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CASE REPORT

An 11-year and 10-month-old girl with purpura and chest pain

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Mucosa-associated lymphoid tissue lymphoma (MALToma) is a type of B-cell lymphoma. Case reports of childhood thymic MALToma and its association with vasculitis are rarely found in the related literature. Herein, we present a report of an 11-year and 10-month-old girl who was initially diagnosed with cutaneous vasculitis characterized by nonthrombocytopenic palpable purpura, positive antinuclear antibody and anti-SSA (Ro) antibody. Eight months later, a thymic mediastinal mass was found. Surgical excision was performed and results of pathological analysis revealed an extranodal marginal zone $CD20^{+}$ B-cell MALToma. Benign response to the chemotherapeutic regimen of Berlin–Frankfurt–Münster group NHL-BFM 90 R2 without relapse was noted in 2 years of follow-up. For the first time, our case demonstrated some clinical evidence of the association between vasculitis and childhood MALToma.
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Introduction

Mucosa-associated lymphoid tissue lymphoma (MALToma) is a type of B-cell lymphoma. In adults, it accounts for up to 8% of non-Hodgkin's lymphoma, and usually occurs in people who are in their 60s. It can attack stomach, orbit, intestine, lung, thyroid, salivary gland, skin, soft tissues, bladder, kidney, and central nervous systems.[1,2] To date, no study has accurately reported on an incidence in a pediatric group. Patients with MALToma may also have underlying autoimmune diseases, such as Sjögren's syndrome and Hashimoto thyroiditis, or disorders such as *Helicobacter pylori* infection.[3,4] It is believed that such a chronic inflammatory process may contribute to the development of MALToma. Vasculitis is an inflammatory disorder, however, only one female patient in her forties with gastric vasculitis and MALToma has been previously reported by Wöhrer et al.[3] Conversely, in children, there

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are no case reports of childhood MALToma with autoimmune diseases in the related literature. We herein present a rare case of childhood thymic MALToma with cutaneous vasculitis.

Case report

An 11-year and 10-month-old Chinese girl visited our emergency department complaining of chest pain, fever, and tachypnea for 6 days. Eight months before admission she was diagnosed with cutaneous vasculitis, which was characterized by nonthrombocytopenic purpura over bilateral lower extremities, positive antinuclear and anti-Sjogren's Syndrome A (SSA) antibodies (Fig. 1A) by the Shands Children's Hospital, Florida, USA. She had been receiving immunomodulator (e.g, azathioprine, hydroxychloroquine sulfate) therapy and steroids since then. In addition, no chest X-ray had been done before this admission. After admission, we confirmed that her septic shock was caused by *Pseudomonas aeruginosa*, and she improved after receiving appropriate treatment and medication.

The initial chest X-ray showed borderline mediastinal widening without interstitial lung edema or pleural effusion (Fig. 1B). A brief cardiac sonography revealed an unknown mass outside of the right side of the heart. A computer tomography (CT) scan demonstrated a huge mass (6.72×5.35 cm^2) over the anterior mediastinal area (Fig. 1C). A well-capsulated, multilobular mass originating from the thymus tissue in the anterior—lateral mediastinal area was found during surgical intervention for mass removal. Pathological findings indicated a malignant lymphoma, extranodal marginal zone B-cell type lymphoma (MALToma) (Fig. 1D).

We checked the immunological profiles of her previous vasculitis. Our case was found to be positive for antinuclear antibody (1:320 titer), anti-SSA (Ro) antibody (120 IU/mL), rheumatoid arthritis (RA) factor (120 IU/mL), and hypergammaglobulinemia [immunoglobulin G (IgG): 30.60 g/L; IgA: 9.89 g/L; IgM: 1.64 g/L]. No evidence of renal involvement was found. As compared with her previous skin appearance, the vasculitis was in the inactive phase. In addition, the possibility of Sjögren's syndrome was excluded by reviewing her related symptoms and based on the results of the Schirmer's test.

The tumor-staging work-up demonstrated that the mass was a localized mediastinal MALToma without metastasis. Treatment with Berlin—Frankfurt—Münster group NHL-BFM 90 R2 regimen was completed over the following 6 months. Despite having high levels of serum SSA (490 AU/mL) and positive RA factor (169 IU/mL) 2 years after tumor excision and chemotherapy, her tumor did not relapse during the 2

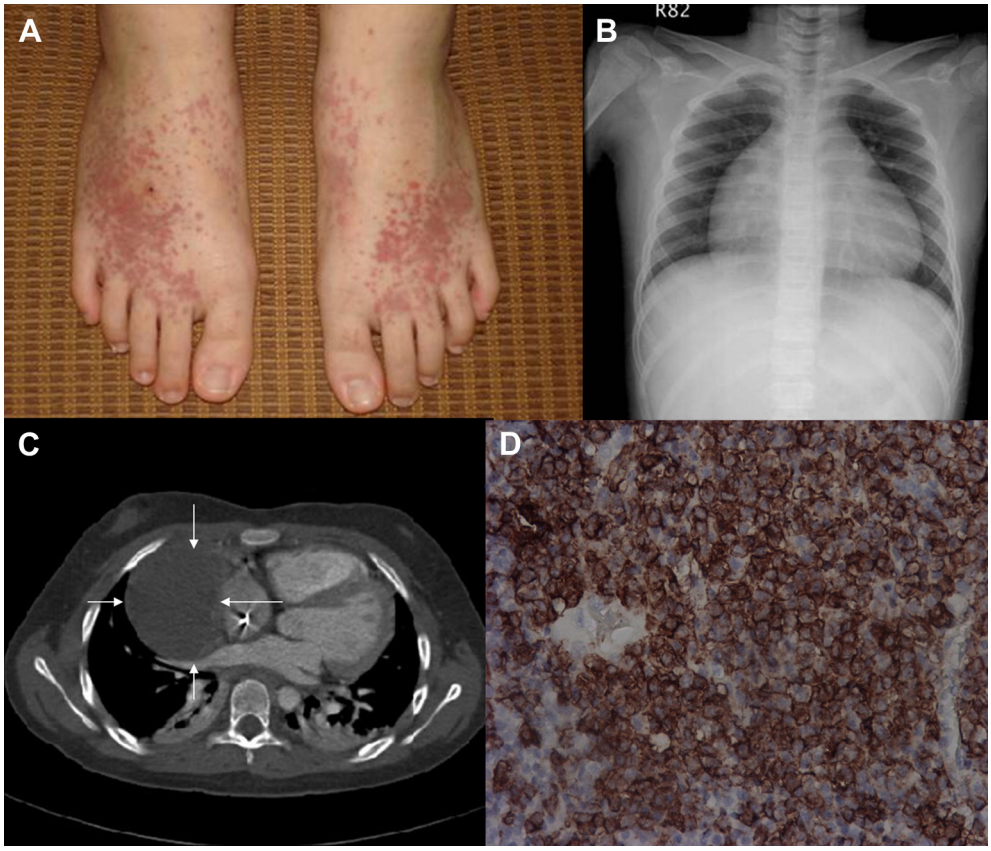

Figure 1. (A) The picture shows nonthrombocytopenic purpura over the girl's bilateral legs. (B) Chest X-ray showed borderline mediastinal widening without interstitial lung edema or pleural effusion. (C) Computer tomography scans demonstrated a huge mass (6.72×5.35 cm^2) in the anterior mediastinal area (white arrows). (D) Pathological analysis revealed a malignant lymphoma, extranodal marginal zone B-cell type lymphoma (mucosa-associated lymphoid tissue lymphoma).

years of clinical follow-up. We regularly followed her malignancy according to her chest radiograph, CT scan, and the level of serum lactate dehydrogenase. Currently, the patient receives hydroxychloroquine and is followed up regularly at pediatric rheumatology and hematology clinics.

Discussion

Our case demonstrated that the thymus could be the original site of childhood MALToma. It was remarkable that our patient who had pre-existing vasculitis was just under the age of 12. Most patients with MALToma also have accompanying autoimmune diseases; these had been older adults with a median age in the 60s.[3] In a review of the related literature, Wöhrer et al reported on 61 patients who had MALToma and autoimmune disease with an average age between 48 and 69 years. One of them had pre-existing vasculitis.[3] Maeda et al reported on a 23-year-old woman with both thymic MALToma and systemic lupus erythematosus. In the current literature, she was the youngest case of MALToma.[5] To the best of our knowledge, our case involves the youngest patient and is the only case of childhood thymic MALToma accompanied by pre-existing vasculitis.

Although the etiology of the MALToma remains unknown, it is clear that marginal zone lymphoma often arises in the setting of chronic inflammation or chronic antigenic stimulation, due to autoimmune disease or infection.[3] The most commonly associated autoimmune disease with MALToma is Sjögren's syndrome. However, our patient did not have Sjögren's syndrome. High titers of anti-SSA and RA factor were consistently noted, even after the completion of lymphoma chemotherapy. One plausible mechanism may be that the autoantibody or autoimmune process may induce the development of mediastinal MALToma.

Some studies regarding gene and immunology in MALToma patients have been reported. One study had revealed that MALToma may be associated with some genetic defects, such as mutation of *API2-MALT1* gene with *t(11,18)*.[6] Another immunology study showed the rising expression of inflammation-dependent cytokine receptors, such as CCR1, CCR8, and CXCR6 in the salivary glands of MALToma patients.[7] Moreover, one of the renowned pathogens associated with MALToma was *H. pylori*.[8] Under the infectious status of *H. pylori*, MALToma development may be facilitated by the autoantibody against *Helicobacter* sonication, IgG, DNA, and stomach extraction.[9]

In our case, we did not ascertain as to whether vasculitis or malignancy occurred first. It is possible that chronic inflammation, such as vasculitis, induces the development of MALToma. Most pediatric patients with MALToma have long-term survival and a good prognosis even with just local therapy alone.[10] As compared with adult-aged patients, both generally have a favorable prognosis. Furthermore, both adult and childhood patients had similar symptoms and signs. For treatment after tumor excision, in the pediatric group, most of the patients received adjuvant systemic chemotherapy. In contrast, in the adult group, they may choose more conservative observation or radiation therapy, except for adjuvant chemotherapy.[5,7,11,12] Regardless, the possibility of malignancy in pediatric patients with autoimmune disease should be kept in mind.[3]

In conclusion, this is the first case report demonstrating the association between childhood vasculitis and thymic MALToma. Underlying autoimmune disease or chronic inflammation may be attributed to the process of oncogenesis.[3] Clinicians might be made aware of the possibility of malignancy in pediatric patients with autoimmune disease.

Conflicts of interest

All contributing authors declare no conflicts of interest.

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