Open Journal of
Clinical & Medical
Case Reports

Volume 5 (2019)
Issue 6

ISSN: 2379-1039

Idiopathic hyper eosinophillic syndrome presenting as urinary incontinence: A case report

Wai Ching Lee*; Sachdeva Pooja; TanYan Denise; Felik Paulus; Tan Leonard; Baikunje Shashidhar

***Wai Ching Lee**

Department of Internal Medicine, General Medicine, Sengkang General Hospital, Singapore

Phone: (65) 6930 2914; Email: deanna.lee.w.c@singhealth.com.sg

Abstract

Urinary presentation of hypereosinophillic syndrome is extremely rare. Our patient is young male who presented with urinary incontinence, hematuria and unexplained diffuse urinary bladder wall thickening in absence of chronic retention of urine. In HES, eosinophils infiltrate various organs and cause damage due to release of inflammatory markers that result in organ dysfunction. This case highlights importance of obtaining full systemic review to identify end-organ damage in any patient presenting with eosinophilia which should include specific enquiry about any urinary symptoms which may be embarrassingto patients and not offered readily to the physician.

Keywords

urinary incontinence; hypereosinophilic syndrome; hypereosinophilia; hematuria; urinary symptoms

Introduction

Diagnosis of Hypereosinophillic syndrome [HES] is made when peripheral blood absolute eosinophil count (AEC) is more than 1500/ microliter on two separate occasions separated by at least a month and/ or tissue infiltration, together with evidence of end organ damage due to eosinophil infiltration and release of inflammatory mediators.

True prevalence of HES is unknown but it is estimated to be 0.36 to 6.3 per 100,000 [2]. Most patients are diagnosed between the ages of 20 and 50 years, it can develop in children [7,8]. Most common presentation is dermatologic (37%), pulmonary (25%), gastrointestinal (14%), cardiac (5%), Neurological (4%) [3]. It is classified in different categories depending on the underlying aetiology driving the eosinophilia such as Primary (or neoplastic) HES, Secondary (or reactive) or Idiopathic.

Case Report

A twenty five year old Asian man presented with urinary incontinence, penile itching and haematuria for three months prior to presentation. He also complained of loose stools 4-5 times a day, mixed with fresh blood, and associated with dull upper abdominal pain for 3 months. Episodic urinary symptoms of incontinence which are unable to control his urine and wetting his clothes with occasional blood at the end of urination. He had no associated fever, no swelling of testes or weight loss. Systemic review was negative for cough, wheeze, breathlessness, chest pain, skin rash, arthralgia, weakness, or numbness or paraesthesia. He had no recent drug exposure, no episodic angioedema and no significant family history. His travel history was unremarkable over the last 6 months; he worked in Singapore but lived in Malaysia; mainly in urban areas. He did not have any exposure to animals or participate in activities with environmental exposure risks such as contact with soil and water. Patient was most concerned with his urinary symptoms as he found it embarrassing socially.

He had some preliminary work up overseas before being seen at our centre. A CT Urogram performed 1 month earlier in another centre showed a thickened bladder wall but no other kidney pathology. His FBC report then was Total White 16.5, Eosinophils 52% Hemoglobin 15.7 platlets 224.

Physical examination revealed a temperature of 36^{o}C, blood pressure 103/63, heart Rate 64/min, respiratory rate 12/min with 100% peripheral oxygen saturation. There was no palpable lymphadenopathy, splenomegaly, hepatomegaly or skin rash. Cardiopulmonary and neurological examinations were within normal limits. There were no penile ulcers and local urogenital pathology.

Investigations revealed marked leukocytosis (34.22 x109/L) with eosinophilia (AEC 29 x109/L, 89%) normal hemoglobin (14.22 mg/dl) and platelets (277 x109/L). His serum electrolytes Sodium (Na) 137mmol/L, potassium (K) 4.1mmol/L, total protein 65 g/L albumin 39 g/L , normal Bilirubin and aminotransferases, BUN 41 mmol/L, Creatinine 69 micromol/L and Troponin T <13ng/L were within normal limits. Further work up for eosinophillia showed that he had raised IgE levels (2833 IU/ml) and LDH (662U/ml), and low folate levels (less than 4.5 pmol/l). An autoimmune screen was negative for ANA, anti-dsDNA, anti-Jo-1, anti- MPO, anti-smith, anti-Ro, anti-La, anti-Scl70ab and ANCA antibodies. He had a normal short Synacthen test, normal vitamin B12 (450 pmol/L), negative screen for human immunodeficiency virus, hepatitis B and hepatitis C, and a negative screen for stool leucocytes, ova cyst and parasites. Urinary screen showed microscopic hematuria and eosinophiluria. Parasite screen for stool, sputum and urine were negative. Infective screen including procalcitonin, blood cultures of two sets, urine cultures, stool cultures were negative. Contrasted CT imaging of his chest, abdomen, and pelvis showed significant urinary bladder wall thickening with no pulmonary, hepatic or kidney pathology. MR imaging of his spine did not show any neurological cause for his incontinence such as caudaequina or conus medullaris involvement. Endoscopy and random biopsies of his stomach and colon showed eosinophils (>50 per HPF) in his gastric stroma and colonic mucosa. Urine cytolocy confirmed eosinophiluria with no malignant cells. Urology was consulted for cystoscopy and biopsy who suggested that gastroendoscopic tissues would be sufficient. Nerve conduction studies of bilateral lower limbs showed no neurological involvement. Echocardiography showed normal

ejection fraction with normal systolic and diastolic function, without valvular pathology. Bone marrow biopsy showed marked eosinophilia (50%) but no immature forms, no granulomas or metastatic tumor cells. Flow cytometry did not show any blasts or B clonal proliferation. Cytogenetics was normal and he did not have the FIP1L1-PDGFR-alpha fusion transcript.

The patient was started on Ivermectin 15mg (200 microgram/kg) once daily for two days to treat empirically for strongyloides infection, as this parasite is prevalent in tropical and subtropical areas but is not always picked up on screening tests. He was started on oral prednisolone 0.5mg/kg when there was no eosinophil response to Ivermectin and also given a second course 2 weeks later to completely cover for the possibility of strongyloides infection. His prednisolone dose was later tapered when his gastrointestinal and genitourinary symptoms improved and his eosinophil counts gradually improved to normal. His gastrointestinal symptoms and then later his urinary symptoms improved and gradually resolved with steroids. Repeated ultrasound scan of the bladder post treatment showed reduced thickening, uroflow was normal and no residual post void urine.

Discussion

Urinary presentation of hypereosinophillic syndrome is extremely rare. Our patient is young male who presented with urinary incontinence and unexplained diffuse urinary bladder wall thickening in absence of chronic retention of urine. The most remarkable abnormality was peripheral eosinophillia hence common causes of eosinophillia such as parasitic infection, sexual infections (Human Immunodeficiency Virus- HIV), drug exposure and allergies were first investigated and excluded on history and initial investigations. He did not have clinical features and laboratory markers suggestive of adrenal insufficiency which was further excluded with appropriate response to adrenocorticotropin (ACTH) administration. The patient had no prodromal symptoms and no history of multisystem involvement raising possibility of autoimmune disorders. He had no personal history of angioedema, asthma or mononeuritis multiplex raising possibility of small vessel vasculitis or granulomatous polyangitis.

In HES, eosinophils infiltrate various organs and cause damage due to release of inflammatory markers that result in organ dysfunction. In our patient, eosinophiluria and tissue demonstration of eosinophills in colonic mucosa and gastric stroma support the diagnosis of eosinophil mediated damage and thus accounting for his gastrointestinal symptoms on presentation.

The most common etiology for overproduction of eosinophills in HES is clonal proliferation of eosinophils resulting from a defect in haematopoetic cells (primary HES) or overproduction of eosinophilpoetic cytokines such as IL-5 [4,5] (Secondary HES). If the cause remains unknown despite aetiologic work- up, it is classified as idiopathic HES. Bone marrow studies which were done in our patient to exclude the clonal proliferation of B cells or myeloid cells were negative, however we were not able to test for T cell clonality. The genetic aberration involving the tyrosine kinase receptor platelet-derived growth factor receptor alpha [PDGFRA] and platelet-derived growth factor beta [PDGFRB]) occur almost exclusively in males [3, 6]. Cytogenetic studies were normal and he was negative for the fusion gene by DNA PCR. The patient did not have other features suggestive of myeloid or lymphoid involvement such as anemia, thrombocytopenia,

hepatosplenomegaly, or lymphadenopathy. Patient also did not have any infective and allergic signs and symptoms with an extremely high eosinophil count to attribute it to solely reactive eosinophilia.

Treatment of HES involves treating the underlying primary cause. However idiopathic HES is often treated first line with a trial of glucocorticoids [7,11]. The overall goals of therapy are reduction of the absolute eosinophil count (AEC) to below 1.5 x 109/L (1500 cells/microL), amelioration of signs and symptoms, and prevention of disease progression and organ infiltration [8]. The presence of end-organ damage in the setting of hypereosinophillia determines the urgency of treatment [10]. Our patient was treated with 2 courses of Ivermectin 15mg (200 microgram/kg) once daily for two days to treat possible strongyloides infection and prednisolone 35 mg once a day (0.5 mg/kg). Patient showed remarkable response and eosinophills counts drop by 30 percent within 24 hours and 75 percent by 72 hours and completely normalized within two weeks of treatment. The patient showed improvement in his urinary symptoms with steroid treatment.

Figures

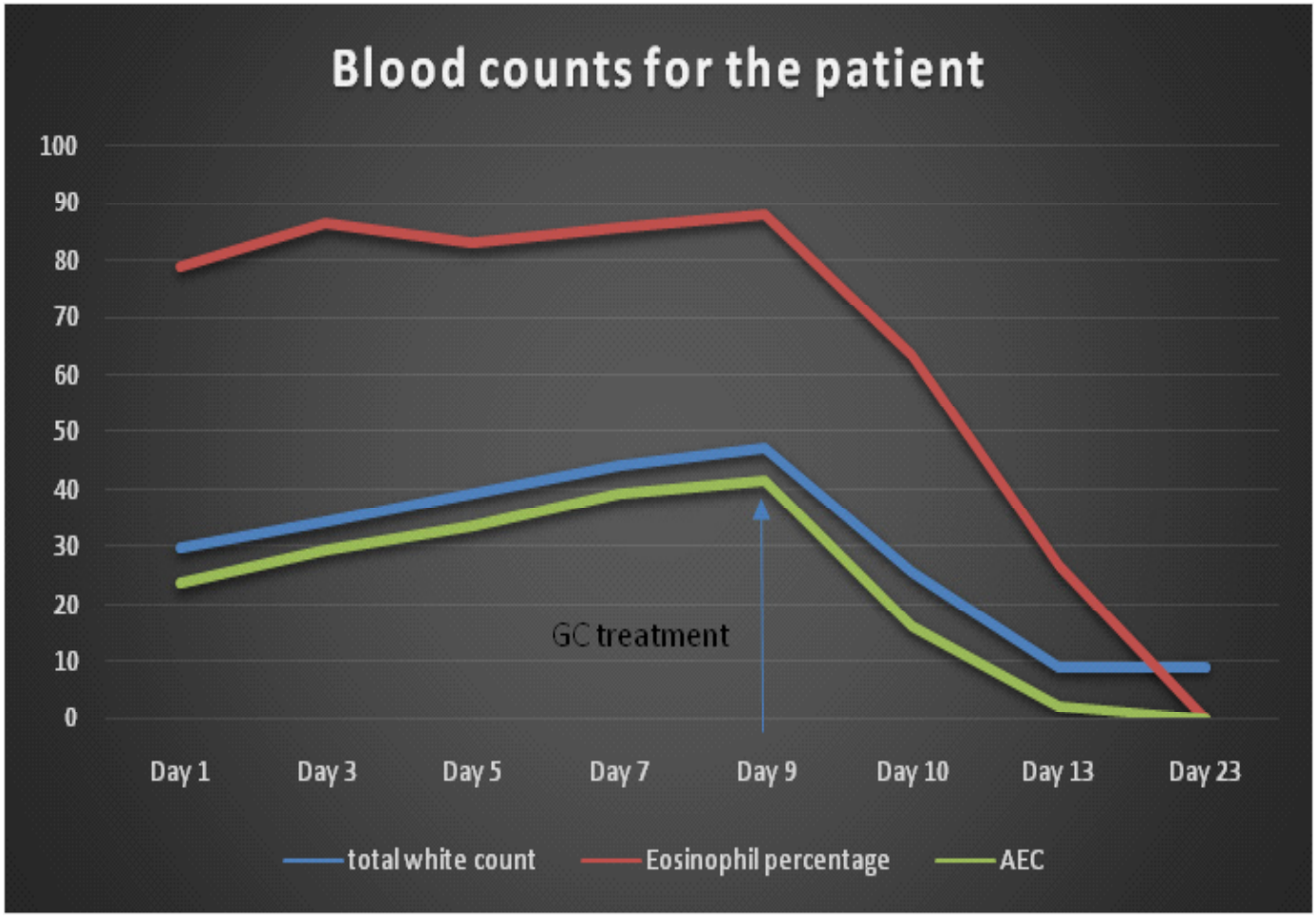

Figure 1: Chart showing patient's trend of Blood counts from presentation till follow up

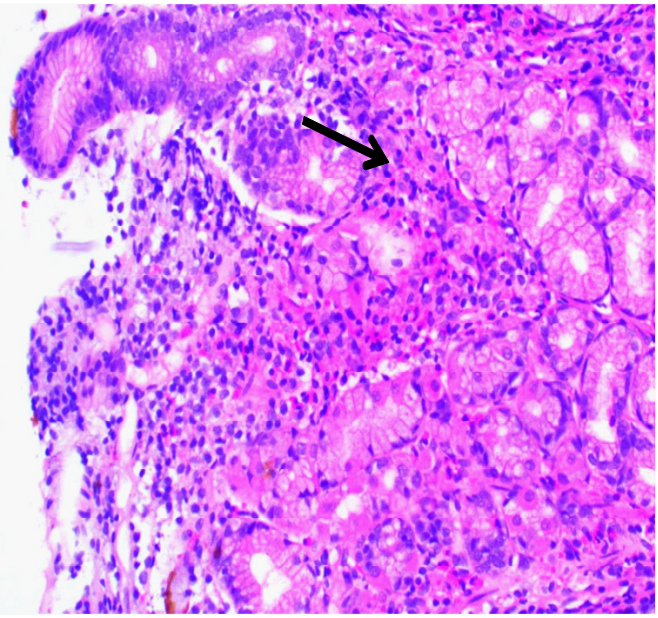

Figure 2: Gastric biopsy showing eosinophil infiltration. (Eosinophils are stained in bright pink)

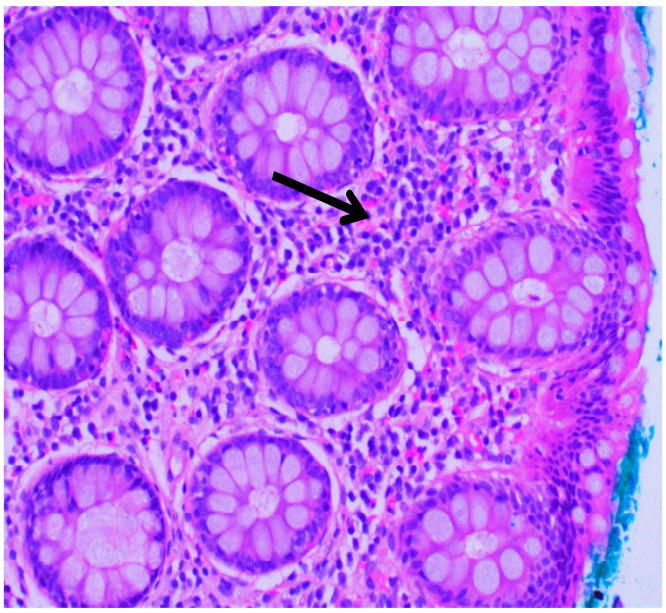

Figure 3: Colonic biopsy showing eosinophil Infiltration (Eosinophils are stained in bright pink)

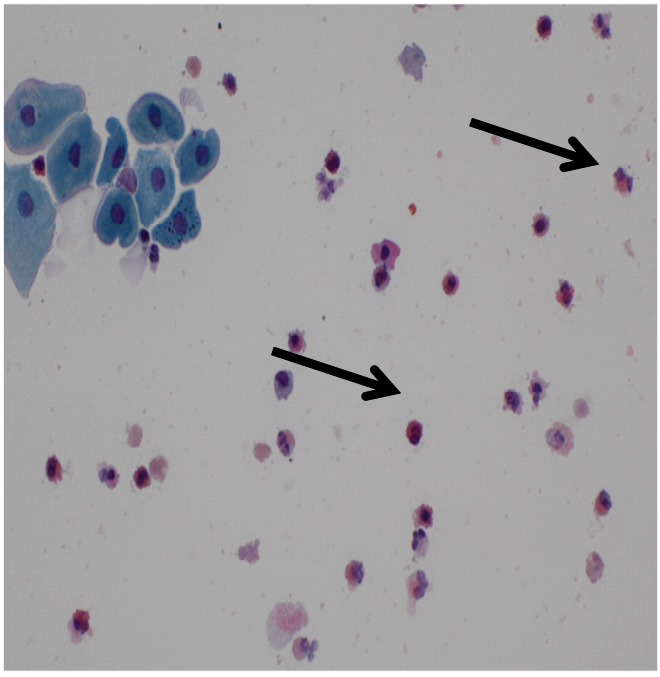

Figure 4: Urine Cytology showed Eosinophills (Eosinophils are stained in bright pink)

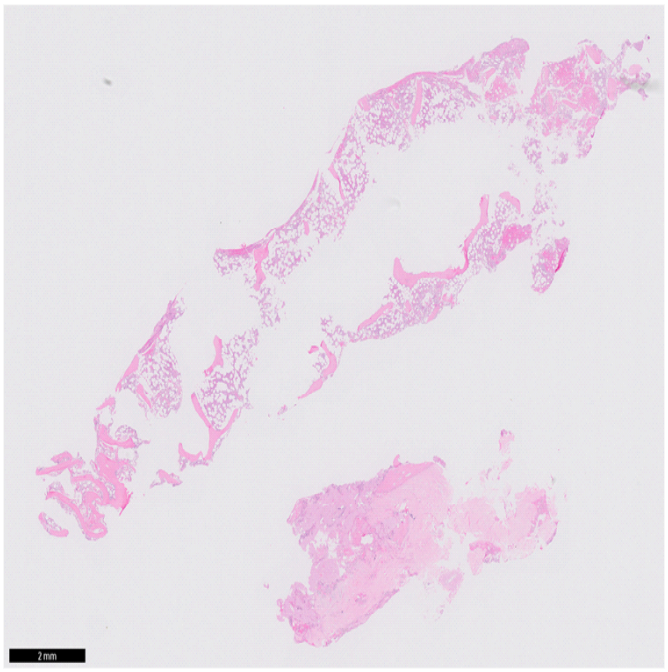

Figure 5A: GBone Marrow Aspirate showed Eosinophils (Eosinophils are stained in bright pink)

Low power view of bone marrow trephine. Normocellular for the patient's age (H&E 2x)

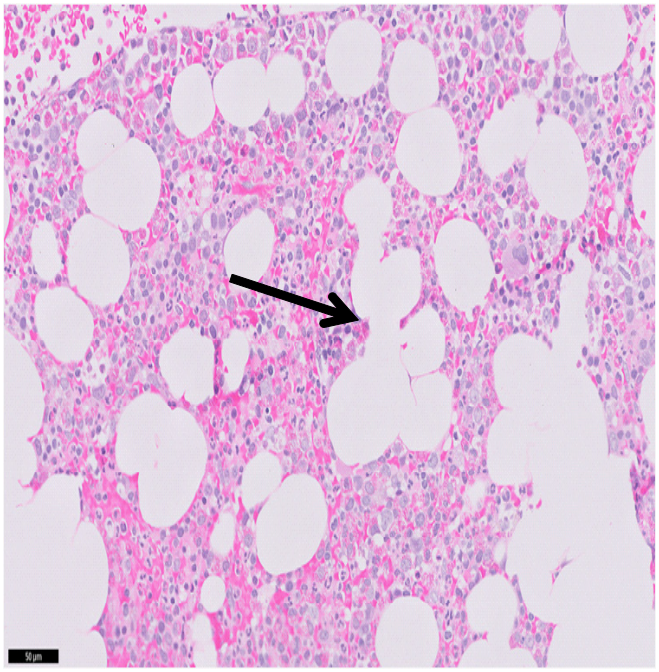

Figure 5B: Bone Marrow Aspirate showed Eosinophils. Raised myeloid to erythroid ratio. Hyperplastic myeloid lineage with complete maturation to segmented granulocytes and eosinophils comprising 40-50% of the marrow population (H&E 20x)

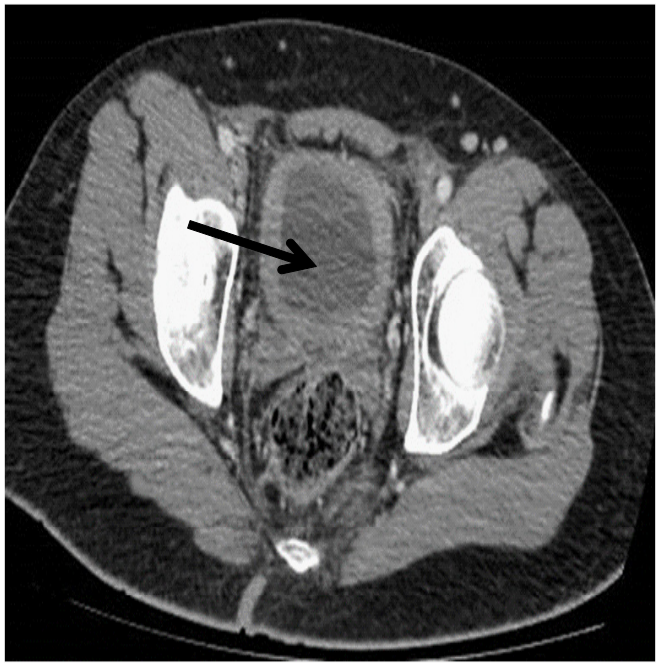

Figure 6: CT (Computed Tomography) images of Thorax, abdomen and Pelvis showing urinary bladder diffuse thickening.

Conclusion

Urinary presentation of HES is possible and it follows the pathophysiology of disease, however it is extremely rare or under-reported, and our patient is the first case in our experience.

A full systemic review to identify end-organ damage in any patient presenting with eosinophilia should include specific enquiry about any urinary symptoms as some of these symptoms such as urinary incontinence may be embarrassing to patients and not offered readily to the physician.

References

1. Contemporary consensus proposal on criteria and classification of eosinophilic disorders and related syndromes. Valent P, Klion AD, Horny HP, Roufosse F, Gotlib J, Weller PF, Hellmann A, Metzgeroth G, Leiferman KM, Arock M, Butterfield JH, Sperr WR, Sotlar K, Vandenberghe P, Haferlach T, Simon HU, Reiter A, Gleich GJ J Allergy Clin Immunol. 2012; 130(3):607. Epub 2012 Mar 28.

2. Incidence of myeloproliferative hypereosinophilic syndrome in the United States and an estimate of all hypereosinophilic syndrome incidence. Crane MM, Chang CM, Kobayashi MG, Weller PF J Allergy ClinImmunol. 2010; 126(1): 179.

3. Hypereosinophilic syndrome: a multicenter, retrospective analysis of clinical characteristics and response to therapy. Ogbogu PU, Bochner BS, Butterfield JH, Gleich GJ, Huss-Marp J, Kahn JE, Leiferman KM, Nutman TB, Pfab F, Ring J, Rothenberg ME, Roufosse F, Sajous MH, Sheikh J, Simon D, Simon HU, Stein ML, Wardlaw A, Weller PF, Klion AD J Allergy ClinImmunol. 2009; 124(6): 1319.

4. Mechanisms of eosinophilia in the pathogenesis of hypereosinophilic disorders. Ackerman SJ, Bochner BS Immunol Allergy Clin North Am. 2007; 27(3): 357.

5. Idiopathic hypereosinophilic syndrome. In: Eosinophils: Biological and clinical aspects, Makino S, Fukuda T (Eds), CRC, Boca Raton 1992. p.403

6. Patients with myeloid malignancies bearing PDGFRB fusion genes achieve durable long-term remissions with imatinib. Cheah CY, Burbury K, Apperley JF, Huguet F, Pitini V, Gardembas M, Ross DM, Forrest D, Genet P, Rousselot P, Patton N, Smith G, Dunbar CE, Ito S, Aguiar RC, Odenike O, Gimelfarb A, Cross NC, Seymour JF Blood. 2014 Jun; 123(23): 3574-7.

7. The idiopathic hypereosinophilicsyndrome.Weller PF, Bubley GJ Blood. 1994; 83(10): 2759.

8. Hypereosinophilic syndrome in childhood: clinical and molecular features of two cases.Farruggia P, D'Angelo P, Acquaviva A, Trizzino A, Tucci F, Cilloni D, Messa F, D'Ambrosio A, AricòMPediatrHematolOncol. 2009; 26(3): 129.

9. Biologic Agents for the Treatment of Hypereosinophilic Syndromes. Kuang FL, Klion AD. J Allergy Clin ImmunolPract. 2017; 5(6): 1502.

10. How I treat hypereosinophilic syndromes. Klion AD Blood. 2015; 126(9): 1069.

11. Heterogeneity of human eosinophil glucocorticoid receptor expression in hypereosinophilic patients: absence of detectable receptor correlates with resistance to corticotherapy. Prin L, Lefebvre P, Gruart V, Capron M, Storme L, Formstecher P, Loiseau S, Capron A ClinExpImmunol. 1989; 78(3): 383.

Manuscript Information: Received: February 02, 2019; Accepted: April 16, 2019; Published: April 30, 2019

Authors Infomation: Wai Ching Lee[1]*; Sachdeva Pooja[2]; TanYan Denise[3]; Felik Paulus[4]; Tan Leonard[5]; Baikunje Shashidhar[6]
[1,2]Associate Consultant, Department of Internal Medicine, General Medicine, Sengkang General Hospital, Singapore.
[3]Associate Consultant, Department of Internal Medicine, Hematology, Sengkang General Hospital, Singapore.
[4]Associate Consultant, Department of Anatomical Pathology, Singapore General Hospital, Singapore.
[5]Senior Consultant; Department of Anatomical Pathology, Singapore General Hospital, Singapore.
[6]Senior Consultant, Department of Internal Medicine, Nephrology, Sengkang General Hospital, Singapore.

Citation: Lee WC, Pooja S, Denise TY, Paulus F, Leonard T, Shashidhar B. Idiopathic hyper eosinophillic syndrome presenting as urinary incontinence: A case report . Open J Clin Med Case Rep. 2019; 1534.

About the Journal: Open Journal of Clinical and Medical Case Reports is an international, open access, peer reviewed Journal focusing exclusively on case reports covering all areas of clinical & medical sciences.
Visit the journal website at www.jclinmedcasereports.com
For reprints and other information, contact info@jclinmedcasereports.com