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Pruritus as a Paraneoplastic Symptom of Thymoma

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We describe the first cases in the literature, to our knowledge, of pruritus as a paraneoplastic symptom of thymoma. The first case is a 36-year-old woman who developed significant generalized pruritus without rash during her second pregnancy, which did not resolve after delivery and which was recalcitrant to topical steroids, antihistamines, and dry skin care. An

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extensive pruritus laboratory workup was performed and was negative (Table 1). A chest computed tomography (CT) performed 14 months after the onset of pruritus demonstrated a 7.5 × 4.3 cm anterior mediastinal mass that infiltrated the mediastinal fat and abutted the great vessels (Fig. 1*A* and *B*; Table 2). CT-guided fine needle aspiration of the mass and a repeat core biopsy was nondiagnostic but consistent with thymic sampling. Immunohistochemistry for Hodgkin's disease (HD) was negative. Based on the very high clinical suspicion of thymoma, she underwent three cycles of neoadjuvant cisplatin, cyclophosphamide, and doxorubicin chemotherapy with good response. Her pruritus resolved 3 days after her first cycle. She had a complete thymectomy, and final pathology demonstrated a Masaoka-Koga stage II World Health Organization type B2 thymoma. The patient is undergoing surveillance, without recurrence of disease or pruritus, now 2 years postoperatively.

The second case is a 60-year-old woman who presented with 12 months of intermittent generalized pruritus without rash. A pruritus laboratory workup was negative (Table 1). A family history revealed HD in a maternal grandmother. A chest radiograph obtained routinely for work showed an anterior mediastinal mass. CT revealed a 9.2 × 7.7 × 11.7 cm mass, with indentation of the right atrium (Fig. 1*C* and *D*; Table 2). CT-guided core biopsy was consistent with thymoma. Clinically, she had a stages I or II thymoma and underwent a complete thymectomy. Final pathology demonstrated a Masaoka-Koga stage I World Health Organization type AB thymoma. Her pruritus resolved immediately after surgery. She is undergoing surveillance, without recurrence of disease or pruritus, now 2 years postoperatively.

DISCUSSION

To our knowledge, this is the first case report of generalized pruritus as a paraneoplastic symptom heralding the diagnosis of thymoma. Paraneoplastic pruritus develops before a clinically evident cancer, is not caused by direct effect of the tumor, and resolves after treatment.[1] The most common malignancy associated with generalized pruritus is HD, where the prevalence rate is approximately 20% to 30%, and the severity of pruritus is associated with shorter survival.[2] Generalized pruritus without rash can be associated with multiple systemic diseases including liver disease, end-stage renal disease, and as a paraneoplastic symptom of malignancies.[1] The standard workup for generalized pruritus without rash (as reported in Table 1) includes evaluation of complete blood count with differential, liver function, renal function, and thyroid function and ruling out malignancy/lymphoma, viral infection (ie, HIV, hepatitis B/C), cholelithiasis, medication-related pruritus, and autoimmune conditions. Skin biopsy in the absence of a primary cutaneous lesion is nonspecific and is of low yield.

Thymomas are frequently associated with autoimmune conditions and paraneoplastic syndromes including myasthenia gravis and pure red cell aplasia.[3] Paraneoplastic skin conditions associated with thymoma that have been reported include mixed connective tissue disease, dermatomyositis, systemic lupus erythematous, acrokeratosis, pemphigus, and lichen planus, which each have an associated clinically apparent rash.[4]

Thymoma is the most common neoplasm of the anterior mediastinum and represents 20% of anterior mediastinal tumors.[5] However, the differential diagnosis of an anterior mediastinal mass includes teratoma, seminoma, lymphoma, and also nonmalignant conditions. An anterior mediastinal mass in a patient with generalized pruritus is more likely to be attributed to HD than thymoma. Given the significant upfront treatment differences between HD and thymoma, making the distinction between these two tumors is critical. The differential diagnosis of generalized pruritus in association with an anterior mediastinal mass should also include thymoma.

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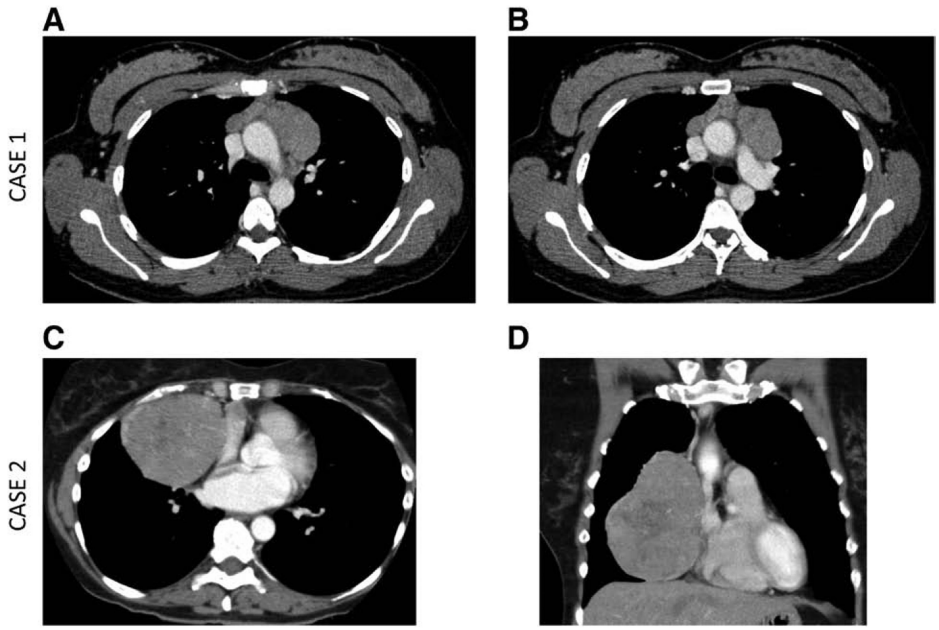

FIGURE 1.

Computed tomography axial views of case 1 demonstrating abutment of proximal great vessels including aorta and pulmonary artery at different planes (*A* and *B*). Computed tomography (*C*) axial view and (*D*) coronal view of case 2 demonstrating indentation of the right atrium.

TABLE 1

Evaluation of Pruritus

Evaluation	Case 1	Case 2
Distribution of pruritus	Generalized but most bothersome on bilateral lower extremities and hands and feet	Generalized but most bothersome on upper extremities and back
Interventions attempted	No resolution after a normal vaginal delivery No improvement with antihistamines, topical moisturizers, or topical steroids	None
Constitutional symptoms, including fevers, night sweats, unintentional weight loss >10%	None	None
Physical examination, including skin, lymph node, liver/spleen examination	Normal	Normal
Thyroid-stimulating hormone	Normal	N/A
Complete blood count + differential	Normal	Normal
Serum chemistry/renal function	Normal	Normal
Serum liver function tests	Normal	N/A
Serum lactate dehydrogenase	Normal	N/A
Serum erythrocyte sedimentation rate and C-reactive protein	Normal	N/A
Other autoimmune work-up[a]	N/A	Negative
Hepatitis B + C panel	Negative	N/A
Other infectious work-up[b]	Negative	N/A
Right upper quadrant ultrasound	Normal, no cholelithiasis	N/A
Change in medications	No	No

[a]Case 2 had the following autoimmune workup: antinuclear antibody, rheumatoid factor, cyclic citrullinated peptide antibody IgG, anti-neutrophil cytoplasmic antibody, myeloperoxidase antibody, proteinase-3 antibody, SCL-70 antibody, Sjogren's screen (anti-SS-A/Ro and anti-SS-B/La antibodies).

[b]Case 1 had toxoplasma, strongyloides, and quantiFERON-tuberculosis serologies sent.

TABLE 2

Characteristics of Cases

Characteristic	Case 1	Case 2
Baseline CT imaging findings	7.5 × 4.3 cm left anterior mediastinal lobulated, homogeneous mass Infiltrates the mediastinal fat Abuts mediastinal vessels (superior vena cava, descending aorta, and main pulmonary artery)	9.2 × 7.7 × 11.7 cm right anteromedial mediastinal well-circumscribed, lobulated, heterogeneous mass Moderate indentation of the right atrium Abuts mediastinal vessels (aorta, superior vena cava) and right lung
Pre-surgical biopsy	Yes CT-guided FNA (nondiagnostic) CT-guided biopsy (nondiagnostic)	Yes CT-guided biopsy (diagnostic for thymoma)
Clinical Masaoka-Koga stage	III	I or II
Neoadjuvant therapy	Yes CAP chemotherapy × 3 cycles	No
Operative findings	Well-circumscribed main tumor mass towards the left of midline and a much smaller, apparently separate 2 cm well-circumscribed tumor mass to the right of midline	Encapsulated tumor Nodule palpated in right upper lobe
Type of resection	Median sternotomy approach: complete thymectomy and radical mediastinal dissection	Median sternotomy approach: complete thymectomy, radical mediastinal dissection, and wedge excision of RUL lung nodule
Pathologic Masaoka-Koga stage	II No clearly defined capsule -well-defined, discrete, microscopic foci of thymic tumor scattered throughout the surrounding mediastinal fat	I Encapsulated tumor Wedge RUL biopsy showed an organizing pneumonia pattern
WHO type	B2	AB
Resection status[a]	R0	R0
Adjuvant therapy	None	None

FNA, fine needle aspiration; CAP, cisplatin, cyclophosphamide, and doxorubicin; RUL, right upper lobe; WHO, World Health Organization.

[a]Resection status: R0 = complete, R1 = microscopic, and R2 = macroscopic.