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Case Report

Regression of an ALK-Negative Cerebral Inflammatory Myofibroblastic Tumour by Steroid Therapy: A Case Report and Literature Review

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Abstract

Introduction: Inflammatory myofibroblastic tumours (IMTs) are non-neoplastic lesions characterized by collagenous stroma and polyclonal mononuclear infiltrates. IMTs typically arise in the lung, retroperitoneum or abdominal region but rarely in the central nervous system (CNS). The primary therapeutic option is surgical resection, and other therapies are currently controversial.

Case report: We report a case of 23-year-old male ALK-negative cerebral IMT patient from Han population via steroid therapy. No relapse is observed at the follow-up visit.

Conclusion: These results support the role of internal medication and promote the use of personalized therapy in genome-profiled IMTs.

1. Introduction

Inflammatory myofibroblastic tumours (IMTs) are generally known as inflammatory pseudo-tumours (IPs). They are featured with non-neoplastic lesions with heterogeneous pathologies, including collagenous stroma, fibrous xanthoma, xanthomatous pseudotumours, plasma cell granulomas, plasma cell/histiocytoma complexes and pseudosarcomatous myofibroblastic proliferation [1]. The prevalence globally ranges from 0.04% to 0.7% regardless of gender and race [2]. The reported rate of mortality at 1 year was 4.4% (95% CI: 2.1%-8.9%) [3]. IMTs are IMTs mainly occur in lungs and infrequently in other organs such as the central nervous system (CNS) [4]. Neuropathology is mandatory for IP diagnosis, and surgical resection is recommended as the priority option [5]. Other alternative therapies, such as internal medication, are rarely discussed in publications. Here, we report one case of anaplastic lymphoma kinase (ALK)-negative CNS-IP successfully treated with steroids.

2. Case Presentation

A 23-year-old male patient presented with acute onset of weakness of the right limbs and dysarthria. He denied a family history of CNS disorders and tumour diseases. The neurological examination showed normal vital signs and normal muscle tension of the left limbs but decreased muscle tension and reinforced deep tendon reflexes of the right limbs in parallel with positive right Babinski's reflex. Slurred speech, right haemiparesis (4/5 muscle strength diffusely) and hypoesthesia of the right limbs were also observed without negative meningeal signs or cognitive regression.

Blood biochemical tests revealed moderately enhanced antistreptolysin O (491 IU/ml) and C-reactive protein (4.97 mg/L). Levels of sexual hormones, tumour markers, thyroid hormone, erythrocyte sedimentation rate and cardiac enzymes were normal. Anti-leptospiral antibodies, antineutrophil cytoplasmic antibodies and antinuclear antibodies were negative. The electrocardiogram, electroencephalogram and CT angiography were also performed without any remarkable findings, whereas the cerebral CT scan revealed a low-density lesion adjacent to the left centrum semiovale and periventricular region. On MRI, the lesion was hypointense on T1-weighted images and hyperintense with perifocal oedema on T2-weighted and fluid-attenuated inversion recovery (FLAIR) images (Figure 1A-1C). Biochemical tests of cerebrospinal fluid (CSF) revealed increased protein (0.56 g/L) and immunoglobulin (43 mg/L) levels. The patient was initially suspected of brain infarction and viral encephalitis. Unfortunately, paralysis of the right limbs (1/5 muscle strength) progressed immediately. When the biopsy pathologically indicated diffuse polymorph inflammatory infiltrate by foamy macrophages and lymphocytes (Figure 2A), his therapeutic management switched to 20 mg dexamethasone administered intravenously daily for two weeks until the muscle strength of the right limbs was restored to 4/5.

Fluorescence in situ hybridization (FISH) analysis thereafter indicated negativity for an ALK rearrangement (Figure 2B).

The patient relapsed with persistent dysarthria and haemiparesis of the right limbs two weeks later. He was then administered high-dose methylprednisolone (1000 mg/day intravenously for seven consecutive days) and subsequent oral prednisone at 10 mg/day for three months until he completely recovered without any abnormal neurological symptoms. Cerebral MRI also confirmed the remarkable shrinkage of the lesion with perifocal oedema (Figure 1D-1F). At follow-up visits, he remained active without recurrence, consistent with the ongoing mass regression noted in cerebral MRI images (Figure 1G-1I).

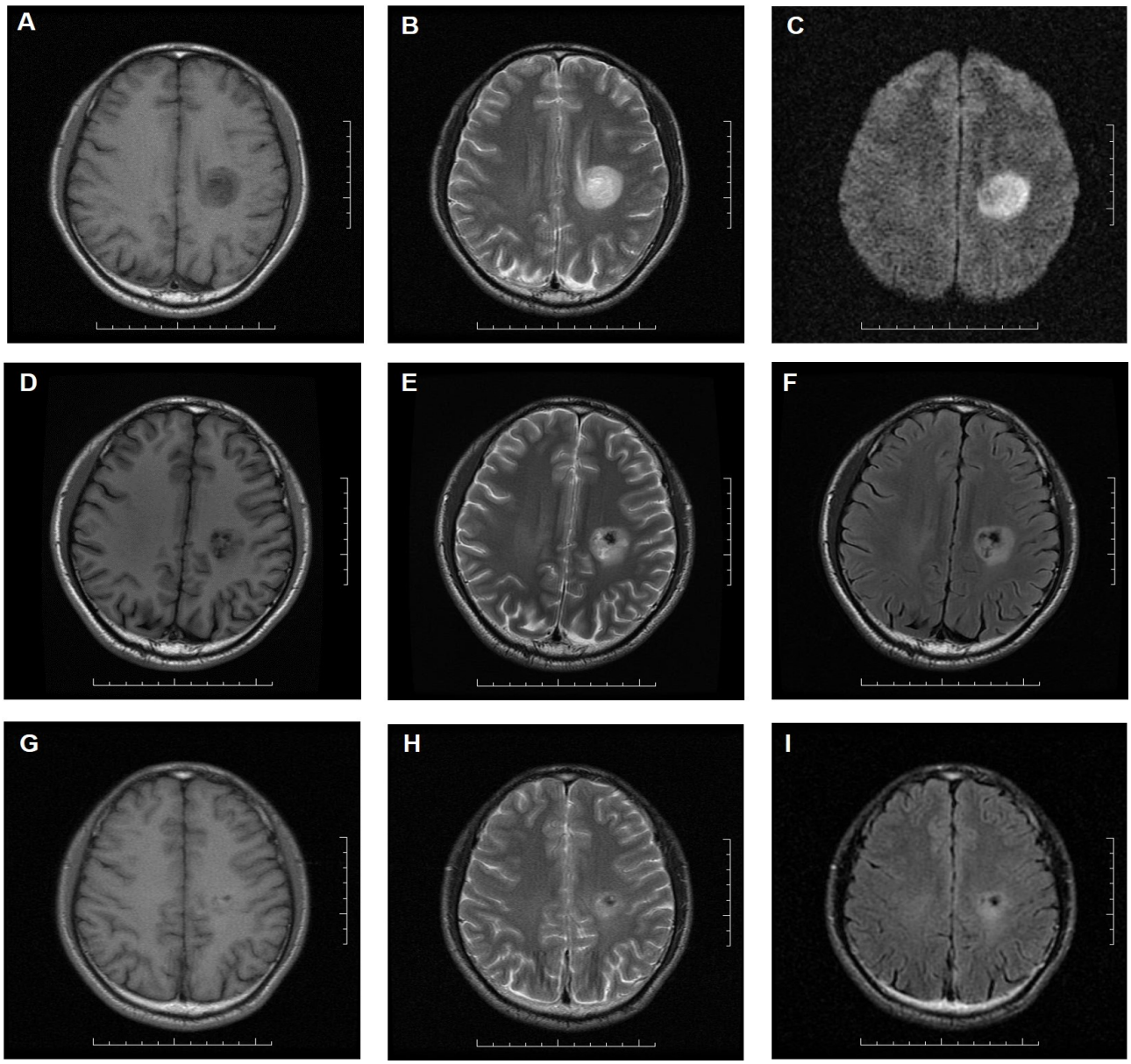

Figure 1. MRI image of the patient two days after onset. Axial T1-weighted sequence image showing a hypointense round lesion with perifocal oedema located in the left centrum semiovale and periventricular region (A). The mass is hyperintense on axial T2-weighted imaging (B). FLAIR sequence is utilized to improve the contrast of fluid and surrounding tissue, assisting the delineation. The hypointense mass is also shown on the FLAIR sequence image (C). The cerebral MRI images showed apparent shrinkage of the lesion on T1 (D), T2 (E) and DWI (F) images three months post steroid therapy. At the follow-up visit, ongoing shrinkage of the cerebral lesion was observed on T1 (G), T2 (H) and DWI (I) images.

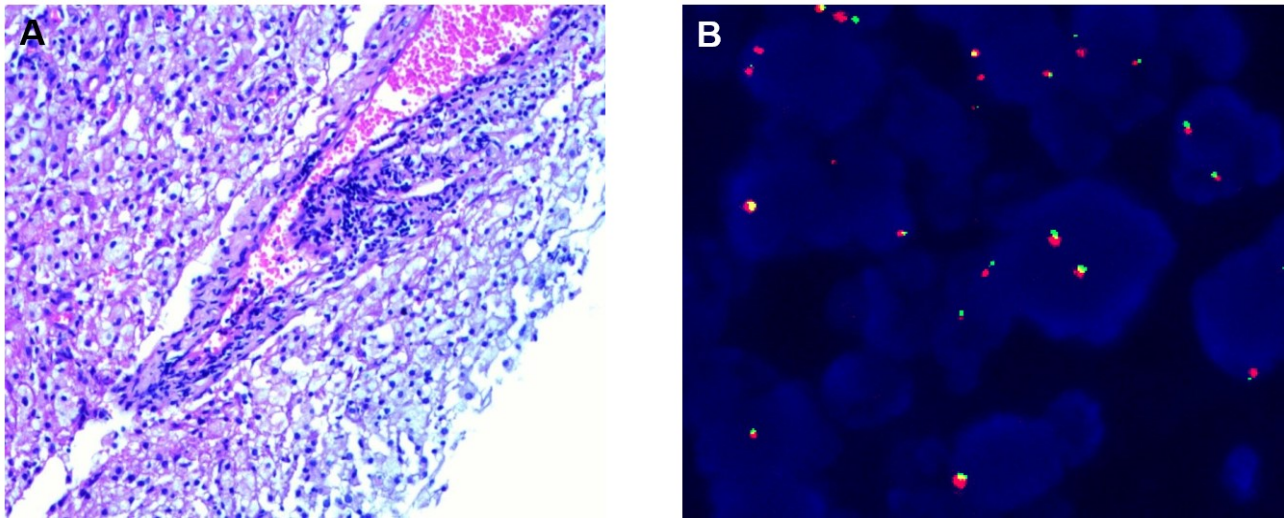

Figure 2. Microscopic features of IP (Hematoxylin & eosin staining.and FISH staining). Within the entire microscopic field, the diffusive polymorph inflammatory infiltration was mainly composed of lipid-containing foamy macrophages, lymphocytes, and plasma cells. Perivascular aggregation of small lymphocytes and a few plasma cells was observed (magnification ×100). The cytological atypia suggestive of atypical lymphoid proliferation and lymphoid follicles or granulomas were absent (A). FISH staining of the cerebral lesion sample indicated negativity for ALK rearrangement. ALK fusion was considered negative for rearrangement when red and green signals appeared adjacent, or yellow (fused) signals were seen(B).

3. Discussion and Conclusion

The early concept of IPs mostly consists of overwhelming inflammatory or reactive processes, but ALK gene rearrangements at chromosome 2p23 in a subset of IMT patients indicated additional neoplastic pathogenesis with poor prognosis [6,7].

Active autoimmune status, such as Crohn's disease, is reported to induce IPs in certain cases, accompanied by elevated levels of serum immunoglobulin [4,8]. The enrichment of IgG4 positive plasma cells was alsoreported in four cases with IP-CNS reported by Lui et al. [9]. Negative IgG4 expression was noted in IMT samples, which is consistent with its normal serum levels [10].

Our case proved the efficacy of steroids in ALK negative cerebral IPs, other than surgical resection as previously reported [11]. In one case of IP-CNS with dominant plasma cell infiltrate, steroid therapy demonstrated promising efficacy without aggravation or relapse in the 16-month follow-up [12]. The efficacy of steroid therapy with minor complications was also noted in one case of pulmonary IP [13]. Additionally, successful treatment with mycophenolate mofetil might elicit that immune inhibition (glucocorticoids and immune suppressors) potentially achieve a good response by attenuating the inflammatory activity of plasma- or inflammatory cell-infiltrated IPs [14].

Aberrant ALK expression (rearrangement or aneuploidy) has been described in approximately 50% of IMTs [15,16]. In our case, the negative ALK fusion of the cerebral lesion (Figure 2B) reflected its benign clinical behaviour and promising prognosis. ALK fusion includes ROS1, NTRK3 and RET genes [17,18]. Substantial evidence in vitro and in vivo indicated that the ALK fusion protein, might induce malignant transformation related to mitogenic, antiapoptotic and potential DNA repair abilities [19]. Itdefined a subset of IMTs with tumour-like biological features that were also sensitive to ALK inhibition [20]. The success of crizotinib treatment was reported in at least half of ALK-positive IMT caseand also minor ALK-negative IMT patients [21-23]. Crizotinib was recommended as a treatment due to IMT patients' superior response to this ALK inhibitor. The positive ALK fusion in IMTs was distinctive nuclear membranous reactivity by IHC. In IMT cohort from one prospective study, ALK positive group was defined as over 15% of cells staining positive or showing gene rearrangement by IHC or FISH [23]. To date, no fusion protein was reported in ALK negative IMTs [18].

Previous studies indicated that the involvement of local inflammation in IMT pathogenesis, eliciting the therapeutic role of anti-inflammatory agents including steroids [24]. The reported intervention of steroids in IMTs is rare, therefore, the mechanistic studies are controversial. In some cases, the utilization of corticosteroids may promote IMT proliferation with resultant relapse [25]. For negative oncogene expression subgroups, steroid therapy alone or combined with surgical resection as adjuvant role is recommended for curative aims.

The current investigation of IMTs defined a series of gene aberrations including ALK, ATRX, FAT1, FCRL4, FOXO1, NUTM2B, PIK3CA, SMAD4, TP53 and ROS1 [26]. Other novel tyrosine kinase inhibitors including entrictinib and alectinib were also introduced with clinical efficacy in IMTs case. The unique neoplastic variety of IMTs necessitates conceptive strategies of personalized therapy originating from tumour disease, aiming to improve the prognosis of IMTs in future clinical practice [19,27].

List of Abbreviations

ALK	Anaplastic lymphoma kinase
CNS	Central nervous system
CSF	Cerebrospinal fluid
DWI	Diffusion weighted imaging
FISH	Fluorescence in situ histology
IMT	Inflammatory myofibroblastic tumour
IPs	Inflammatory pseudo-tumours

Ethics Approval and Consent to Participate

Not applicable.

Consent for Publication

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

Availability of Data and Material

Data generated during this study are included in this published article.

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Competing Interests

The authors declare no competing interests.

Author′s Contributions

YJG and CJX collected and interpreted the clinical data. QD completed the pathology analysis. YD and LLW wrote the manuscript and graphical illustrations. All authors critically revised and approved the manuscript.

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