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Evaluating the Diagnostic Accuracy of Fine Needle Aspiration Cytology in Anaplastic Thyroid Carcinoma: A Case Report and Literature Review

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Abstract

Background: Anaplastic thyroid carcinoma (ATC) is a rare and the most aggressive malignancies originating from the thyroid gland, characterized by rapid progression, local invasion, and a poor prognosis. Timely and accurate diagnosis of ATC is crucial for guiding appropriate management strategies and improving patient outcomes. Fine needle aspiration cytology (FNAC) is useful as a rapid initial diagnostic tool for evaluating thyroid nodules and guiding subsequent clinical management.

Methods: This case series aims to evaluate the diagnostic accuracy and correlation between FNAC and histopathological examination in cases of ATC. The study focuses on three patients, who were diagnosed with ATC from FNAC, followed by surgical resection with histopathological analysis

Results: The patients, one male (44 years old) and two females (45 and 47 years old), exhibited cytological findings in Bethesda VI, malignant categories consistent with ATC. The histopathological examination revealed the tumor was Anaplastic Thyroid Carcinoma

Conclusion: This study demonstrates FNAC's have a consistent findings with histopathology in three patients. These serial cases showed that FNAC still valuable for initial diagnosis because exhibited consistent cytological and histopathological findings for diagnosis tool. A multimodal approach, clinical judgment and imaging, is recommended to enhance diagnostic precision.

Keywords: *anaplastic, thyroid, carcinoma, FNAC, Diagnostic*

Introduction

Anaplastic thyroid carcinoma (ATC) is a rare and highly aggressive malignancy of the thyroid gland, accounting for less than 2% of all thyroid cancers.[1] Despite its low incidence, ATC contributes disproportionately to thyroid cancer mortality due to its rapid progression, local invasiveness, and resistance to conventional treatments. Early and accurate diagnosis of ATC is paramount, as it directly influences management strategies and patient outcomes[2]. Fine-needle aspiration cytology (FNAC) has emerged as a critical diagnostic tool for evaluating thyroid nodules, offering a minimally invasive, cost-effective method to rapidly identify malignancies.[3]

The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) plays an essential role in standardizing the interpretation and reporting of thyroid FNAC results. TBSRTC categorizes cytology findings into six diagnostic groups, each associated with a specific risk of malignancy and clinical management recommendation. ATC

typically falls under Category VI, the "malignant" group, which includes high-grade malignancies with cytological features such as marked pleomorphism, necrosis, and atypical mitoses. The classification system aids pathologists and clinicians in determining the level of suspicion for malignancy and deciding on appropriate follow-up or surgical intervention[4].

The diagnostic role of FNAC in ATC is often challenged by its histological overlap with other thyroid malignancies, such as poorly differentiated and undifferentiated thyroid cancers.[5] Morphological variations and the rarity of ATC further complicate cytological evaluation, leading to potential misdiagnoses or diagnostic delays. Distinguishing ATC from other thyroid tumors is crucial because of its distinct treatment requirements and prognostic implications. This highlights the need for a comprehensive assessment of FNAC's diagnostic performance in ATC.[5]

This study aims to evaluate the diagnostic accuracy of FNAC in ATC by correlating cytological findings with histopathological results. Through the analysis of three ATC cases, this article seeks to provide insights into the strengths and limitations of FNAC in the context of thyroid malignancies. Furthermore, the findings underscore the importance of a multidisciplinary approach involving clinical, radiological, and histopathological inputs to enhance diagnostic precision.

By examining the cytomorphological characteristics and diagnostic pitfalls of FNAC in ATC, this study contributes to the existing body of knowledge and offers practical recommendations for optimizing diagnostic approaches. This article aims to evaluate the diagnostic accuracy of FNAC in ATC by analyzing a series of cases from our institution. We focus on the cytomorphological features, diagnostic pitfalls, this study seeks to contribute to the optimization of diagnostic approaches for this rare but lethal malignancy.

Methods

This case series aims to evaluate the diagnostic accuracy and correlation between FNAC and histopathological examination in cases of ATC. The study focuses on three patients, who were diagnosed with ATC from FNAC, followed by surgical resection with histopathological analysis. The patients, one male (44 years old) and two females (45 and 47 years old), exhibited cytological findings in Bethesda VI, malignant categories consistent with ATC

This study analyzed three cases of thyroid malignancy diagnosed as anaplastic thyroid carcinoma (ATC) using fine-needle aspiration cytology (FNAC) and confirmed through histopathological examination. The cases were identified from patients presenting with rapidly enlarging thyroid masses and clinical symptoms suggestive of ATC, including dysphagia, hoarseness, and neck pain. FNAC was performed by cytopathologists using a 23-gauge needle. The collected cytological material was processed using conventional smears stained with hematoxylin-eosin and Giemsa stains for morphological evaluation.

The cytological findings of each case were assessed for features characteristic of ATC, including highly pleomorphic cells, multinucleated giant cells, rhabdoid cells, and necrosis. These features were interpreted according to the Bethesda System for Reporting Thyroid Cytopathology (Category VI, malignant). Following the FNAC diagnosis, the patients underwent surgical resection of the thyroid tumors. Histopathological confirmation was achieved by examining formalin-fixed, paraffin-embedded tissue sections stained with hematoxylin and eosin (H&E).

The cytological smears were assessed for Cellularity (scanty, moderate, or high), Cell shape and arrangement (single cells or clusters), nuclear features (pleomorphism, hyperchromasia, prominent nucleoli), mitotic activity and necrosis. The cytological and histopathological findings were compared to assess the concordance between FNAC and the final histopathological diagnosis. The diagnostic performance of FNAC was evaluated based on its ability to accurately identify ATC. Any challenges or discrepancies encountered during the diagnostic process were documented, emphasizing the importance of correlating cytological, histopathological, and clinical findings for a comprehensive diagnostic approach in ATC.

Results

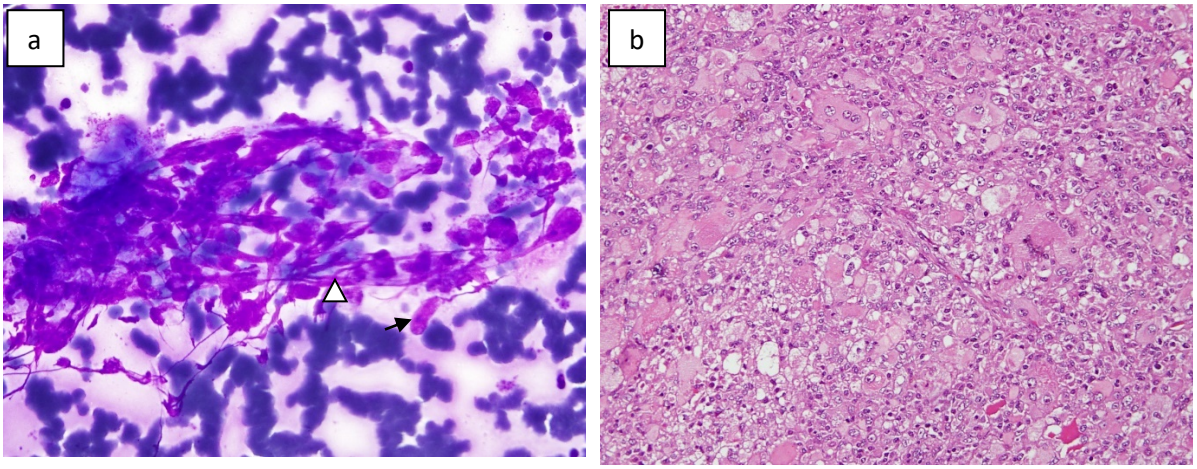
Three patients presenting with rapidly enlarging thyroid masses and compressive symptoms were evaluated using fine-needle aspiration cytology (FNAC). The patients included one male (44 years old) and two females (45 and 47 years old). Cytological examination of FNAC samples revealed features characteristic of anaplastic thyroid carcinoma (ATC), including highly pleomorphic tumor cells, multinucleated giant cells, necrotic debris, and abundant mitotic figures. The cytological findings from FNAC are presented in table 1 and based on these findings, all cases were classified as Bethesda Category VI (malignant).

Table 1. The cytological features findings from FNAC

Patient No	Sex	Age (years)	Cellularity	Cell shape and arrangement	Nuclear features	Mitotic activity	Necrosis
1	M	44	moderate	Spindle cell, clustering with mark of fibrosis	Severe pleomorphisme, hyperchromasia, prominent nucleoli	Not seen	Present
2	F	45	High	Epithelioid and multinucleated giant cell, Single cell and clustering	Severe pleomorpisme, hyperchromasia, prominent nucleoli (some multiple)	Present	Present
3	F	47	High	Rhabdoid, plasmacytoid and epithelioid cell, clustering	Severe pleomorphisme	Present	Present

Histopathological examination of the surgical specimens confirmed the diagnosis of ATC in all three cases. The cytological finding from patient number one, we looking for the moderate cellularity with tumors cell clustering (figure 1.a). The cells shape are predominantly spindle (figure 1.a) mimicking sarcomatoid look with area of extensive fibrosis (figure 1.a). The histological features included well-differentiated thyroid carcinoma component, in another side we can find tumor cells with spindle-shaped nuclei arranged in an intersecting pattern, resembling a storiform pattern (1.c) and extensive necrosis and fibrosis (1.c).

undifferentiated pleomorphic tumor cells arranged in sheets and nests, extensive areas of necrosis, and evidence of vascular invasion. In this study, In all three cases, we still found areas of well-differentiated thyroid carcinoma but unfortunately, we did not perform immunohistochemistry (IHC) due to the limited availability of antibodies in our laboratory. Comparison of cytological and histopathological findings demonstrated complete concordance between the two diagnostic modalities. The cytological features observed on FNAC accurately reflected the histopathological characteristics of ATC in all cases, emphasizing the diagnostic reliability of FNAC.



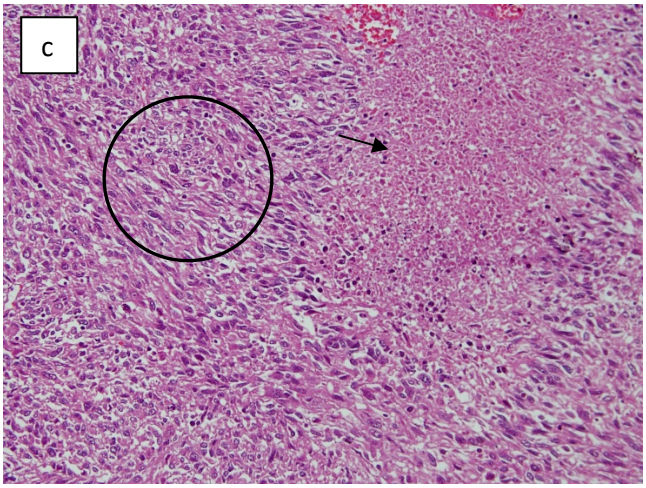
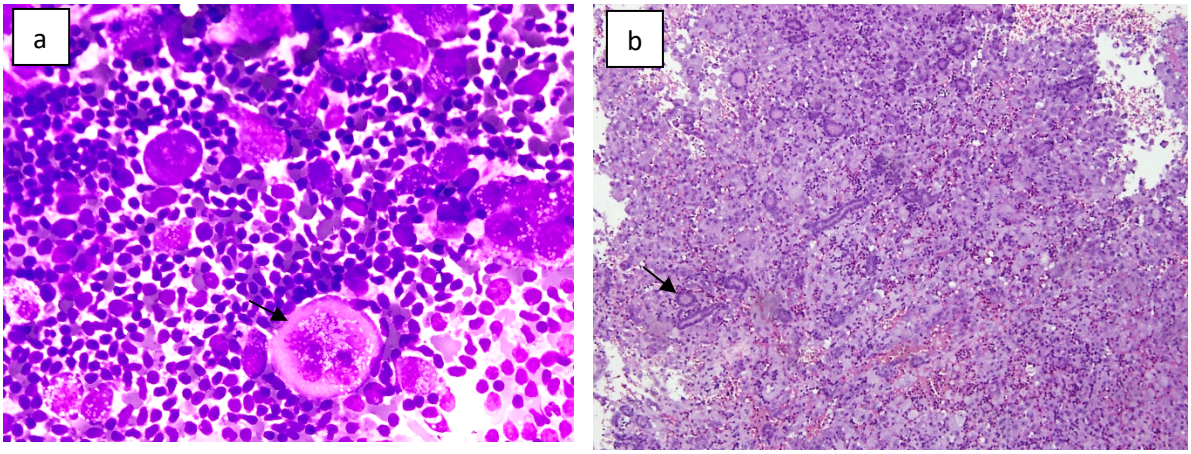


Figure 1. Case number one. A. In these smears, a moderately cellular aspirate is observed, with clusters of tumor cells exhibiting spindle-shaped nuclei (arrow) and prominent fibrosis (head arrow), B. In histopathology examination, some areas, a component of well-differentiated carcinoma is still present, C. The correlation with histopathology finding reveals tumor cells with spindle-shaped nuclei arranged in an intersecting pattern, resembling a storiform pattern (circle), extensive necrosis (arrow).

The cytological finding from case number two, we observe a highly cellular specimen consisting of a diffuse distribution of singly arranged cells with markedly pleomorphic nuclei. The nuclear morphology varies, including plasmacytoid, epithelioid and multinucleated giant cells (figure 2.a). Histopathological examination also reveals residual follicular structures with colloid (figure 2.b). This histopathological image reveals a highly pleomorphic tumor characterized by significant nuclear atypia. The nuclei exhibit marked variation in size and shape, with some appearing hyperchromatic and irregular. A notable feature is the presence of multinucleated giant cells (figure 2.c), which are scattered throughout the field, contributing to the aggressive morphology of the tumor. Additionally, there is a high mitotic activity, including atypical mitoses, indicating rapid cellular proliferation. The background also contains a mixed inflammatory infiltrate, which may be reactive or associated with tumor necrosis (figure 2.c).



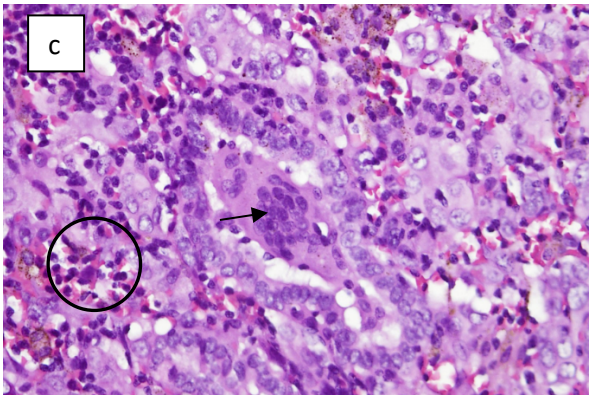


Figure 2. Case number two. A. In these smears, a highly cellular aspirate is observed, with diffuse distribution of singly arranged cells with pleomorphic nuclei include epithelioid, plasmacytoid and multinucleated giant cell (arrow), B. In histopathology examination, residual follicular structures with colloid (arrow). C. Correlating with histopathology, we identify areas with markedly pleomorphic nuclei (arrow), a distribution of multinucleated giant cells, numerous atypical mitoses and necrosis (circle).

This cytology finding from case number three demonstrates a highly cellular sample with significant nuclear pleomorphism. The tumor cells are arranged predominantly in a dispersed, single-cell pattern with occasional clusters (figure 3.a). The nuclei exhibit marked variation in size and shape, with some appearing enlarged, hyperchromatic, and irregular. The cytoplasm appears scant to moderate, with some cells displaying an eosinophilic or vacuolated appearance (rhabdoid cell). Additionally, atypical mitotic figures are observed, indicating a high proliferative activity. The background shows necrotic debris and scattered inflammatory cells, which may suggest tumor necrosis or a reactive inflammatory response.

This histopathological image of the same tumor previously described in the cytology smear further confirms its highly aggressive nature. The tissue exhibits marked cellular pleomorphism, with tumor cells displaying extreme variation in nuclear size and shape. Numerous multinucleated giant cells are present, along with abundant atypical mitoses, indicating a high proliferative index. The background consists of necrotic debris and a dense inflammatory infiltrate, which may reflect tumor necrosis and host immune response. The tumor cells also demonstrate scattered eosinophilic cytoplasm and irregular chromatin distribution, consistent with a high-grade malignancy (figure 3.b).

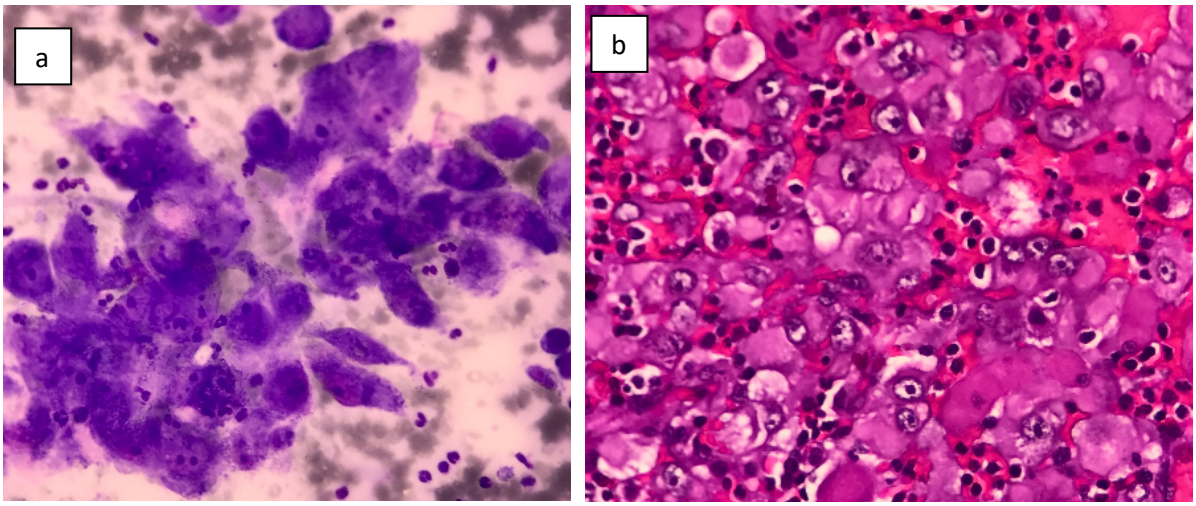


Figure 3. Case number three. A. In these smears a highly cellular aspirate, with significant nuclear pleomorphism. The tumor cells are arranged predominantly in a dispersed, single-cell pattern with occasional clusters a highly cellular aspirate is observed, B Correlating with histopathology examination exhibits marked cellular pleomorphism, with tumor cells displaying extreme variation in nuclear size and shape with some cells displaying an eosinophilic or vacuolated appearance (rhabdoid cell) . Numerous multinucleated giant cells are present, along with abundant atypical mitoses, indicating a high proliferative index.

Discussions

Our study highlights FNAC's high diagnostic accuracy for ATC, consistent with the literature. Anaplastic thyroid carcinoma (ATC) is the aggressive form of thyroid cancer, often presenting with rapid growth, extensive local invasion, and early metastasis. Cytologically, ATC exhibits high cellularity with marked pleomorphism and loss of thyroid follicular architecture. Some aspirates exhibit moderate cellularity, partly influenced by the extensive fibrosis and hyalinization present in certain tumors[6]. When fibrosis is predominant, the reduced cellular yield can make interpretation more challenging[7].

ATC demonstrates a heterogeneous cytomorphology, often classified into three main cell types, there are spindle cells (resembling sarcomatoid tumors, these elongated cells have hyperchromatic nuclei and scant cytoplasm), giant cells (multinucleated tumor cells, sometimes mimicking osteoclast-like giant cells) and epithelioid cells (large polygonal cells with prominent nucleoli, which may resemble undifferentiated carcinoma from other organs)[8].

Nuclear atypia in ATC is profound, with marked nuclear pleomorphism, coarse chromatin, and frequent mitotic figures, including atypical mitoses. The presence of tumor necrosis, high mitotic activity, and inflammatory infiltrates further supports the diagnosis[9]. Unlike well-differentiated thyroid carcinomas, ATC typically lacks colloid material and follicular structures, making it cytologically distinct. The smear background is frequently necrotic, extensive inflammation predominantly neutrophils,"abscess-like" (figure 1.c) and hemorrhagic, reflecting the high-grade nature of the tumor.[10]

The Bethesda system for thyroid cytology have a such criteria for diagnosis ATC, there is a aspirate usually show moderately to markedly cellular, neoplastic cells are arranged as isolated cells and/or in variably sized groups. The FNAC showed a variety of cytomorphological features including epithelioid, spindle-shaped and range in size from small to giant cells. Plasmacytoid and rhabdoid cell shapes may be seen[4]. Nuclei show enlargement, irregularity, extreme pleomorphism with bizarre and macronuclei, spindle-shaped nuclei, clumping of chromatin with parachromatin clearing, multinucleation, pseudoinclusion, eccentric nuclear placement and coarse chromatin. Necrosis and extensive inflammation (predominantly neutrophils, 'abscess-like'), apoptosis and necrosis. These findings corresponded to the histopathological findings obtained after tumor resection with heterogenous histologic features including pleomorphic, giant cell and sarcomatoid morphology.[4] This study demonstrates FNAC's have a consistent findings with histopathology in three patients.

Some cases of anaplastic thyroid carcinoma (ATC) exhibit areas of co-existing well-differentiated or poorly differentiated thyroid carcinoma, with papillary thyroid carcinoma (PTC) being the most common precursor, though follicular carcinoma, oncocytic carcinoma, poorly differentiated (insular) carcinoma may also be involved[10–12]. The present of well differentiated thyroid carcinoma supports the notion that ATC develops through the dedifferentiation of a pre-existing well-differentiated thyroid malignancy, progressing through a multistep process of tumor evolution. In this three case, we can still identification of well differentiated thyroid carcinoma component.

Anaplastic thyroid carcinoma (ATC) remains a formidable diagnostic and therapeutic challenge due to its rarity, aggressive behavior, and rapid progression[13]. In this study, the diagnostic accuracy of fine-needle aspiration cytology (FNAC) for ATC was evaluated through three cases, all of which demonstrated concordant cytological and histopathological findings. The results reaffirm FNAC's role as a valuable initial diagnostic tool for thyroid malignancies, particularly in resource-limited settings where timely diagnosis is crucial for initiating management[14,15].

The cytomorphological features observed in FNAC samples, such as marked pleomorphism, multinucleated giant cells, necrosis, and high mitotic activity, are hallmark characteristics of ATC. However, these features may overlap with other poorly differentiated thyroid malignancies or metastatic carcinomas. This highlights the importance of correlating FNAC findings with clinical and radiological data[16]. In cases where the cytological diagnosis is equivocal, ancillary techniques, such as immunohistochemistry (IHC), provide critical support for accurate diagnosis. The use of markers like pancytokeratin, PAX8, and vimentin, along with the absence of thyroglobulin and TTF-1, is instrumental in distinguishing ATC from other thyroid and non-thyroid tumors[17].

Despite the diagnostic utility of FNAC, certain limitations must be acknowledged. Sampling errors, tumor heterogeneity, and the potential for misinterpretation of cytological features can occasionally result in diagnostic discrepancies[16]. Furthermore, the aggressive nature of ATC often leads to extensive necrosis, which may compromise the adequacy of cytological samples[18,19,]. These challenges underscore the necessity of integrating FNAC findings with histopathological confirmation and clinical judgment to ensure diagnostic precision.

The findings of this study emphasize the importance of a multidisciplinary approach in managing ATC. The concordance observed between FNAC and histopathology in all three cases validates the reliability of FNAC in diagnosing ATC. However, the aggressive course of this malignancy necessitates prompt and comprehensive treatment strategies. Early recognition and accurate diagnosis, facilitated by FNAC, play a pivotal role in optimizing patient outcomes, particularly when combined with advanced imaging modalities and tailored therapeutic interventions.

Conclusions

These serial cases showed that FNAC still valuable for initial diagnosis because exhibited consistent cytological and histopathological findings for diagnosis tool. Fine-needle aspiration cytology (FNAC) of anaplastic thyroid carcinoma (ATC) typically reveals high cellularity with a predominantly discohesive arrangement of tumor cells, exhibiting marked nuclear pleomorphism, hyperchromasia, and irregular nuclear contours. A key feature is the presence of multinucleated giant cells, alongside numerous atypical mitoses indicating a high proliferative rate. The tumor cells may show spindle, epithelioid, or pleomorphic morphology, often with scant to moderate cytoplasm, and a background of necrotic debris and inflammatory cells. The absence of colloid and follicular structures helps distinguish ATC from other thyroid malignancies, while histopathological, immunohistochemical (IHC), and molecular studies are essential for definitive diagnosis.

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Declarations of competing interest

No potential competing interest was reported by the authors.

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