Criteria for referral to national complex neurofibromatosis 1 service

Guy's and St. Thomas' NHS Foundation Trust London &
Manchester University NHS Foundation Trust

Brain glioma / glial neoplasm

Any adult or child with brain or spine glioma or glial neoplasm (This is a diagnosis made by a neuro-radiologist)

Scan yearly for first 5 years after diagnosis and then long-term follow-up under complex NF1 (most gliomas that require treatment, do so in the first five years after diagnosis.

DNET (dysembryoplastic neuroepithelial tumour)

Any adult or child with the above to be followed long-term by national service until a diagnosis has been made on histology (DNET cannot be distinguished reliably from glioma on brain MRI)

Aqueduct stenosis

This could be caused by a glioma, web or periaqueductal proliferation of glial cells. NF1 patients may remain stable for many years and then deteriorate acutely with hydrocephalus

Optic pathway glioma

Children with OPG

1) All children with OPG for 2 years after diagnosis (most children with OPG who need treatment will do so in the first 2 years after diagnosis) / or children with OPG and deteriorating vision / precocious puberty / abnormal visual examination

2) OPG and significant learning problems
3) Not possible to test vision due to developmental or cognitive problems
4) Treated with chemotherapy
5) Treated with radiotherapy
6) Referred for second opinion
7) Any other neurological or ophthalmological problem that threatens vision or overlaps with neurovascular or inflammatory disease

Adults with OPG

1) Treated with chemotherapy
2) Treated with radiotherapy
3) Significant learning problems
4) Any other neurological or ophthalmological problem that threatens vision or overlaps with neurovascular or inflammatory disease or demyelination

The service works closely with regional neuro-oncology teams to ensure NF1 patients entered into relevant clinical trials. Please let us know about any children with NF1 and OPG so we can ensure their long term outcome is recorded

Multiple sclerosis (There is an increased frequency of all types of multiple sclerosis in NF1 and clinical signs of NF1 and multiple sclerosis overlap).

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Patients will be followed by both NF1 and MS specialists

Radiologically isolated demyelination

(50% risk of developing MS)

Clinically isolated syndrome

Vasculopathy

Includes intracranial e.g.moya moya, aneurysm, haemorrhage, vascular malformation, renal artery stenosis

Cord compression / cauda equina compression caused by neurofibromas

(Many patients do not require intervention despite neuroimaging findings. The cord compression is normally in the high cervical cord).

The complex NF1 service is involved in decision making about timing of surgery. Patients are followed-up, unless they have had surgery and do not have significant deficit

Symptomatic neurofibromas

1) Neurofibromas that cause one or more of persistent pain/nocturnal pain, rapid growth, change in texture or new or unexplained neurological deficit and require FDG PET CT. **N.B. The decision to undertake PET imaging and the interpretation of results is a complex issue. To avoid unnecessary radiation we recommend that patients with symptoms are referred to the national centres prior to PET imaging**

2) Symptomatic neurofibromas causing **significant**
   a) Neurological deficit
   b) Impaired respiratory function
   c) Impaired sphincter function
   d) Haemorrhage
   e) Severe infection
   f) Limb overgrowth, extensive internal neurofibromas/ extensive neurofibromas involving the skull base/ face
   g) Symptomatic neurofibromas that are not operable and are being considered for MEK inhibitors

Atypical neurofibroma (atypical neurofibromatous neoplasm of uncertain biologic potential)

People with previous resection of neurofibroma(s) reported to be atypical on histology by expert pathologists (these are associated with increase risk of future MPNST)

Neurofibromatous neuropathy

People with this axonal neuropathy have an increased risk of developing malignant peripheral nerve sheath tumour

Malignant peripheral nerve sheath tumour

Any past history or current history of MPNST (People with past history of MPNST are at increased risk of developing new MPNST)

Gastrointestinal stromal tumour (GIST)

These tumours may present with abdominal pain, change in bowel habit or haemorrhage

Sarcoma

Include bone sarcoma and rhabdomyosarcoma

Other Tumours

Phaeochromocytoma
Breast cancer < 50 years (increased risk in NF1 and requires screening from 40 years)
Cancer of colon, thyroid, lymphoma, leukaemia, melanoma other malignancy – increased risk

Pseudarthrosis of long bone

Adults and children seen once by Complex NF1 service to ensure no other bone dysplasia/ adequate vitamin D and referral to specialist pseudarthrosis team / adult rehabilitation team

Unusual NF1 phenotype

Legius syndrome
Kyphoscoliosis causing respiratory impairment
Spinal phenotype
Whole gene deletion – increased risk of malignancy

Genetic Counselling for people with mosaic NF1

Patients with mosaic NF1 should first have RNA based mutation analysis via the Manchester lab. If the results are normal they are then eligible for skin biopsy from café au lait macules (for melanocyte culture) or neurofibroma removal (for Schwann cell extraction and culture). The specific tissues are necessary to identify the causative mutation for genetic counselling.
Contact Dr Emma Burkitt Wright (Manchester) or Dr Dragana Josifova (GSTT).