Giant cell arteritis in silence: A case report and literature review

Kangping Cui, Ahmed Shah, Sandeep Dhillon, Arthur Lau, Asghar Naqvi, Salem Alowami

ABSTRACT

Introduction: Giant cell arteritis (GCA) is a type of large vessel vasculitis of unknown etiology, and it typically manifests with cranial or constitutional symptoms.

Case Report: We report a case of asymptomatic GCA identified incidentally on an excisional biopsy for scalp squamous cell carcinoma (SCC), whose temporal artery biopsy performed subsequently showed transmural lymphocytic and granulomatous infiltrate with giant cells. To our best knowledge, this is the only case ever reported on incidental GCA in the setting of cutaneous SCC.

Conclusion: Our case highlights the challenges in GCA diagnosis when the lack of clinical symptoms conflicts with the pathology findings. Confirmatory tests including ultrasound, magnetic resonance imaging (MRI), and temporal artery biopsy, investigations for extra-cranial manifestations of the GCA, along with regular surveillance are warranted for diagnostic clarification and treatment guidance.

Keywords: Giant cell arteritis, Hypertrophic actinic keratosis, Squamous cell carcinoma, Temporal artery biopsy

INTRODUCTION

Giant cell arteritis, also known as temporal arteritis, is a type of large vessel vasculitis of unknown etiology [1, 2]. It classically affects the temporal artery and leads to arterial wall inflammation, intimal hyperplasia, and loss of external elastic lamina. If untreated results in vessel occlusion and tissue ischemia [1]. Histologically, giant cells are not needed to make a diagnosis of giant cell arteritis but are helpful if present.

CASE REPORT

An 82-year-old man presented to the rheumatology clinic with a biopsy report showing giant cell arteritis, discovered incidentally. His past medical history included squamous cell carcinoma (SCC) of the scalp, coronary artery disease, dyslipidemia, hypertension, renal calculi, and presyncope (not yet diagnosed). His home medications include fludrocortisone, sertraline, and atorvastatin. He underwent SCC excision, which was located on the superior aspect of the right frontal-partial scalp. Histologically, invasive squamous cell carcinoma was diagnosed in the background of hypertrophic actinic keratosis (Figure 1). Moreover, the vessel had transmural dense lymphocytic and granulomatous inflammatory infiltrate with giant cells (Figure 1B). The disruption of
external elastic lamina was also identified (Figure 2). Clinically, however, no cranial or constitutional symptoms were present. Patient’s C-reactive protein (CRP) was elevated at 30 mg/L and erythrocyte sedimentation rate (ESR) 45 mm/h. Ultrasound on the temporal arteries was negative for features of GCA. Magnetic resonance imaging was not performed due to the presence of bare metal stents. The patient underwent temporal artery biopsy subsequently which showed chronic inflammation of arterial blood vessels with focal granulomatous features and loss of elastic lamina, consistent with temporal arteritis (Figure 2A and B). The patient was subsequently started on prednisone and continued to do well clinically.

Figure 1: Squamous cell carcinoma with giant cell arteritis in background of hypertrophic actinic keratosis. (A) H&E (20×), (B) H&E (40×), (C) H&E (40×), with arrows pointing at the area of temporal arteritis.

Figure 2: Subsequent temporal artery biopsy. (A) H&E, with arrow-head pointing to the granulomatous inflammation (100×). (B) Miller stain, with arrow pointing at the loss of elastic lamina (100×).

DISCUSSION

The diagnosis of GCA is based on a combination of clinical features, laboratory investigations, and biopsy evidence. Given the lack of clinical symptoms, our patient would not be classified as having GCA based on the 1990 American College of Rheumatology (ACR) classification criteria [2], despite the compatible pathology results. Based on the location of the excisional biopsy for SCC, the arteries captured were likely the distal branches of superficial temporal artery. The presence of vasculitis was further supported by temporal artery biopsy. Given the potential devastating consequences of GCA, treatment was initiated.

To the best of our knowledge, an incidental finding of GCA in the context of SCC has only been reported once in the literature. Misselevitch et al. [3] reported a case of SCC of vocal cord and epiglottis in a patient who lacked GCA symptoms. In the tumor sample a single artery showed GCA lesion. To date, our case represents the only incidental GCA case found in a cutaneous SCC excisional biopsy. Additional reports on the incidental identification of GCA changes in various malignancy have been summarized in Table 1. Incidental GCA findings in the female genital tract has been reported in literature [4–6].

<table>
<thead>
<tr>
<th>ID</th>
<th>Malignancy</th>
<th>Clinical GCA symptoms*</th>
<th>GCA pathology description</th>
<th>Temporal artery biopsy results</th>
</tr>
</thead>
<tbody>
<tr>
<td>N/A [3]</td>
<td>SCC of vocal cord</td>
<td>No clinical evidence of giant cell arteritis</td>
<td>From the excised tissue, a single artery was affected by the giant cell arteritis lesion</td>
<td>Not done</td>
</tr>
<tr>
<td>74F [7]</td>
<td>Invasive ductal carcinoma of the breast</td>
<td>Malaise and a 14-day persistent fever</td>
<td>Coincidental pathologic findings of GCA in the same biopsy specimen</td>
<td>Unclear but authors mentioned that “no other artery was involved by GCA”</td>
</tr>
</tbody>
</table>
Concurrent GCA and malignancy have been previously reported. Our group has previously reported giant cell arteritis associated with overlying basal cell carcinoma [8]. Whether the presence of GCA in the setting of malignancy represents an increased association between the two is unclear, as literature evidence is conflicting [15–18]. Existing evidence suggests that the presence of multinucleated giant cells and mononuclear cells are a reactive response to various epithelial malignancies [19–23]. Therefore, it is possible that the observed GCA represents reactive changes of inflammatory cells secondary to the primary tumor. However, as Orbo et al. [11] pointed out in their reported case of endometrial carcinoma that the presence of arteritis at a different location (cranial arteritis) in the patient argues against a local reactive process secondary to the tumor, but rather

<table>
<thead>
<tr>
<th>ID</th>
<th>Malignancy</th>
<th>Clinical GCA symptoms*</th>
<th>GCA pathology description</th>
<th>Temporal artery biopsy results</th>
</tr>
</thead>
<tbody>
<tr>
<td>86M</td>
<td>BCC of scalp</td>
<td>Asymptomatic per authors</td>
<td>Histopathology showed giant cell arteritis in the tissue deep to the excised tumor. The report described “striking inflammatory changes with luminal obliteration and frequent mural giant cells”</td>
<td>Not done</td>
</tr>
<tr>
<td>83M</td>
<td>BCC of left temporal region</td>
<td>Symptomatic with headaches, jaw claudication, and proximal muscle pain in upper limbs. No vision or other neurological symptoms</td>
<td>A portion of presumed temporal artery noted from the tissue showed mural-based granulomatous inflammation associated with fibrinoid necrosis obliterating the internal and external arterial elastic laminae</td>
<td>Positive based on the BCC excision tissue</td>
</tr>
<tr>
<td>78F</td>
<td>Suspected multiple myeloma but resolved after GCA treatment</td>
<td>Positive for constitutional symptoms but patient denied headache or visual problems</td>
<td>Positron emission tomography (PET) scan showed diffuse fluorodeoxyglucose (FDG) uptake in carotid, subclavian arteries and thoracic aorta, suggesting arteritis</td>
<td>Positive for GCA</td>
</tr>
<tr>
<td>N/A</td>
<td>Renal transitional cell carcinoma</td>
<td>N/A</td>
<td>Increased tracer uptake involving the aorta, with thickened aortic wall, and proximal branches of the aorta, including the carotid, iliac, femoral, and subclavian arteries</td>
<td>Unclear, authors reported “the patient had biopsy proven giant cell arteritis”</td>
</tr>
<tr>
<td>68F</td>
<td>Endometrial carcinoma</td>
<td>No history of weight loss, fever, fatigue or night sweats</td>
<td>Histologically, an extensive arteritis with giant cells of small- and medium-sized arteries in the myometrium, tubes and ovaries were identified</td>
<td>+</td>
</tr>
<tr>
<td>75F</td>
<td>Brenner tumors of the ovaries</td>
<td>Asymptomatic</td>
<td>Identified incidentally in a bilateral salpingo-oophorectomy specimen obtained as a result of an ovarian cyst</td>
<td>Positive</td>
</tr>
<tr>
<td>74F</td>
<td>Pancreatic carcinoma</td>
<td>Patient denied fever, headache, scalp tenderness, jaw claudication, and visual disturbances</td>
<td>PET scan showed arteritis, involving the aorta, truncus brachiocephalicus, subclavian arteries, axillaries, external carotid arteries, vertebral arteries, and superficial temporal arteries</td>
<td>Not done Doppler ultrasonography of superficial temporal arteries showed a characteristic periluminal dark “halo sign”</td>
</tr>
<tr>
<td>71M</td>
<td>Diffuse large B-cell lymphoma</td>
<td>None</td>
<td>PET scan showed inflammatory changes of the aorta</td>
<td>Transmural mononuclear cell infiltrate with disruption of the internal elastic membrane and giant cells consistent with GCA</td>
</tr>
</tbody>
</table>

*The presence of any of the cranial vessel ischemic symptoms, constitutional symptoms, or polymyalgia rheumatica symptoms.
supports a coincidence of systemic GCA identified in a primary tumor biopsy. Our case supports this argument.

Silent GCA, which has been studied previously, often refers to patients with constitutional symptoms (including fever of unknown origin) and raised ESR but no clinical evidence of cranial or other large artery involvement or polymyalgia rheumatica. Based on this definition, the reported prevalence was between 9% and 46% [24–28]. The reported clinical outcome of silent GCA varies, with some studies showing a relatively good outcome [24, 26] while others showing no difference in treatment outcomes [25, 28]. However, incidental GCA without constitutional symptoms or any other clinical GCA features, as illustrated in our case, is rarely reported. This highlights the challenges in recognizing such cases.

CONCLUSION

Our case highlights the challenges in GCA diagnosis when the lack of clinical symptoms conflicts with the pathology results. Confirmatory temporal artery biopsy, investigations for extra-cranial manifestations of the GCA, along with regular surveillance are warranted for diagnostic clarification and management guidance.

REFERENCES


*********

Author Contributions

Kangping Cui – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Ahmed Shah – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Sandeep Dhillon – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Arthur Lau – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Asghar Naqvi – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Guarantor of Submission

The corresponding author is the guarantor of submission.

Source of Support

None.

Consent Statement

This case does not use any specific patient identifiers, and the pictures are of microscopic histology and immunohistochemistry that cannot be used for patient identification purposes. In the department of pathology, we do not directly interact with patients, but all efforts have been made in great detail to anonymize the case as much as possible.

Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

Copyright

© 2020 Kangping Cui et al. This article is distributed under the terms of Creative Commons Attribution License which permits unrestricted use, distribution and reproduction in any medium provided the original author(s) and original publisher are properly credited. Please see the copyright policy on the journal website for more information.