Case Report

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Ataxia telangiectasia: a rare case report from Nepal

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Introduction and importance: Ataxia telangiectasia (A-T) is a rare autosomal recessive neurodegenerative disorder with early childhood onset. It is characterized by ataxia, oculocutaneous telangiectasia, immunodeficiency, and lymphoid-origin cancer predisposition due to ataxia telangiectasia mutated gene mutations.

Case presentation: The authors present a 19-year-old girl with spastic movements since 18 months, leading to wheelchair dependence. Ocular telangiectasia, dystonic posture, and slurred speech were evident. Diagnosis involved elevated alpha-fetoprotein levels and typical brain imaging.

Clinical discussion: A-T due to ataxia telangiectasia mutated gene mutations located on chromosome 11q22-23. It has varied presentations categorized by age and features. Timely diagnosis relies on characteristic symptoms, lab findings, and imaging. Radiation sensitivity and increased cancer risk underscore cautious radiation use.

Conclusion: A-T is a complex disorder with no cure. Genetic counseling for parents is vital. Its poor prognosis due to infection susceptibility and cancer risk necessitates supportive care. Comprehensive management, including genetic counseling and careful surveillance, is imperative.

Keywords: ataxia telangiectasia, autosomal recessive disorder, cerebellar atrophy, elevated alpha-fetoprotein, oculocutaneous telangiectasia

Introduction

Ataxia telangiectasia (A-T) is a rare autosomal recessive progressive neurodegenerative disorder, typically diagnosed in early childhood. It is characterized by ataxia, oculocutaneous telangiectasia, immunodeficiency, and a predisposition to certain cancers, particularly of lymphoid-origin[1–3]. This condition is caused by mutations in the ataxia telangiectasia mutated (ATM) gene, located on chromosome 11q22-23, which lead to defective DNA repair mechanisms and genome instability[4]. Diffuse atrophy of the cerebellum occurs due to the loss of Purkinje fibers. Various complications may arise due to the abnormal immune system. Unfortunately, there is no cure for this condition; only symptomatic and supportive management is available. Parents should receive counseling regarding the prognosis, and genetic counseling should also be offered. We present the case of a 19-year-old Muslim girl who presented with abnormal body movements and difficulty in walking. The case has been report following Surgical CAse REport (SCARE) guideline[5].

HIGHLIGHTS

- This case of Ataxia telangiectasia (A-T) is a rare presentation, particularly in Nepal, emphasizing the importance of documenting unique cases in diverse populations.
- Diagnostic challenges in A-T, including the significance of characteristic symptoms, elevated alpha-fetoprotein levels, and neuroimaging for timely diagnosis, are highlighted.
- The case underscores the need for comprehensive clinical management, including symptom-based treatment, genetic counseling, and physiotherapy.
- The report emphasizes the risk of radiation sensitivity and increased cancer susceptibility in A-T, calling for cautious radiation use and diligent cancer surveillance.

Case presentation

A 19-year-old Muslim girl presented with complaints of abnormal body movement and difficulty in walking. The abnormal body movement was spastic and jerky, present in both the upper and lower limbs bilaterally. It began at the age of 18 months. The spastic movement was predominantly noticeable in the neck, leading to the head pushing posteriorly. There was an extension of all limbs for the same duration. During her childhood, she experienced difficulty in crawling, creeping, and sitting. This difficulty gradually progressed to the point where she has been

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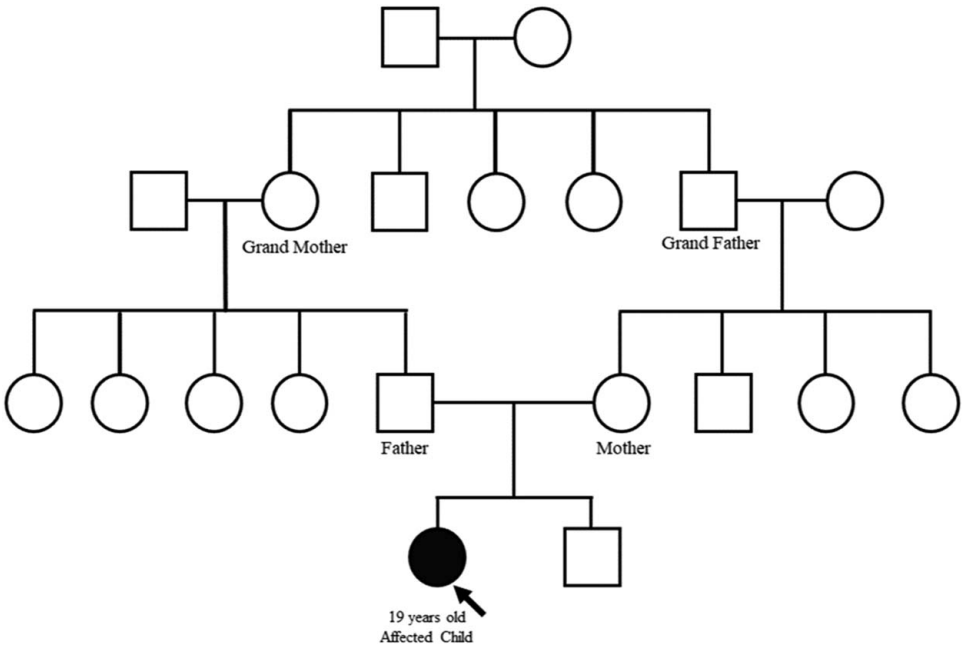

Figure 1. Pedigree chart of a 19-year-old female showing history of consanguineous marriage in the family.

confined to a wheelchair since the age of two. The patient had no history of fever, cough, difficulty in breathing, neck rigidity, loss of consciousness, foaming in mouth, tongue biting, blurring of vision, or sensory deficits. Her bowel and bladder functions were normal, and her menstrual cycles were regular. She had pneumonia at 6 months of age. She also has had frequent episodes of respiratory tract infection. Additionally, there was a history of consanguineous marriage, as evidenced by the pedigree chart of the family (Fig. 1).

On physical examination, her Glasgow Coma Scale was 15 out of 15, demonstrating alertness, consciousness, and full orientation. Cognitive function was within normal limits, including intact memory, attention, language skills, executive functions, visuospatial skills, mathematical abilities, and abstract thinking. She exhibited round, regular, and reactive pupils measuring 3 mm. Bilateral ocular telangiectasia was observed. Additionally, she displayed a dystonic posture and slurred speech. All cranial nerves were found to be intact. The cerebellar signs, dysdiadochokinesia was present, and the finger-to-nose test showed abnormal results. Bilateral muted plantar responses were noted. Sensory tests showed intact function. During the motor examination, there was a decrease in calf bulk bilaterally and increased muscle tone in all limbs. Deep tendon reflexes were graded as one. She also exhibited pes cavus in her both feet. The child had characteristic ocular telangiectasia (Fig. 2) and cerebellar signs. Hence, A-T was clinically diagnosed.

During routine laboratory investigations, her complete blood count, serum B12 level, vitamin E level, and electrolytes all were in normal range. However, her serum alpha-fetoprotein (AFP) level was elevated, measuring 144.79 ng/ml. Her lymphocyte count and serum immunoglobulin levels were slightly towards the lower margin of the normal range. A plain MRI of the brain and spinal cord was performed, revealing diffuse cerebellar atrophy and straightening of cervical and lumbar lordosis due to muscle spasm. In Figure 3 (A–D), we illustrate cerebral atrophy observed in T2-weighted axial sections of the head, coronal T2-weighted section, T1-weighted section, and axial FLARE section. Figure 4 (A, B) highlights straightening of cervical and lumbar lordosis respectively in T2-weighted sagittal sections of the cervical and

Figure 2. Ocular telangiectasia in a 19-year-old female.

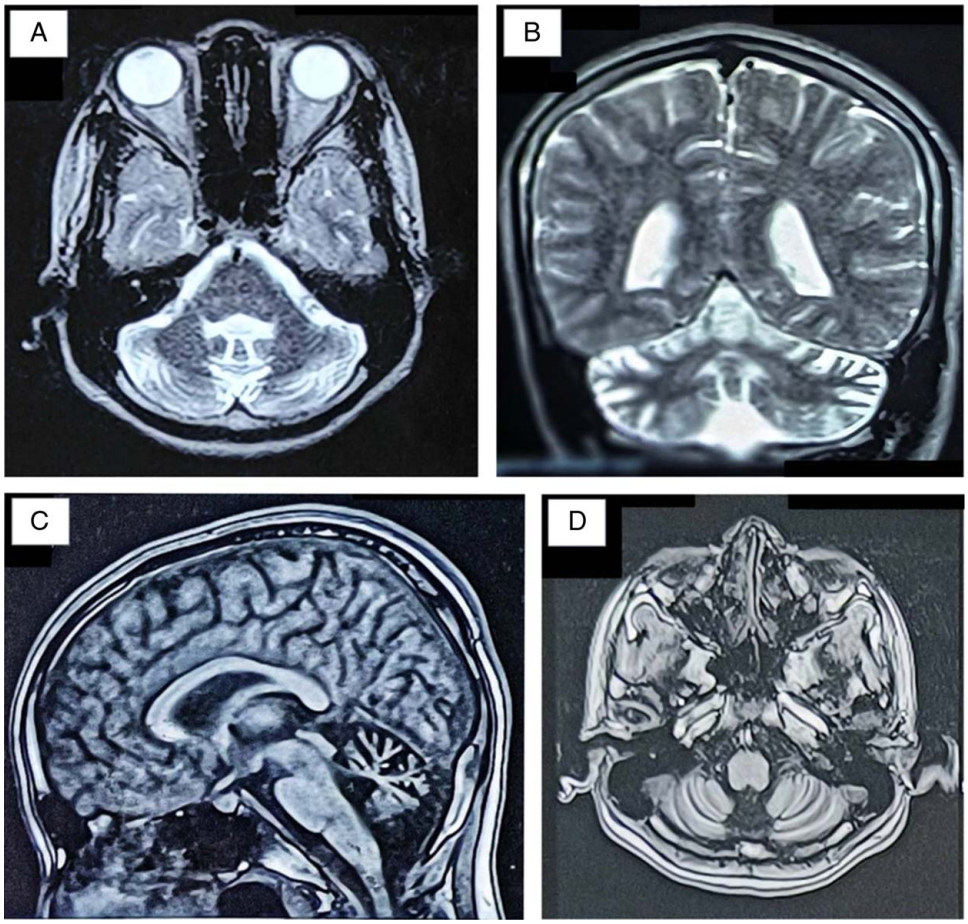

Figure 3. Various MRI of the head are presented, showcasing features suggestive of cerebellar atrophy. The images include: (A) T2-weighted MRI axial section, (B) T2-weighted MRI coronal section, (C) T1-weighted MRI sagittal section, and (D) FLARE axial section of the head.

lumbar regions. The elevated AFP levels, along with typical features on MRI of the brain, confirmed A-T.

Furthermore, the patient was counseled about the condition she had, and there was a suggestion for genetic testing to confirm the diagnosis. However, due to financial constraints experienced by the parents, genetic testing was not pursued at that time.

In terms of management, the patient was treated symptomatically. She was prescribed clonazepam 0.5 mg and other supportive measures. Furthermore, the patient was referred for physiotherapy. The patient's parents were counseled about the prognosis.

Discussion

A-T, also known as Louis–Bar syndrome, is a rare inherited progressive neurodegenerative disorder that affects multiple systems[6]. It is inherited in an autosomal recessive pattern and is due to mutation in the ATM gene located on chromosome 11q22-23[7]. ATM gene is important in DNA repair mechanisms. The prevalence of the disease is between one in 40 000 to one in 100 000[1]. Neuroimaging reveals the presence of diffuse progressive degeneration in various regions of the cerebellum. This degeneration is linked to the loss of Purkinje fibers within the cerebellum[1].

There is different presentation of A-T. It can be categorized as classic/typical/ early onset on basis of characteristic features and as variant/atypical/adult onset on basis of some characteristic's features, or less severe or late onset of features[1]. The typical presentation of ataxia can be recognized in early childhood. The child attends gross motor milestone at a normal age, but child have history of frequent falls and difficulty walking as child age. Later as the disease progresses child has to depend upon wheelchair, as seen in our case. The prominent telangiectasias usually occurs by the age of 5 years[8]. The bulbar conjunctiva is a common site for telangiectasia, as seen in our case.

In our presented case, the child exhibits spastic and jerky movements, that made them incapable of carrying out routine activities[9]. There is frequent history of respiratory illness such as pneumonia, bronchiectasis, etc. occurring in child[1]. Our case also had frequent history of respiratory illness. She had history of pneumonia when she was just 6 months old. The is child is sensitive to ionizing radiation. Even the diagnostic dose of radiation is harmful to children. These children have increases chances of having cancers especially of lymphoid-origin. Hence, it is crucial to use radiation judiciously, when necessary and in balanced dose.

The diagnosis is usually done clinically by identification of ataxia and oculo-telangiectasia or skin telangiectasia. However, the absence of awareness of A-T makes it difficult in early

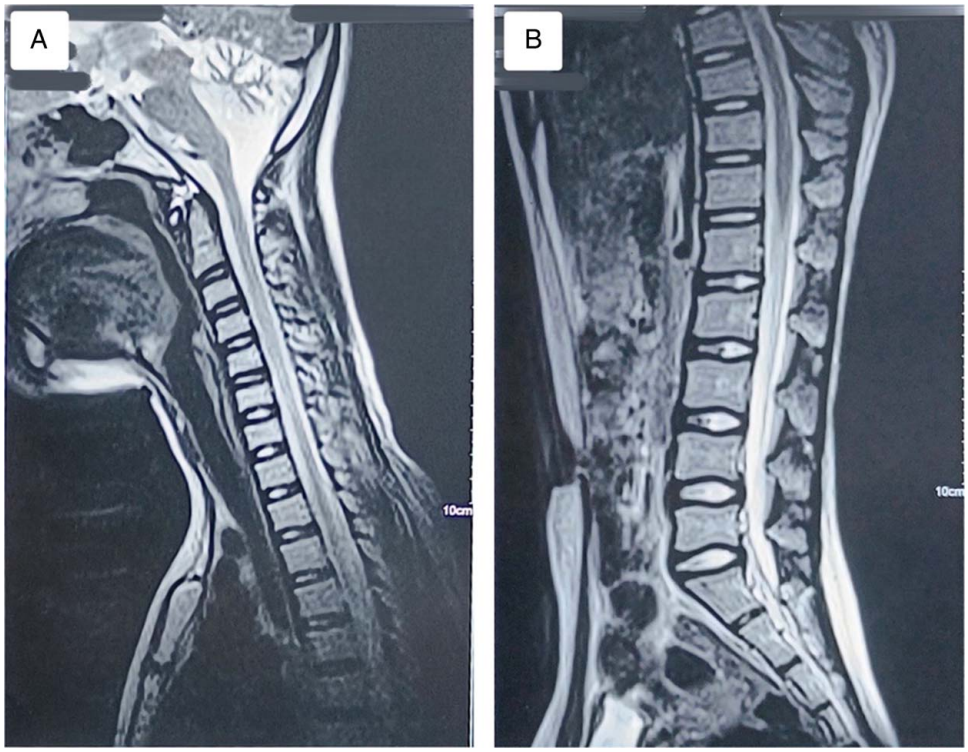

Figure 4. T1-weighted sagittal section of the cervical and lumbar regions of the spine are presented, depicting the straightening of cervical and lumbar lordosis, respectively: (A) shows the cervical region, and (B) shows the lumbar region.

diagnosis. Conditions like ataxia telangiectasia-like disorder (ATLD), as well as ataxia oculomotor apraxia type 1 (AOA1) and type 2 (AOA2), contribute to diagnostic challenges due to their similarities in presentation[10]. However, the laboratory finding often reveal elevated serum AFP level, low lymphocyte count and other immunological abnormalities. MRI reveals cerebellar atrophy. MRI is best imaging modality as there is no exposure to ionizing radiation. Our case had elevated level of AFP as well as cerebellar atrophy was seen in MRI scan. Cytogenetic and molecular test confirms the diagnosis.

The management of A-T involves only symptomatic and supportive treatment. The parents should be counseled about the progression of the affected child as well as a genetic counseling should be done. Some literatures have recommended the multidisciplinary treatment and use of antioxidant and mutation-targeted approaches[11,12].

Conclusion

A-T is a complex disorder that affects multiple systems. It is important to do genetic counseling for the parents, a crucial step that serves to decrease the probability of future occurrences of the disorder among their offspring. The prognosis for individuals affected by this condition is generally poor, largely due to an elevated susceptibility to infections and various forms of cancer. As of now, treatment options remain primarily symptomatic and supportive, aiming to alleviate the associated symptoms and enhance the individual's quality of life. The multifaceted nature of A-T underscores the necessity for a comprehensive approach to care, with a focus on proactive genetic counseling, vigilant infection management, and diligent cancer surveillance.

Ethical approval

Ethical approval was not required for this case report.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

P.M. and A.U.: wrote the original manuscript, reviewed, and edited the original manuscript; A.U., P.M., A.U., S.S., S.A., A.Y., B.G., S.B., and L.T.: reviewed and edited the original manuscript.

Conflicts of interest disclosure

Authors have no conflict of interest to declare.

Research registration unique identifying number (UIN)

1. Name of the registry: not applicable.
2. Unique identifying number or registration ID: not applicable.
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Guarantor

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Data availability statement

All the required information is in manuscript itself.

Provenance and peer review

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