causes of ataxia

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Sheffield Ataxia Centre

the Sheffield ataxia clinic was set up in 1994

aims:

achieve a diagnosis in all progressive ataxias

study the natural history of different ataxias

offer support and regular follow up

promote research

forge collaborations with other ataxia centres

Sheffield Ataxia Centre

accredited as Ataxia Centre of Excellence

by Ataxia UK in 2007

appointment of dedicated ataxia nurse with support from Ataxia UK (first 3 years)

appointment of an additional Consultant (2014) with an interest in Ataxias and a second ataxia nurse (2014) now all fully funded by STH Trust

referral bias?

interested in all ataxias both sporadic and familial/genetic

most patients referred do not have a diagnosis

research work in immune ataxias eg gluten ataxia and primary autoimmune cerebellar ataxia

practicalities

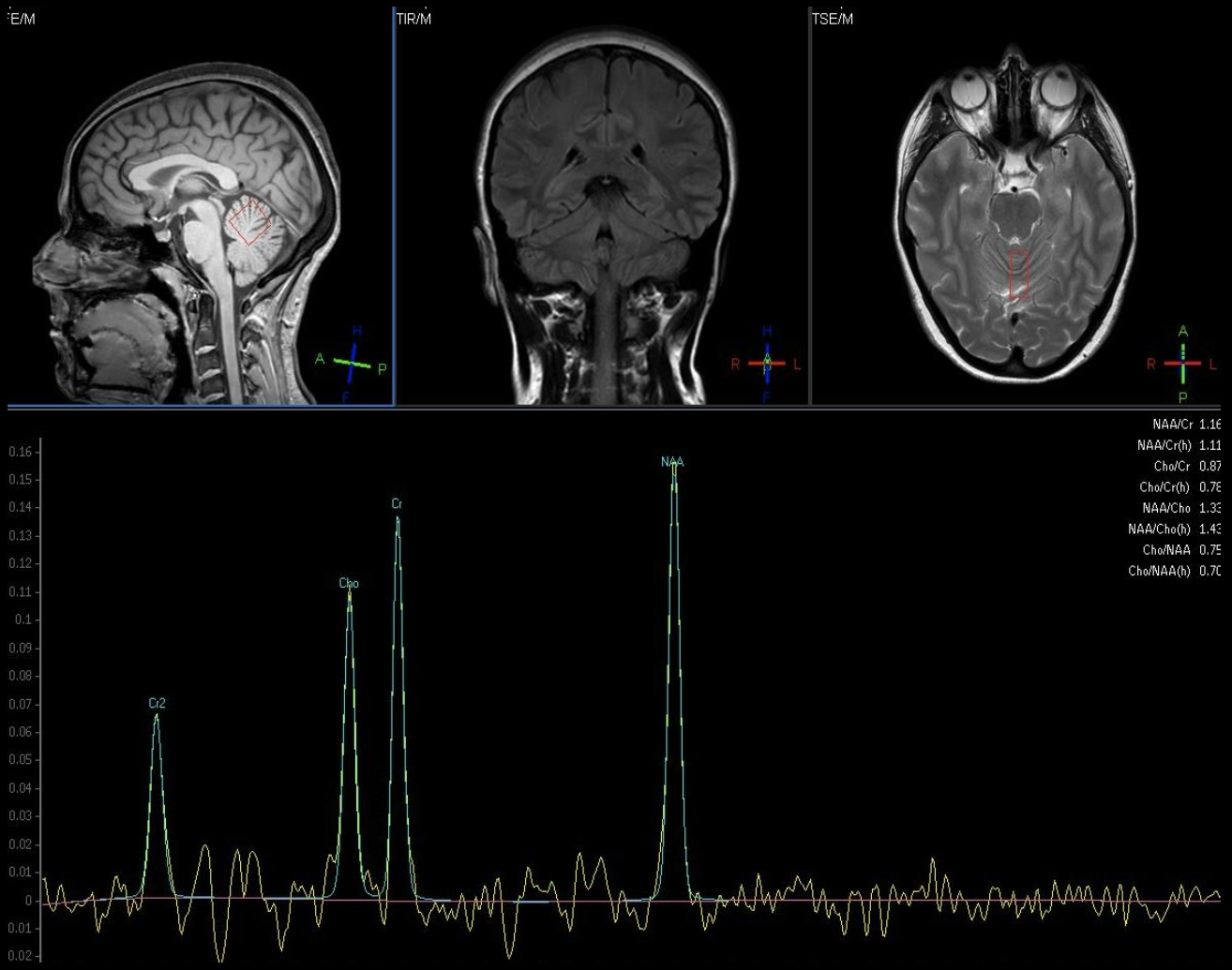
patients referred from all over the UK and abroad

initial assessment and regular FU (6-12 months)

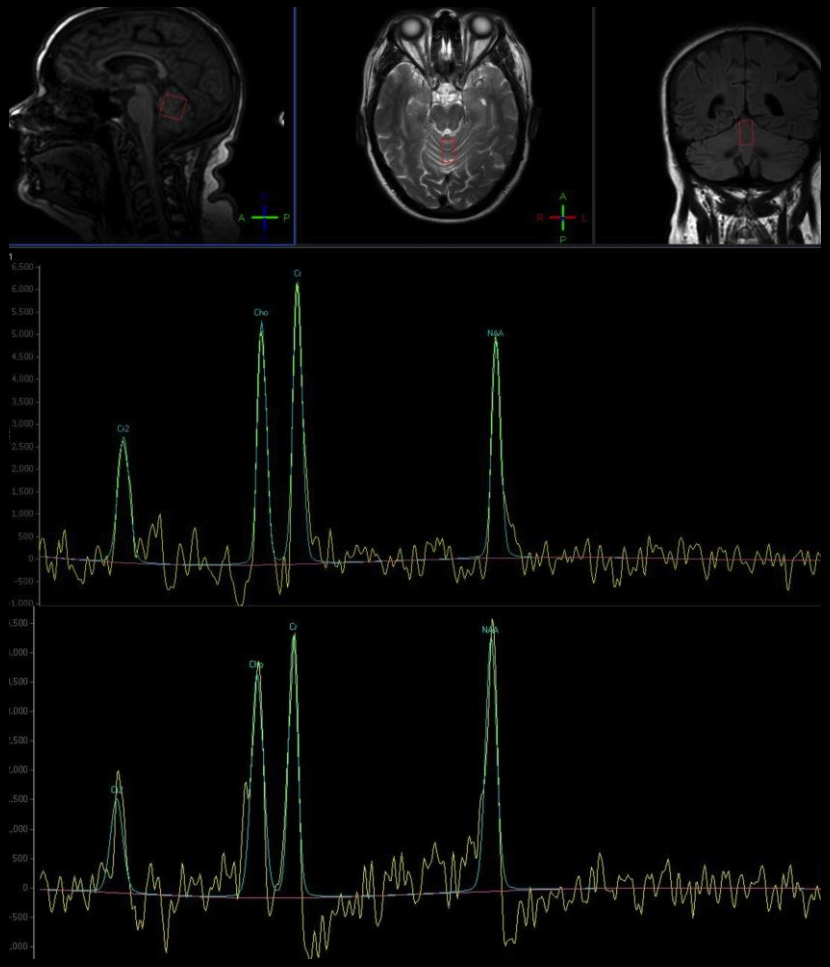
brain imaging including MR spectroscopy of the cerebellum

access to genetic testing (local and good collaboration with many labs in UK and abroad)

regular Consultant review particularly for patients where a diagnosis has not been made


E/M
TIR/M
TSE/M
NAA/Cr 1.1
NAA/Cr(h) 1.11
Cho/Cr 0.87
Cho/Cr(h) 0.7
NAA/Cho 1.3
NAA/Cho(h) 1.4
Cho/NAA 0.7
Cho/NAA(h) 0.7
Cr2
Cho
Cr
NAA

before and after gluten free diet



the role of the consultant

don’t underestimate the importance of clinical skills and expertise in diagnosing ataxias

new generation sequencing is not the answer to all diagnoses

the importance of clinical observation means that we can identify new entities eg primary autoimmune cerebellar ataxia

gain experience in the natural history of ataxias

the role of the ataxia nurse

address practical aspects at home, issues at work, access to support, physio, OT and speech and language therapy etc

available at the end of the phone between appointments

able to spend much more time in discussing the implications of ataxia

works closely with the Consultant

for patients with known diagnosis can help with follow ups

the role of the ataxia nurse

motivate patients to help themselves

eg

alcohol ataxia

Gluten ataxia

can run more specialist clinics with input from other specialist nurses eg MSA-C

causes of ataxia

a total of 1288 patients assessed

(10 new patients per month)

259 familial (20%)

1029 sporadic (80%)

causes of sporadic ataxia

idiopathic sporadic ataxia (ISA)	262/1029 (25%)
gluten ataxia	235/1029 (23%)
alcohol related	143/1029 (14%)
genetic cause	132/1029 (13%)
MSA-C	125/1029 (12%)
paraneoplastic	28/1029 (3%)
anti-GAD ataxia	24/1029 (2%)

under 2% in order of frequency: phenytoin, cerebellitis, superficial siderosis, opsoclonus myoclonus ataxia, ataxia with palatal tremor

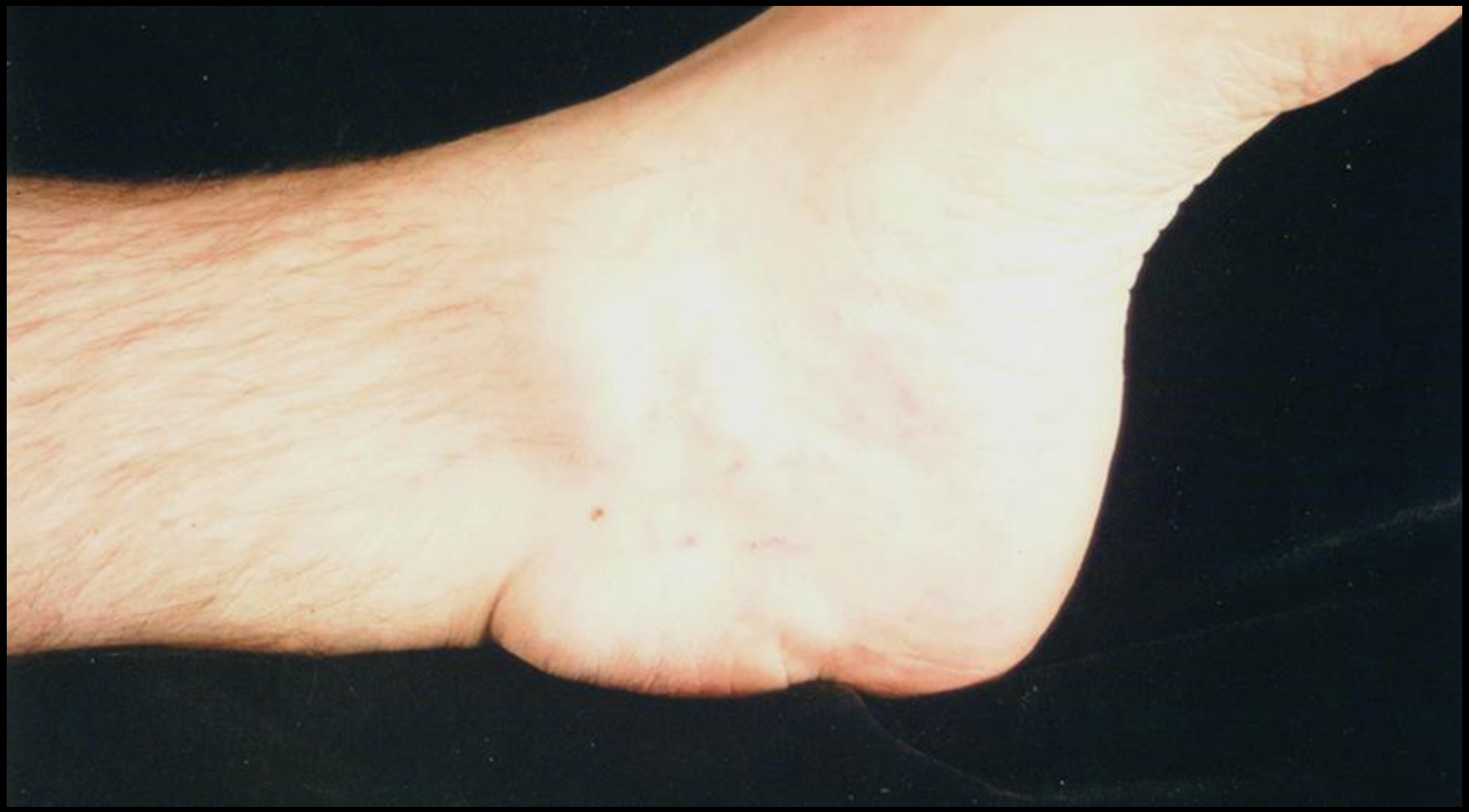
imaging in newly diagnosed CD

44% had abnormal MR spectroscopy of the cerebellum

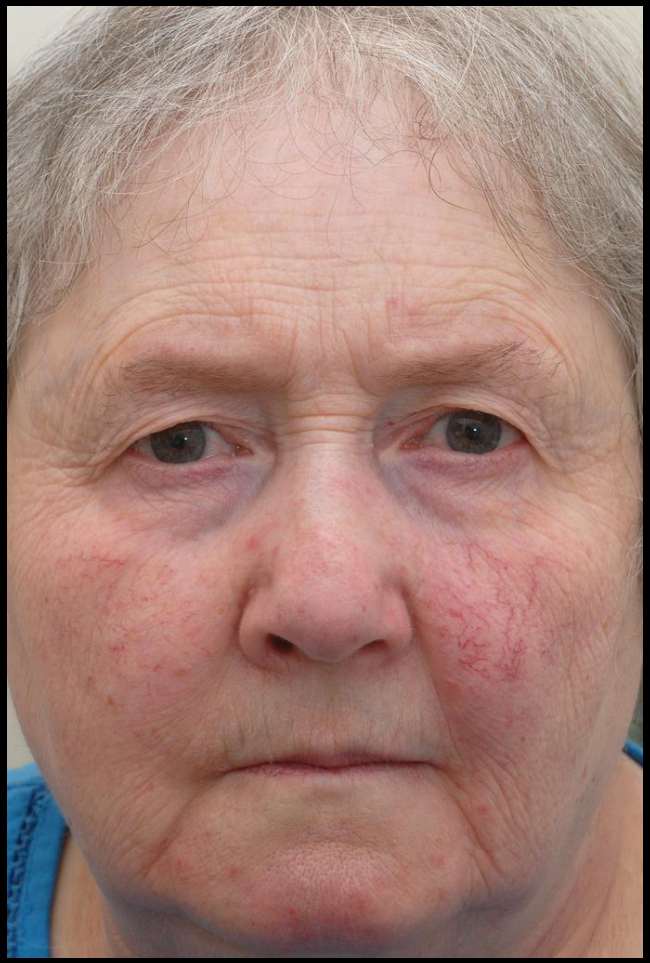
(3% controls)

56% of patients with abnormal MRS had clinical evidence of balance problems

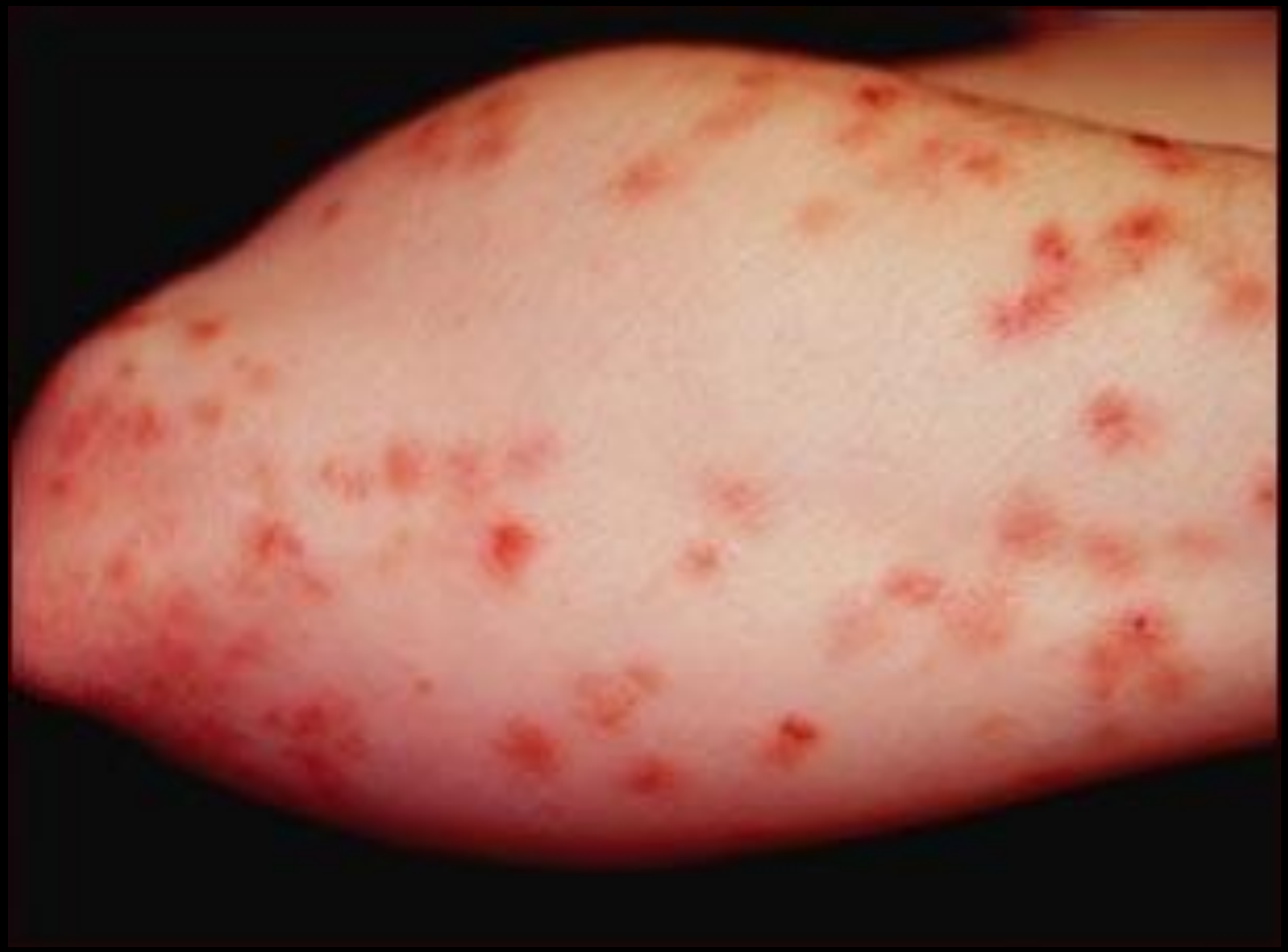
examination clues



examination clues



examination clues



genetic causes in sporadic ataxia

132/1029 (13%)

FA 39, mitochondrial 22, SCA6 15, EA2 13, fragile X 6

SPG7 7

2 or less includes

SCA1, SCA2, SCA14, SCA15, SCA28, AOA2, Cockaynes, NP-C, Krabe's, XP, CTX, amyloid, AT, ARSACS, congenital, dysplasia, Tay-Sachs, Holmes

out of all idiopathic sporadic cases a genetic cause was found in 132/132+262= 34%

familial ataxias

259 ie 20% of the whole group of 1288

AD 183 (71%)

AR 75 (29%)

AD commonest types

EA2 28, SCA6 24, SCA2 8, SCA3 4, SCA7 4

two or less

SCA1, SCA8, SCA 13, SCA 14, SCA 15, SCA 17, SCA 22, SCA 28, mitochondrial, AOA2

familial ataxias

AR 75 (29% of all familial cases)

FA 25, SPG7 4, NP-C 2, mito 1, (EA2 2)

genetic characterisation in all familial ataxias 45%

next generation sequencing

20 patients with results so far (16 with family history, 4 early onset)

positive in 7 patients (35%)

3 SCA14, 3 EA2, 1 ARSACS, 1 SPG7

genetic testing just for SPG7 (ataxia with mild spastic paraparesis) 11 positive patients

diagnostic yield after assessment at the Sheffield Ataxia Centre

based on data from 1071 patients

48% a diagnosis was achieved after investigations at the Sheffield Ataxia Centre

13% a diagnosis was already known (mainly genetic cases)

39% no diagnosis and ongoing assessments and investigations (genetic and other)

overall diagnostic yield was 55%

conclusions

commonest genetic ataxias in the UK:

FA, EA2, SCA6

total number of potentially genetic ataxias -all with family history plus all genetically confirmed sporadic cases: 30%

genetic characterisation in familial ataxias: 45%

EA2 can present with progressive ataxia without being episodic

SPG7 and SCA14 are proving to be common causes of progressive ataxia

conclusions

commonest causes of sporadic ataxias in the UK:

gluten, alcohol, genetic and MSA-C

idiopathic sporadic ataxias account for 20% of all ataxias

some ISAs are likely to prove to be genetic but some are likely to have an immune aetiology

thank you