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ATAXIA - TELANGIECTASIA – A HISTORICAL REVIEW AND A PROPOSAL FOR A NEW NAME: ATM SYNDROME

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Abstract

The authors review ataxia telangiectasia, emphasizing historical aspects, genetic discoveries and the clinical presentations of the classical and atypical forms. Our conclusion is that the term ataxia telangiectasia is a misnomer because it represents a multisystem entity with pleomorphic neurological and systemic manifestations. ATM syndrome is proposed as a more adequate designation for this entity.

Keywords

ataxia-telangiectasia; cerebellar ataxia; immunodeficiency; malignancies; oculocutaneous telangiectasia; alpha-fetoprotein

Ataxia telangiectasia (A-T) is a rare autosomal recessive neurodegenerative disease caused by mutations in the A-T gene (ATM) characterized by progressive neurological dysfunction in association with multisystem abnormalities and cancer predisposition.^{1,2,3} It occurs in 1 out of 88,000 live births in the USA (1 in 300,000 and 1 in 40,000 live-births) with onset of symptoms in infancy, particularly between the ages of two and five years.^{1,3} Classical neurological signs include progressive cerebellar ataxia; oculomotor abnormalities, particularly ocular apraxia; movement disorders, such as chorea; and cognitive dysfunction. The condition presents with multisystem involvement, which includes immunodeficiency, sinopulmonary infections, radiosensitivity, cancer predisposition, oculocutaneous telangiectasia and elevated serum alpha-fetoprotein levels.^{1,2,3,4,5,6} The gene responsible for this disorder, ATM (ataxia telangiectasia mutated), codes for the protein kinase ATM, which plays an important role in DNA damage repair.^{1,2,3,5,7} After the genotype was defined, it became evident that there is a wide spectrum of phenotypic manifestations, including the classical phenotype with mild and severe forms and childhood and adult onset, as well as

atypical clinical presentations without oculocutaneous telangiectasia.^{8,9,10,11,12,13} Our aim is to present a historical review and discuss a new proposal for defining this entity.

Historical Review

The term ataxia-telangiectasia (A-T) was initially proposed by Boder and Sedgwick in 1957,^{6,14,15} however this clinical entity received other designations that include Louis-Bar syndrome, suggested by Centerwall and Miller in 1958, and Boder-Sedgwick syndrome, suggested by Sagarra (1959), Jablonsky (1969) and François (1972).⁶ The first eponym relates to Madame Louis-Bar, a Belgian neurologist who published a case report in 1941 describing a nine-year-old boy with progressive cerebellar ataxia and extensive cutaneous telangiectasia.^{6,16} She included this new disease in the group of phakomatoses.^{6,16} For the next couple of decades, A-T was referred to worldwide as Louis-Bar syndrome, until 1964, when Martin¹⁷ published the manuscript *Aspect choréothétosique du syndrome d'ataxie-télangiectasie*, stating that there was a previous description of A-T in the literature, published in French by Syllaba and Henner (1926) fifteen years before the classical description by Louis-Bar.¹⁷ In fact, Syllaba and Henner described three adolescent Czech siblings with progressive chorea and dystonia in association with ocular telangiectasia.¹⁸ Subsequently, in 1968, Henner confirmed that the disease described previously was in fact A-T.⁶ Two other important studies were published in 1957, one by Boder and Sedgwick¹⁴ and another by Biemond.¹⁹ Boder and Sedgwick described eight patients with classical A-T, suggesting the name “ataxia-telangiectasia”.^{6,15} They also reported the absence of the thymus and ovaries in their cases.¹⁵ Biemond published another case series with neuropathological findings in which he described the familial nature of this disorder and the presence of extrapyramidal manifestations.¹⁹ later, several groups published case series of A-T patients, including Wells and Shy (1957), Centerwall and Miller (1958), Boder and Sedgwick (1958, 1960, 1963) and Dunn et al. (1964).^{4,6,14,15} The 1963 publication of Boder and Sedgwick evaluated the clinical features of 101 cases of A-T and found cerebellar ataxia (100 % of cases), oculocutaneous telangiectasia (100% of cases), characteristic facies (98%), choreoathetosis (91 %), progeric changes of the skin and hair (88%), eye movement apraxia (84%), sinopulmonary infections (83%), familial occurrence (45%) and mental retardation (33%).²⁰ In 1964, Dunn et al. published a case report of two Canadian patients with A-T in which they described neuropathological findings and atrophy of the thymus, adrenals, spleen and lymphoid tissues, as well as bronchiectasis and the presence of bilateral ovarian dysgerminoma.⁴ In 1972, Waldmann et al. described the presence of high levels of serum alpha-fetoprotein in patients with A-T.²¹ In 1884, Byrne et al. described a sibship of three ataxic patients, associated to dystonia, chorea, dementia, peripheral neuropathy, with IgE deficiency, chromosomal abnormalities, but, without telangiectasias or alpha-fetoprotein elevation.²² The authors proposed that A-T should be defined as a syndrome of “multiple neurological system degeneration, immunological attrition, chromosomal instability and predisposition to malignancy”.²² In 1993, Friedman and Weitberg published a case report about a 17-year old boy with cerebellar ataxia associated to dystonia, myoclonus, pyramidal signs, seizures, recurrent sinopulmonary infections, persistent lymphopenia, immunoglobulin deficiency, and elevated alpha-fetoprotein, but without telangiectasia.¹³ The authors proposed a new definition for this entity, as “ataxia with immune deficiency”.¹³

A-T – Genetic Discoveries

In 1988, Gatti et al. mapped the A-T gene to chromosome 11q22-23.²³ In 1995, Savitsky et al. (an international consortium led by Shiloh and Collins) identified the defective gene responsible for A-T (ATM).²⁴ Subsequently, in 1996 and 1997, multiple cell cycle checkpoints and the product of the ATM gene, the protein kinase ATM, were described. Since then, several mutations have been found in the ATM gene, including truncating mutations, which result in the total absence of ATM kinase activity, and one missense or splice site mutation, leading to decreased kinase activity.^{7,12,25,26} In general, mothers of A-T children who are heterozygous for the ATM mutation and are therefore carriers have a high risk of developing breast cancer.²⁷ In 2001, Stewart et al. studied ATM kinase activity levels in cells from A-T patients and suggested that this activity correlates with the degree of neurological symptoms in these patients (residual A-T mutated protein function is related to a less severe phenotype).²⁵ In a seminal study in 2012, Verhagen et al. showed that the presence of ATM protein and residual kinase activity correlates with the phenotype in A-T patients (a genotype-phenotype study).⁷ Patients without ATM kinase activity showed the classical phenotype of A-T while the presence of residual ATM kinase activity correlated with a milder and atypical phenotype, including the absence of telangiectasia, normal endocrine and pulmonary function, normal immunoglobulins, significantly lower X-ray hypersensitivity in lymphocytes and extended lifespan.⁷ Verhagen et al. also showed that cancer occurs later in life in these patients.⁷

The A-T phenotype after the genotype was defined

In previous studies of A-T published before the discovery of the ATM gene, the frequency of cerebellar ataxia and ocular and cutaneous telangiectasia was very high (around 100 % of cases).^{4,14,15,20,28} However, after the A-T gene was identified several studies emphasized the presence in genetically proved cases of A-T of atypical clinical pictures that did not include cerebellar ataxia or ocular and cutaneous telangiectasia.^{8,11,22,29,30,31,32,33} Trimis et al. published a case report of a six-year-old girl with genetically proved A-T but an unusual absence of neurologic symptoms.¹⁰ Alterman et al. studied two siblings with A-T and severe cellular phenotype but mild neurological clinical presentation.¹² Moin et al. evaluated clinical and laboratory features of 104 patients with A-T and found that cerebellar ataxia was present in all of the patients.³⁴ However, ocular and cutaneous telangiectasia was present in 87 and 73 of the cases, respectively.³⁴ In a Brazilian case series of 10 patients with A-T, half of the cases did not have ocular or cutaneous telangiectasia (Teive et al., unpublished data). The most relevant case series of A-T with atypical clinical manifestations are shown in Table 1. Different movement disorders have been described in patients with A-T, including dystonia, myoclonus, chorea, parkinsonism and postural, rest, and kinetic tremor.³⁵⁻⁴² The most common movement disorders described in A-T patients are shown in Table 2.

A new proposal for a definition of A-T

It is now known that various diseases associated with DNA damage response (DDR) manifest with neurological symptoms and immunodeficiency.^{1,2,3,7,12, 43,44} These can

simulate A-T phenotypically and include diseases such as A-T-like disorder (ATLD - Mre11 deficiency) and Nijmegen breakage syndrome (NBS, or nibrin/Nbs1 deficiency), with microcephaly and mental retardation, without ataxia, apraxia or telangiectasia, and A-T (Fresno), a mixture phenotype (A-T and NBS) with mutations in the ATM gene.^{1,2,3,44} In 2007, Gatti et al. proposed a disease category called XCIND syndrome, an acronym for X-ray irradiation sensitivity, cancer susceptibility, immunodeficiency, neurological abnormality and double-strand DNA breakage.⁴⁵ Now that the ATM gene has been identified, the genotype-phenotype correlation of A-T confirms that the clinical picture of this condition is very broad, with non-classical presentations with and without neurological abnormalities, with movement disorders (chorea, dystonia), without cerebellar ataxia and without ocular and cutaneous telangiectasia. These cases are described as atypical cases of A-T, or A-T variants. However, in our opinion, it is time to replace the name A-T by ATM syndrome. In summary, ATM syndrome represents a neurodegenerative disorder with multisystem involvement due to the absence or reduced levels of ATM protein and kinase activity. The syndrome is characterized by the presence of movement disorders, such as cerebellar ataxia, dystonia, chorea and myoclonus, in association with systemic abnormalities such as immunodeficiency, malignancies, oculocutaneous telangiectasias and an increase in alpha-fetoprotein levels.^{1,2,3,7,12,27,34,43,45,46,47,48.}

Conclusion

Although the eponym Louis-Bar syndrome and the name A-T are well known around the world, they are inappropriate for this disease as Madam Louis-Bar was not the first to describe this disorder and, furthermore, the syndrome can present with other movement disorders in addition to ataxia telangiectasia, and a significant number of cases do not present with telangiectasia at all. Thus, we propose naming this important disease ATM syndrome.

References

1. Crawford, TO.; Shiloh, Y. Ataxia-Telangiectasia. In: Brice, A.; Pulst, SM., editors. Spinocerebellar degenerations. The ataxias and spastic paraplegias. Butterworth Heinemann Elsevier; Philadelphia, PA, USA: 2007. p. 202-221.
2. Treuner, K.; Barlow, C. Ataxia-Telangiectasia. In: Pulst, SM., editor. Genetics of movement disorders. Academic Press; San Diego, CA, USA: 2003. p. 195-203.
3. Sahama I, Sinclair K, Pannek K, Lavin M, Rose S. Radiological imaging in ataxia telangiectasia: a review. *Cerebellum*. 2014 Mar. (Published online).
4. Dunn HG, Meuwissen H, Livingstone CS, Pump KK. Ataxia-Telangiectasia. *Canad Med Ass J*. 1964; 91:1106–1118. [PubMed: 14229760]
5. McConville CM, Stankovic T, Byrd PJ, McGuire GM, Yao QY, Lennox GG, Taylor AM. Mutations associated with variant phenotypes in ataxia-telangiectasia. *Am J Hum Genet*. 1996; 59:320330.
6. Sedgwick, RP.; Boder, E. Ataxia-Telangiectasia. In: Vinken, PJ.; Bruyn, GW.; Klawans, HL.; De Jong, JMBV., editors. Handbook of Clinical Neurology. 60. Hereditary Neuropathies and Spinocerebellar atrophies. Elsevier Science Publishers; Amsterdam, The Netherlands: 1991. p. 347-423. Revised Series 16
7. Verhagen MM, Last JJ, Hogervorst FB, et al. Presence of ATM protein and residual kinase activity correlates with the phenotype in ataxia-telangiectasia: a genotype-phenotype study. *Hum Mutat*. 2012; 33:561–571. [PubMed: 22213089]

8. Willems PJ, Van Roy BC, Kleijer WJ, Van der Kraan M, Martin JJ. Atypical clinical presentation of ataxia telangiectasia. *Am J Med Genet.* 1993; 45:777–782. [PubMed: 8456862]
9. Churchyard A, Stell R, Mastaglia FL. Ataxia telangiectasia presenting as an extrapyramidal movement disorder and ocular motor apraxia without overt telangiectasia. *Clin Exp Neurol.* 1991; 28:90–96. [PubMed: 1726561]
10. Trimis GG, Athanassaki CK, Kanariou MM, Giannoulia-Karantana AA. Unusual absence of neurologic symptoms in a six-year old girl with ataxia-telangiectasia. *J Postgrad Med.* 2004; 50:270–271. [PubMed: 15623968]
11. Stell R, Bronstein AM, Plant GT, Harding AE. Ataxia telangiectasia: a reappraisal of the ocular motor features and their value in the diagnosis of atypical cases. *Mov Disord.* 1989; 4:320329.
12. Alterman N, Fattal-Valevski A, Moyal L, et al. Ataxia-telangiectasia: mild neurological presentation despite null ATM mutation and severe cellular phenotype. *Am J Med Genet A.* 2007; 143A:1827–1834. [PubMed: 17632790]
13. Friedman JH, Weitberg A. Ataxia without telangiectasia. *Mov Disord.* 1993; 8:223–226. [PubMed: 8474496]
14. Boder E, Sedgwick RP. Ataxia-telangiectasia; a familial syndrome of progressive cerebellar ataxia, oculocutaneous telangiectasia and frequent pulmonary infection. *Pediatrics.* 1958; 21:526–554. [PubMed: 13542097]
15. Sedgwick RP, Boder E. Progressive ataxia in childhood with particular reference to ataxia telangiectasia. *Neurology.* 1960; 10:705–715. [PubMed: 14444443]
16. Louis-Bar D. Sur un syndrome progressif comprenant des tlangiectasies capillaires cutanes et conjonctivales symtriques, disposition naevode et de troubles crbelleux. *Confin Neurol (Basel).* 1941; 4:32–42.
17. Martin L. Aspect choroathtosique du syndrome d'ataxie-tlangiectasie. *Acta Neurol (Belg).* 1964; 64:802–819.
18. Syllaba L, Henner K. Contribution l'indpendance de l'athtose double idiopathique et congnitale. Atteinte familiale, syndrome dystrophique, signe du rseau vasculaire conjonctival, intgrit psychique. *Rev Neurol.* 1926; 1:541–562.
19. Biemond, A. Palaeocerebellar atrophy with extra-pyramidal manifestations in association with bronchiectasis and telangiectasis of the conjunctiva bulbi as a familial syndrome. In: van Bogaert, L.; Radermecker, J., editors. *Proc. 1st Intern. Congr. Of Neurological Sciences*; Brussels. 1957; London: Pergamon Press; 1957. p. 206
20. Boder, E.; Sedgwick, RP. Ataxia-telangiectasia. A review of 101 cases. In: Walsh, G., editor. *Little Club Clinics in Develop.* London: Heinemann Medical Books; 1963. p. 110-118.
21. Waldmann TA, McIntire KR. Serum-alpha-fetoprotein levels in patients with ataxia-telangiectasia. *Lancet.* 1972; 2:1112–1115. [PubMed: 4117204]
22. Byrne E, Hallpike JF, Manson JI, Sutherland GR, Thong YH. Ataxia-without-telangiectasia. Progressive multisystem degeneration with IgE deficiency and chromosomal instability. *J Neurol Sci.* 1984; 66:307–317. [PubMed: 6597863]
23. Gatti RA, Berkel I, Boder E, Braedt G, Charmley P, Concannon P, et al. Localization of an ataxia-telangiectasia gene to chromosome 11q22-23. *Nature.* 1988; 336:577–580. [PubMed: 3200306]
24. Savitsky K, Bar-Shira A, Gilad S, Rotman G, Ziv Y, Vanagaite L, et al. A single ataxia telangiectasia gene with a product similar to PI-3 kinase. *Science.* 1995; 268:1749–1753. [PubMed: 7792600]
25. Stewart GS, Last JI, Stankovic T, et al. Residual ataxia telangiectasia mutated protein function in cells from ataxia telangiectasia patients, with 576ins137 and 7271T-G mutations, showing a less severe phenotype. *J Biol Chem.* 2001; 276:30133–30141. [PubMed: 11382771]
26. Hoche F, Seidel K, Theis M, et al. Neurodegeneration in ataxia telangiectasia: what is new? What is evident? *Neuropediatrics.* 2012; 43:119–129. [PubMed: 22614068]
27. Boder E, Sedgwick RP. Ataxia-telangiectasia. (Clinical and immunological aspects). *Psychiatr Neurol Med Psychol Beih.* 1970; 13–14:8–16.
28. Paglia LL, Laug A, Weber J, et al. ATM germline mutations in women with familial breast cancer and a relative with haematological malignancy. *Breast Cancer Res Treat.* 2010; 119:443–452. [PubMed: 19404735]

29. Ying KL, Decoteau WE. Cytogenetic anomalies in a patient with ataxia, immune deficiency, and high alpha-fetoprotein in the presence of telangiectasia. *Cancer Genet Cytogenet.* 1981; 4:311–317. [PubMed: 6174206]
30. Taylor AM, Flude E, Laher B, Stacey M, McKay E, Wett J, et al. Variant forms of ataxia-telangiectasia. *J Med Genet.* 1987; 24:669–677. [PubMed: 3430541]
31. Maserati E, Ottolini A, Veggioti P, Lanzi G. Pasquali Ataxia-without-telangiectasia in two sisters with rearrangements of chromosomes 7 and 14. *Clin Genet.* 1988; 34:283–287. [PubMed: 3228996]
32. Lanzi G, Balottin U, FRanciotta D, Maserati E, Ottolini A, Pasquali F, Veggioti P. Clinical, cytogenetic and immunological aspects in 4 cases, resembling ataxia telangiectasia. *Eur Neurol.* 1992; 32:121–125. [PubMed: 1375558]
33. Grabli D, Meneret A, Beaugendre Y, Gaymard B, Apartis E, Tranchant C, et al. Movement Disorders spectrum in adults with ataxia telangiectasia. *Mov Disord.* 2014; (Suppl)
34. Moin M, Aghamohammadi A, Kouhi A, et al. Ataxia-telangiectasia in Iran: clinical and laboratory features of 104 patients. *Pediatr Neurol.* 2007; 37:21–28. [PubMed: 17628218]
35. Huang SJ, Chu Jm, Tsai YT, Wang PJ, Hsieh KH. Ataxia-telangiectasia associated with torticollis: report of a case. *Zhonghua Min Guo Xiao Er Ke Yi Xue Hui Za Zhi.* 1991; 32:191–195. [PubMed: 1776444]
36. de Graaf AS, de Jong G, Kleijer WJ. An early-onset recessive cerebellar disorder with distal amyotrophy and, in two patients, gross myoclonia: a probable ataxia telangiectasia variant. *Clin Neurol Neurosurg.* 1995; 97:1–7. [PubMed: 7788963]
37. Klein C, Wenning GK, Quinn NP, Marsden CD. Ataxia without telangiectasia masquerading as benign hereditary chorea. *Mov Disord.* 1996; 11:217–220. [PubMed: 8684395]
38. Carrilo F, Schneider SA, Taylor AM, Srinivassan V, Kapoor R, Bhatia KP. Prominent oromandibular dystonia and pharyngeal telangiectasia in atypical ataxia telangiectasia. *Cerebellum.* 2009; 8:22–27. [PubMed: 18846412]
39. Saunders-Pullman R, Raymond D, Stoessl AJ, et al. Variant ataxia-telangiectasia presenting as primary-appearing dystonia in Canadian Mennonites. *Neurology.* 2012; 78:649–657. [PubMed: 22345219]
40. Nissenkorn A, Hassin-Baer S, Lerman SF, Levi YB, Tzadok M, Bren-Zeev B. Movement disorder in ataxia-telangiectasia: treatment with amantadine sulfate. *J Child Neurol.* 2013; 28:155–160. [PubMed: 22550086]
41. Charlesworth G, Mohire MD, Schneider SA, Stamelou M, Wood NW, Bhatia KP. Ataxia telangiectasia presenting as dopa-responsive cervical dystonia. *Neurology.* 2013; 81:1148–1151. [PubMed: 23946315]
42. Shaikh AG, Zee DS, Mandir AS, Lederman HM, Crawford TO. Disorders of upper limb movements in ataxia-telangiectasia. *Plos One.* 2013; 8:e67042. [PubMed: 23826191]
43. Bott L, Thumerelle C, Cuvellier JC, Deschildre A, Vallée L, Sardet A. Ataxia-telangiectasia: a review. *Arch Pediatr.* 2006; 13:293–298. [PubMed: 16423518]
44. Hasegawa, S.; Imai, K.; Yoshida, K., et al. Whole-exome sequence analysis of ataxia telangiectasia-like phenotype. *J Neurol Sci.* 2014. (<http://dx.doi.org/10.1016/j.jns.2014.02.033>)
45. Gatti RA, Boder E, Good RA. Immunodeficiency, radiosensitivity, and the XCIND syndrome. *Immunol Res.* 2007; 38:87–101. [PubMed: 17917014]
46. Coutinho G, Mitui M, Campbell C, et al. Five haplotypes account for fifty-five percent of ATM mutations in Brazilian patients with ataxia telangiectasia: seven new mutations. *Am J Med Genet A.* 2004; 126A:33–40. [PubMed: 15039971]
47. Gilad S, Chessa L, Khosravi R, Russel P, Galanty Y, Pianе M, et al. Genotype-phenotype relationships in ataxia-telangiectasia and variants. *Am J Hum Genet.* 1998; 62:551–561. [PubMed: 9497252]
48. Chun HH, Gatti RA. Ataxia-telangiectasia, an evolving phenotype. *DNA Repair (Amst).* 2004; 3:1187–1196. [PubMed: 15279807]

Table 1

Atypical Cases/Variants of A-T

Author	No / mild Neurol Manif.	Breast cancer only	No cerebellar ataxia	No oculocutaneous Telangiectasia	Ocular Abnor. (*)	Peripheral Neuropathy	Spinal atrophy
Ying et al. 1981				✓			
Byrne et al. 1984				✓			
Taylor et al. 1987				✓			
Maserati et al. 1988				✓			
Stell et al. 1989				✓	✓ (**)		
Churchyard et al. 1991			✓	✓			
Lanzi et al. 1992				✓			
Willems et al. 1993						✓	✓
Friedman & Weitberg, 1993				✓			
De Graff et al. 1995				✓			
Klein et al. 1996				✓			
Trimis et al. 2004	✓						
Alterman et al. 2007	✓						
Moin et al. 2007				+Ocular= 17/104 +Cutaneous=31/104			
Carrillo et al. 2009			✓	Only on the posterior pharyngeal wall			
Paglia et al. 2010		✓					
Sauders-Pullman et al. 2012			✓	✓			
Charlesworth et al. 2013			✓	✓			
Grabli et al. 2014			✓	✓	✓		

Neurol Manif = Neurological Manifestations;

(*) Ocular abnormalities other than ocular apraxia;

(**) Abnormalities of saccades, absence of smooth pursuit and optokinetic nystagmus, periodic alternating nystagmus.

TABLE 2

Movement disorders described in patients with genetically proved A-T

Reference/Mov Disord	Chorea	Dystonia	Myoclonus	Parkinsonism	Tremor	Other
Huang et al. 1991	Absent	Torticollis	Absent	Absent	Absent	
Churchyard et al. 1991	Absent	Generalized	Absent	Absent	Absent	
Woods et al. 1992	Generalized	Generalized	Absent	Absent	Absent	
De graff et al. 1995	Absent	Absent	Generalized	Absent	Absent	
Klein et al. 1996	Generalized	Absent	Absent	Absent	Absent	
Yanofsky et al. 2009	Absent	Generalized	Absent	Absent	Absent	Dyskinesia
Carrilo et al. 2009	Absent	Oromandibular	Absent	Absent	Absent	
Saunders-Pullman et al. 2012	Absent	Cranio-cervical and brachial	Generalized	Absent	Absent	
Shaik et al. 2013	Absent	Upper Limb Segmental	Generalized	Absent	Upper Limbs Postural/Rest	
Charlesworth et al. 2013	Absent	Cervical Dystonia and DRD	Absent	Absent	Absent	
Nissenkom et al. 2013	Generalized	Absent	Generalized	Present	Absent	
Grabli et al. 2014	Absent	Generalized	Generalized	Absent	Upper Limbs	

Mov Disord = Movement Disorders; DRD= Dopamine Responsive Dystonia