

Case-Based Review

Carcinomatous Polyarthrititis as a Presenting Manifestation of Papillary Carcinoma of Thyroid Gland

Himanshu Pathak, Ray Lonsdale¹, Ketan Dhatariya², Chetan Mukhtyar

Departments of Rheumatology, ¹Histopathology and ²Endocrinology, Norfolk and Norwich University Hospital, Norwich, United Kingdom

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Address for correspondence:

Dr. Himanshu Pathak, Department of Rheumatology, Level 2, East Block, Norfolk and Norwich University Hospital, Norwich NR4 7UY, United Kingdom.
E-mail: himanshu.pathak@nnuh.nhs.uk

Abstract

A 61-year-old female presented with 6 months of polyarthralgia associated with constitutional symptoms. These included weight loss, night sweats, lethargy and worsening mobility and activities of daily living. There was no significant medical history. On examination, she had synovitis of multiple joints. Investigations for rheumatoid factor and anti-cyclic citrullinated peptide antibody were negative. There was an acute phase response in the form of raised erythrocyte sedimentation rate and C-reactive protein. Contrast-enhanced computed tomography showed pancreatic and right ovarian cystic lesions, which turned out to be clinically insignificant. Positron emission tomography-computed tomography demonstrated fluorodeoxyglucose avid lesion in the right hemi-thyroid. Ultrasound of thyroid gland showed a 13 mm hyporeflexive, irregular, subcapsular nodule in the upper lobe with some microcalcification. Fine needle aspiration cytology was diagnostic of papillary carcinoma, confirmed on total thyroidectomy. Arthritis completely resolved within 8 weeks postoperatively. We report the first case of paraneoplastic carcinomatous polyarthrititis in association with a papillary thyroid carcinoma as evidenced by a resolution of joint manifestations and laboratory markers of inflammation posttotal thyroidectomy.

Key Words: Carcinomatous polyarthrititis, papillary carcinoma of thyroid, paraneoplastic, paraneoplastic rheumatic syndromes, polyarthrititis

Introduction

Carcinomatous polyarthrititis is an uncommon but significant cause of asymmetrical arthritis in the elderly. In the absence of a definite etiology, a high suspicion should be maintained to enable an early diagnosis of malignancy and the consequent benefits of early treatment.

Case Report

A 61-year-old female was referred urgently for a 6-month history of polyarthralgia affecting knees, hips, ankles, hands, and shoulders. These symptoms were affecting activities of daily living. She reported weight loss, anorexia, and night sweats. Her past medical history included gastroesophageal reflux disease, osteopenia, depression, and varicose vein surgery. She had been fully independent before these symptoms. There was no recent travel history. Her medication included tramadol 50 mg four times daily and citalopram 40 mg daily. On

examination, she was afebrile with a blood pressure of 130/80 mmHg. There was synovitis of the left second and third metacarpophalangeal joint, left wrist, and both knees. The rest of the examination including urinalysis was normal. Blood investigated showed normocytic anemia with hemoglobin of 103 g/L (120–150) and thrombocytosis of $511 \times 10^9/L$ (150–410). Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were raised at 117 mm/h (0–20) and 228 mg/L (0–10), respectively. Rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) antibodies were negative. The antinuclear antibody was negative. The alkaline phosphatase was raised at 224 U/L (38–126), but the transaminases were normal. Albumin was low at 27 g/L (35–50). Serum creatinine and serum calcium were normal. Serum ferritin was 312 $\mu\text{g/L}$ (23–300). There was no paraproteinemia. Thyroid function was normal. Infection screening was negative for hepatitis B and C, HIV, Borrelia, Coxiella, Chlamydia, and Brucella. X-rays of

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her chest, whole spine, and skeletal survey were normal. X-rays of knees showed moderate medial compartment and patellofemoral osteoarthritis on the right. Right knee arthrocentesis drew straw-colored fluid with raised white blood cells, no crystals or organisms on microscopy and culture. In view of the atypical polyarthritis with constitutional symptoms, she underwent a computed tomography (CT) scan of her chest, abdomen, and pelvis to look for malignancy. This demonstrated a 6.5 cm right ovarian cyst, and a 7 mm cyst in the body of her pancreas. Tumor markers for ovarian, pancreatic, and gut cancer were not raised. IgG4 levels were normal. An upper gastrointestinal endoscopy requested because of her history of chronic gastroesophageal reflux and anemia showed reactive changes at the gastroesophageal junction and a normal duodenum. Positron emission tomography-CT (PET-CT) scan demonstrated fluorodeoxyglucose avid right thyroid lesion [Figure 1]. The left hip and both knees also demonstrated uptake, but the pancreas and the ovary remained “cool.”

She was initially administered simple analgesia. The right knee was aspirated and injected with methylprednisolone depot for therapeutic and diagnostic purposes. Despite these measures, her knee and hip pain did not improve. Oral prednisolone 15 mg once daily and oral methotrexate 15 mg once a week (with once weekly folic acid 5 mg cover) was started while waiting for the PET-CT. The knee pain and swelling improved as did her ESR and CRP. Following the PET-CT result, she was discharged with a plan for outpatient thyroid gland ultrasound, fine needle aspiration cytology, and follow-up in gynecology and gastroenterology clinic for her ovarian and pancreatic cysts, respectively. She was given a plan to reduction plan to stop the prednisolone before the PET-CT scan.

Thyroid ultrasound confirmed a 13 mm nodule in the upper right lobe. Fine-needle aspiration was diagnostic of papillary carcinoma (Thy 5) [Figures 2 and 3]. She was referred to endocrinology and the ENT surgeons for further management. While waiting for her thyroid surgery, she was reviewed in the rheumatology clinic where she described on-going joint pains and swelling after stopping the prednisolone. She had stopped the methotrexate of her own accord due to perceived inefficacy. She underwent total thyroidectomy with uncomplicated postoperative recovery. Histology confirmed a papillary carcinoma of classical type, 10 mm diameter, with vascular invasion and microscopic tumor foci in the left lobe, pT1a(m). Eight weeks after surgery, she was reviewed in the rheumatology clinic. On that follow-up, she had no joint synovitis and the pain had completely resolved. The CRP was 25 mg/L. Her ovarian cyst was diagnosed as benign, and her pancreatic cyst was unchanging, with a plan for annual review by the gastroenterologists. At the most recent follow-up 16 weeks postsurgery, there is no evidence of inflammatory arthritis.

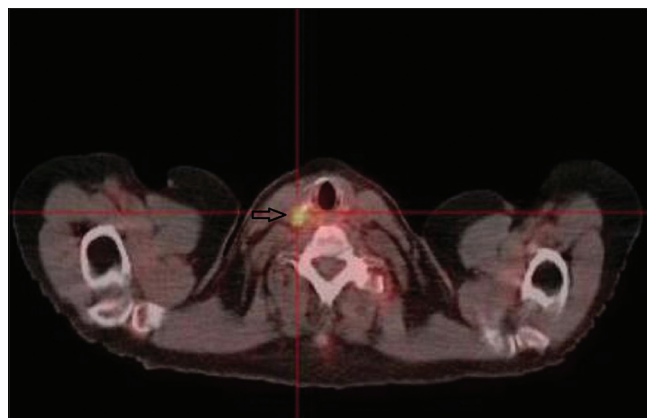


Figure 1: Fluorodeoxyglucose-positron emission tomography-computed tomography showing incidental FDG avid right thyroid nodule (arrow)

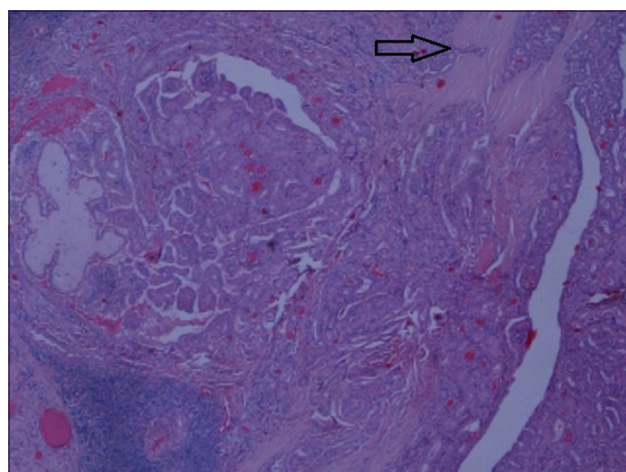


Figure 2: ×20 original magnification showing papillary carcinoma invading through its fibrous capsule into the surrounding thyroid gland (arrow)

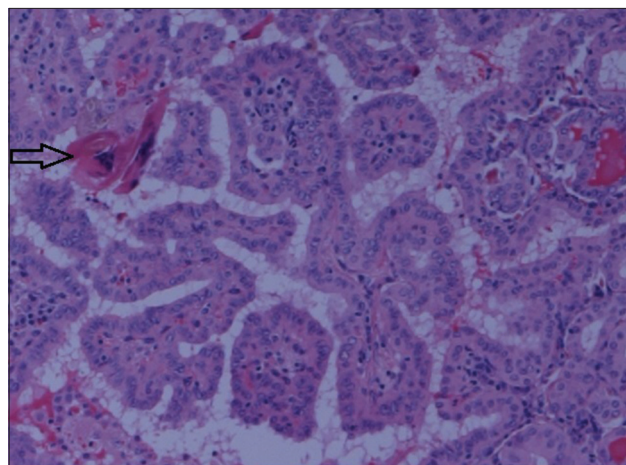


Figure 3: ×100 original magnification image showing tumor forming papillary structures with admixed multinucleated histiocytes (arrow)

Discussion

The main differentials considered for patients presentation were seronegative inflammatory arthritis, adult onset Still's disease, and carcinomatous polyarthritis. Atypical clinical

presentation, absence of immunology for inflammatory arthritis, mildly elevated ferritin, histopathological findings of thyroid cancer, and complete resolution of polyarthritis postthyroidectomy confirmed the diagnosis of carcinomatous polyarthritis. Paraneoplastic syndromes arise from tumor secretion of hormones, peptides, or cytokines.^[1-4] The musculoskeletal manifestations of paraneoplastic syndromes can predate, present synchronously, or follow the malignancy.^[1] Dermatomyositis, leukocytoclastic vasculitis, carcinomatous polyarthritis, polymyalgia rheumatica, hypertrophic pulmonary osteoarthropathy, and remitting seronegative symmetrical synovitis are recognized paraneoplastic rheumatologic phenomenon.^[1,2,4,5] Carcinomatous polyarthritis is usually asymmetrical, migratory, and predominantly involves the lower limb joints. It has been described as “explosive in onset” and mainly affects an elderly age group.^[1,2] Paraneoplastic arthritis is usually seronegative, but concomitant RF and anti-CCP positivity have been reported.^[6] It has been reported in association with neoplasia of the lung, colon, breast, ovary, stomach, oropharynx, hematopoietic, and lymphoid malignancies.^[2,7] Arthritis resolves with treatment of the neoplasm and that is the only definite proof of diagnosis.^[1,2] Papillary carcinoma of thyroid is most common thyroid cancer. The 10-year prognosis of papillary thyroid carcinoma is good (82%).^[8,9] Paraneoplastic syndromes are uncommon with papillary thyroid cancer.^[10] The previous case reports [Table 1] have shown rheumatologic paraneoplastic association of papillary carcinoma of thyroid with connective tissue diseases, dermatomyositis, polymyositis, polymyalgia rheumatica, and adult onset Still’s disease,^[11-19] but we believe this is the first report of a case of papillary thyroid cancer associated with carcinomatous polyarthritis.

In summary, an undifferentiated inflammatory arthritis in an elderly patient should be investigated for possible underlying malignancy. If clinical suspicion is high for occult malignancy than PET-CT scan is a valuable investigation. Carcinomatous paraneoplastic polyarthritis can be a presenting feature of malignancy which resolves with treatment of the underlying malignancy.

Table 1: Rheumatological paraneoplastic syndromes with papillary carcinoma thyroid	
Case reports	Rheumatological paraneoplastic syndromes reported with papillary thyroid cancer
Sola <i>et al.</i> ^[11]	Systemic lupus erythematosus
Thongpooswan <i>et al.</i> ^[12]	Mixed connective tissue disease
Ikeda <i>et al.</i> , ^[13] Shah <i>et al.</i> , ^[14] Lee <i>et al.</i> ^[15]	Dermatomyositis
Kalliabakos <i>et al.</i> ^[16]	Polymyositis
Tabata and Kobayashi ^[17]	Polymyalgia rheumatica
Inoue <i>et al.</i> , ^[18] Ahn <i>et al.</i> ^[19]	Adult onset still’s disease

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Conflicts of interest

There are no conflicts of interest.

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