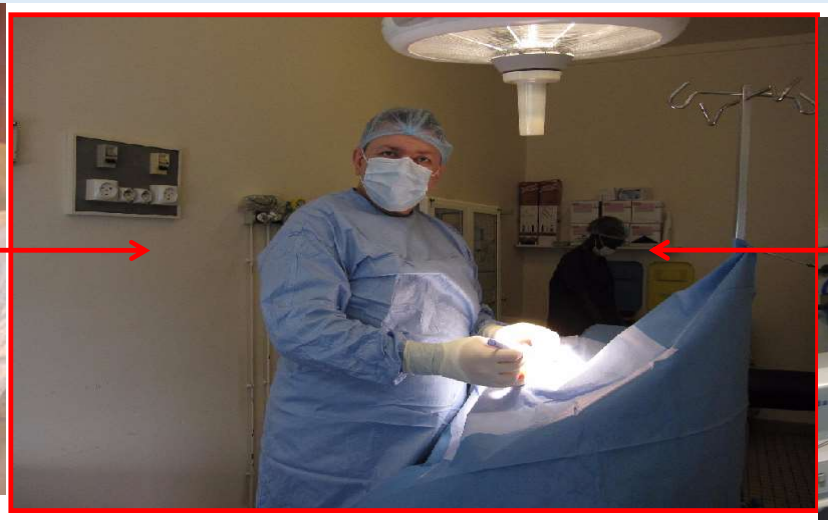


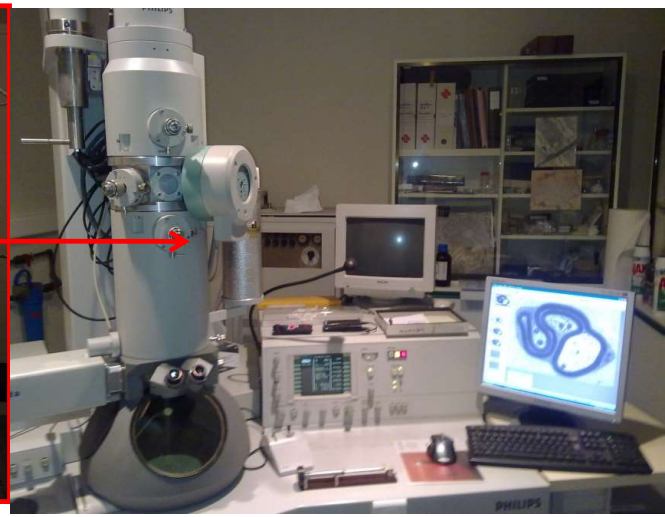




Biopsie « informative »

Dialogue +++



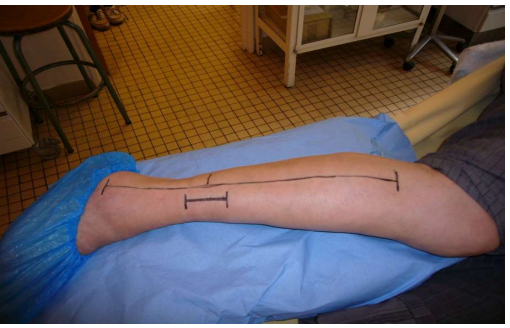


Prescripteur
Indication
Clinique/ENMG

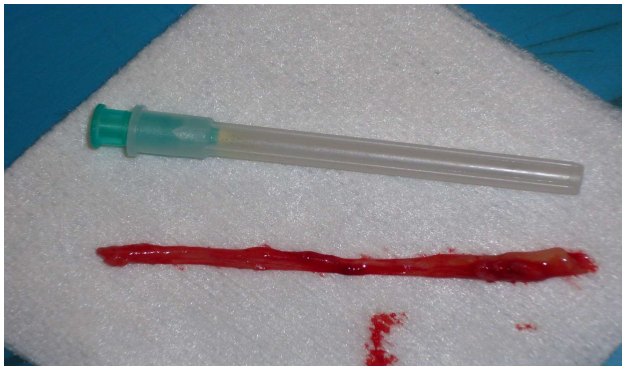
Préleveur
Site
Taille, nbre,
Conditionnement
des prélèvements

Interprète
analyse
biopsie

Biopsie Neuro Musculaire informative

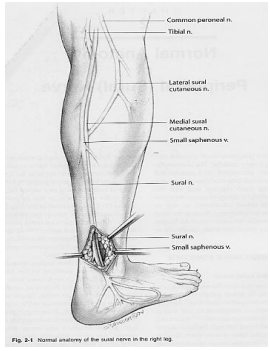


Longueur
Du fragment
3-4 cm

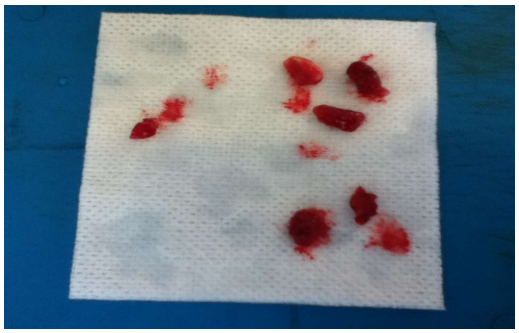


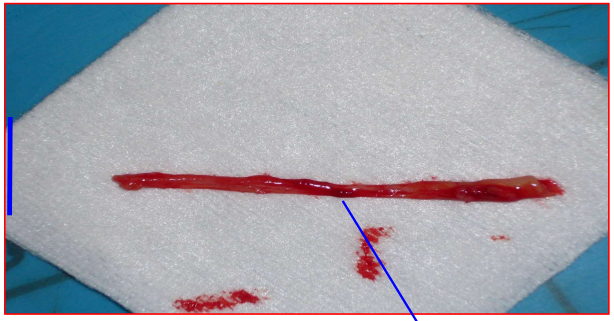
Biopsie informative

Quel nerf prélevé ?
Nerf radial ?



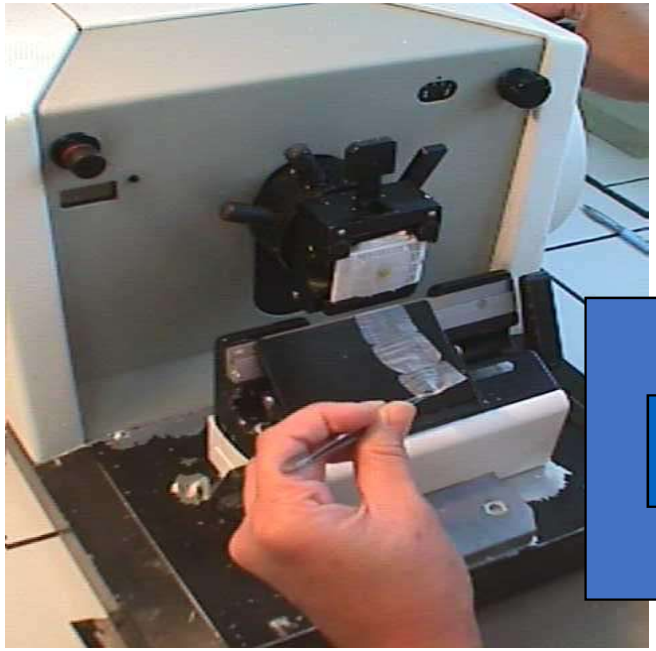
Nbre de fragments
musculaires
6-8

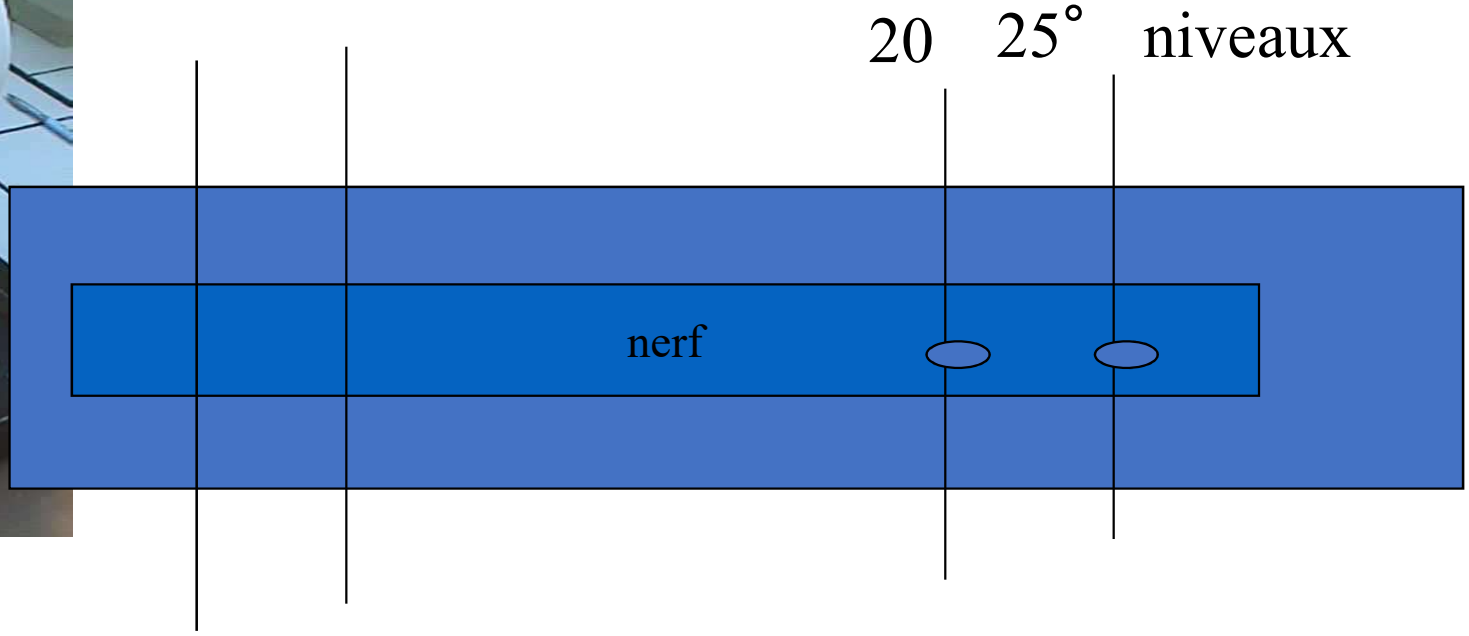




Paraffine
Causes interstitielle

Technique A : paraffine





Epuisement du bloc si nécessaire +++

Répartition sur le muscle ou nerf des lésions de vascularite

(Said et al, 1988, Bennett et al JNNP, 2008, Magy et Vallat, JNNP 2008)

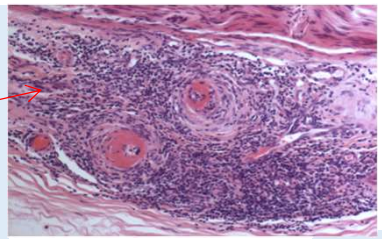
- Vascularite seulement sur le nerf 20 %
- Vascularite seulement sur le muscle 45 %
- Vascularite sur le nerf et le muscle 30 %
- « Rentabilité du nerf » 50 %
- « Rentabilité du muscle » 75 %

Messages-Conclusion

- Neuropathie Evocatrice d'une vascularite : traitement ! Urgence vasculaire du nerf périphérique

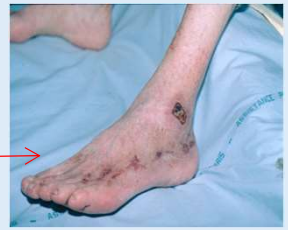
Importance délai diagnostic court ! Biopsie Nerveuse

Neuropathie Traitable voire curable



- **Mononeuropathies Multiples**

- Installation aiguë
- Asymétrie clinique et / ou électrophysiologique



- Signes généraux extra neurologique

La peau !!

- Douleur

- **Polyneuropathie distale symétrique**
  - *Froide , sans signe extra neurologique*
  - *Sans syndrome inflammatoire*
  - *Sans cause retrouvée*

Mais

  - *<u>Evolutive</u>*
  - *<u>Aggravation nette en 6 mois +++</u>*
  - Mais possible plus de 2 ans d'ancienneté si évolutivité , notion de poussée +++

- *Attention aux diagnostiques différentiels si « vasculite lymphocytaire » : lymphome, Sarcoïdose, lèpre, Parvovirus etc Bilan médecine interne*

- Importance du « bon cadre » de vascularite pour le traitement au-delà des corticoïdes +++