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Case Report
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Henoch-Schonlein Purpura in Adult with Gastrointestinal and Renal Involvement

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ABSTRACT

Background: The pathogenesis of Henoch-Schonlein Purpura (HSP), a multisystem organ-involved small vessel vasculitis, is unknown. HSP is more common in youngsters than in adults. HSP is associated with a history of malignancies, medications, vaccinations, and upper respiratory tract infections. Painful purpura, arthritis, stomach discomfort, and renal involvement are symptoms that may be seen in HSP patients. Adult patients had a much higher rate of renal involvement than children. **Purpose:** To report a case of HSP in an adult with gastrointestinal and renal involvement. **Case**: A 45-year-old man complained of an arm, leg, and waist rash for two weeks before admission to the hospital. He also has stomach pains, nausea, and vomiting to deal with. His symptoms have just appeared now for the first time. During a renal function test, blood urea nitrogen (BUN) and creatine serum levels rose. On a urinalysis, proteinuria and microscopic hematuria were found. Leucocytoclastic vasculitis was discovered during the histopathology investigation. HSP diagnosis was based on the ACR and ICC criteria. The patient was given 3x2 tablets of 0.5 mg dexamethasone, 3x2 tablets of cetirizine, 2x10 mg lisinopril, 2x50 mg ranitidine injection, and 2 grams ceftriaxone. **Discussion**: The clinical symptoms of HSP are used to make the diagnosis. In the vast majority of instances, the treatment is only supportive therapy. Corticosteroid usually are usually used for HSP with multisystem organ involvement to reduce pain severity and faster resolution of renal manifestation. **Conclusion:** Follow up on renal function is needed to monitor the worsening of renal disease.

Keywords: Henoch schonlein purpura, gastrointestinal involvement, renal involvement, adult, human and disease.

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BACKGROUND

Henoch-Schonlein Purpura (HSP), formerly known as IgA vasculitis, is an immune complex vasculitis affecting tiny arteries with predominant IgA deposits that often affects the skin, digestive tract, joints, and kidneys, as well as other parts of the immune system. It is predominantly a disease of childhood; it is rarely seen in adults. Proposed triggers include upper respiratory tract infections, medications, vaccinations, and malignancies.[1] HSP often manifests as purpura in the lower extremities without thrombocytopenia, but articular or gastrointestinal signs might occur 30-40% of the time as the first symptom. Arthritis, stomach discomfort, and renal failure are among the other symptoms of HSP, but pulmonary and neurologic complications are also possible. Erythematous, macular, or urticarial eruptions are the most frequent signs of HSP, and within 24 to 48 hours of initiation, they combine and develop into the characteristic deep ecchymoses and/or palpable purpura that characterize the condition. HSP is more common in children than in adults, with a prevalence of 6-22 cases per 100,000 people per year compared to 3.4-14.3 cases per 100,000 people per year. There are almost 1.5 times as many HSP instances in men as there are in women, which is unusual for a vasculitide.[2]

Henoch-Schonlein Purpura's cause is still a mystery. This vasculitis is caused by the deposition of IgA1-carrying immune complexes on the tiny vessels,

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resulting in the injury and subsequent clinical symptoms. The bulk of the related genes have been involved in inflammation and immunological regulation, and some have been connected to the development of HSP. Class II alleles of the human leukocyte antigen (HLA) have the strongest genetic link to illness. Infectious agents, foods, medications, immunizations, insect bites, and so on have all been shown to have a role in the start of HSP in several epidemiological investigations.[3]

Among the most striking distinctions between adults and children is that adults are more likely to have substantial renal involvement and even end-stage renal disease.[4] Due to invasion of polymorphs or mononuclear cells, leucocytoclastic vasculitis (LCV) with necrosis of the blood vessel wall has occurred. There may be RBCs and fibrin thrombi that have been extravasated.[5] There are two kinds of criteria to establish the diagnosis of HSP; (1) the ACR (American College of Rheumatology) in 1990, and (2) the ICC (International Consensus Conference) in 2006 (EULAR/PRINTO/PRES).[6]

In most cases, HSP is a self-limiting disease with a low fatality rate. Most of the time, the goal of therapy is to provide relief from the symptoms of a condition.[2] Children's long-term renal recovery prospects are great; however, adult patients' long-term recovery prospects are substantially less favorable. End-stage renal disease is prevalent, as is mortality from HSP, which is most often due to gastrointestinal involvement. Purpura and cutaneous relapses are also common.[7] Recurrences occur in 30-40% of individuals during the first year of illness, although they are usually less severe and short-lived than the original symptoms.[2]

CASE REPORT

On January 13th 2019, a 45-year-old male was admitted to Dr. Soetomo General Hospital Surabaya's emergency room with chief complaint of rashes on both arms, thighs, legs and waist. The red rashes have been present since two weeks before being hospitalized. The rash appeared on his thighs and spread to his legs, arms, and waist. He never complained about his rash being itchy and painful. He complained of a burning sensation on the rash, nausea, and vomiting 1 day before admission.

Before hospitalization, he received antibiotics, loratadine, and omeprazole, but there was no improvement. This is the first time he has had the disease. He had diabetes for 1.5 years and had his left leg amputated a year ago. He was taking metformin and insulin for his diabetes. The patient had been taking the metformin by himself since November and last consumed it in the middle of December. There were no history of food and drug allergy, no history of atopy in his family, and none of the family members had the same complaint. No complaint about bleeding spontaneously on any other part of his body. No prior history of using traditional medicine, vaccination, hypertension, or weight loss.

The patient's general physical examination was compos mentis, he looked well with no sign of anemia, icterus, cyanotic or respiratory distress. There was no conjunctivitis, no enlargement of the lymph nodes. The blood pressure was 110/70 mmHg, pulse rate was 80 times per minute, respiratory rate was 18 times per minute and body temperature was 36.5 °C. No abnormalities found on thoracic and abdominal examination. No swelling on his extremities. The dermatological examination of the region antebrachial dextra sinistra, femoral dextra sinistra, cruris dextra sinistra, and thoracal posterior revealed there were multiple palpable purpuras varying in size from 0,5 cm to 1 cm. The diascopy test was negative.

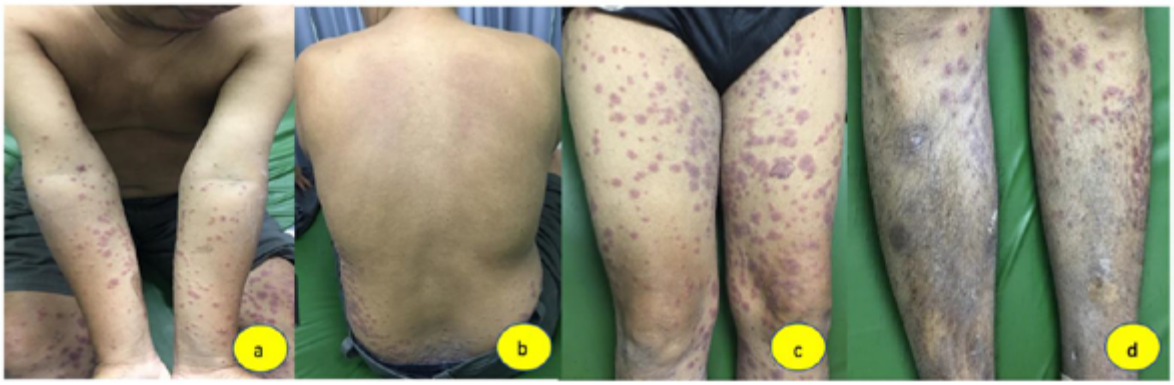

Figure 1. Dermatological state before the treatment. (a) multiple palpable purpuras of varying in size on both arms. (b) multiple palpable purpuras of varying size around the waist. (c) multiple palpable purpuras of varying size on both thighs. (d) multiple palpable purpuras of varying size on both legs.

Laboratory results at the first visit revealed a complete blood count, urinalysis, and renal function test. Blood examination showed that the patient had mild anemia (hemoglobin 9 g/dL), hypoalbuminemia (serum albumin 2.89 g/dL), and hyperglycemia (blood glucose 299 mg/dL). Blood urea nitrogen (BUN) 37 mg/dL and creatinine serum 2.15 mg/dL, markers of renal function, were higher than normal. Urinalysis showed protein +2, bilirubin +1, blood 5+, leucocyte 1+, and microscopic leukocyte 0-2, erythrocyte 25-50. The histology examination revealed that the epidermis showed atrophy and a shortening of the rete ridges. On the dermis, there was infiltration neutrophil and lymphocytes on capillary blood vessels and necrosis of other blood vessels. The conclusion of the histopathology examination was leukocytoclastic vasculitis concordant with HSP.

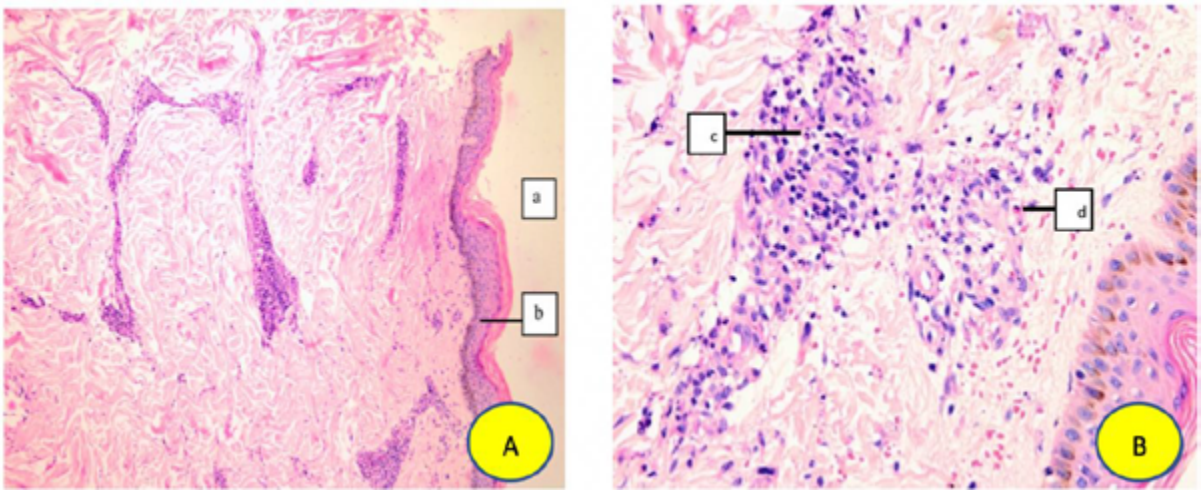

Figure 2. A. Skin Biopsy with Hematoxylin-Eosin coloring at 100x magnification showed atrophy (a) and shortened rete ridges in the epidermis (b). B. At 400x magnification, a skin biopsy stained with Hematoxylin-Eosin revealed neutrophil (c) and lymphocyte infiltration on the capillary blood vessel (d).

The patient was consulted to Internal Department and was given lisinopril 1x5 mg, ceftriaxone 2x1 gram, ranitidine 2x 50 mg, novorapid 6 units, and levemir 12 units at night. The surgery department performed wound care for the left diabetic foot. The patient was treated with dexamethasone 0.5 mg 3x2 tablets, cetirizine 2x10 mg, ceftriaxone 2x1 gram, lisinopril 1x5mg, ranitidine 2x50 mg, novorapid 6 units, levemir 12 units at night. After 15 days, the lesion disappeared.

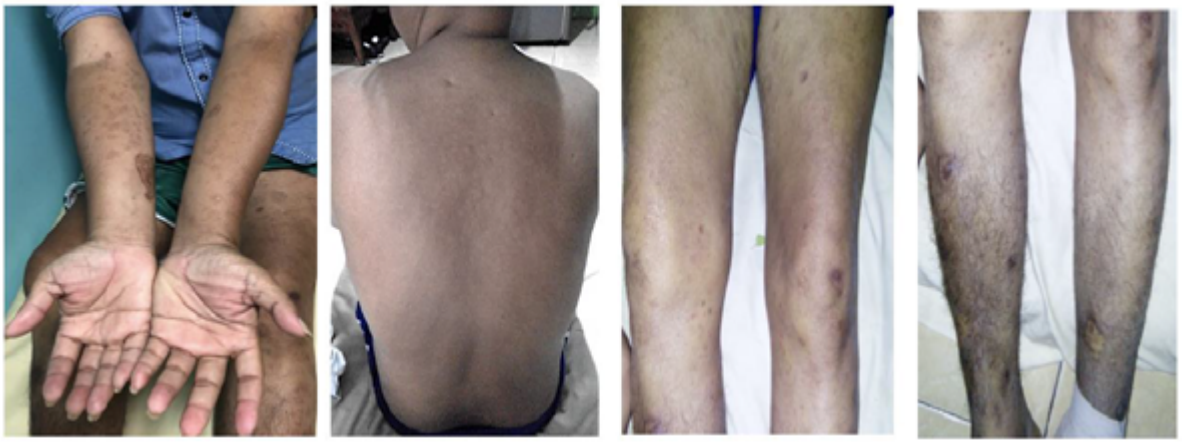

Figure 3. Dermatological state 2 weeks after treatment. On both arms, there were no palpable purpura; on both arms, there were hyperpigmented macules unsharply marginated.

Table 1. Clinical Progression and Treatment

	Day 1	Day 6	Day 11	Day 12
Subjective/objective				
Rash	+++	++	+	-
Abdominal pain	-	-	-	-
Joint pain	-	-	-	-
Palpable purpura	++	+	-	-
Fasting blood glucose (mg/dL)	172	165	145	139
Blood pressure (mm Hg)	110/70	140/80	130/80	130/80
Therapy				
Dermatology and Venereology Department				
Dexamethasone 0.5 mg	3 x 2 tablet	2 x 2 tablet	2 x 1 tablet	-
Cetirizine 10 mg	2 x 1 tablet	2 x 1 tablet	+	-
Fusidic acid 2% ointment	-	+	-	-
Internal Department				
Ceftriaxone 2x1 gram	+	+	-	-
Ranitidine 2x50 mg i.v	+	+	-	-
Novorapid 6 unit s.c a.c	-	-	+	+
Levemir 12 units s.c a.c	+	+	+	+
Lisinopril 5 mg	-	+	+	+

a.c: ante cunam; i.v: intravenous; s.c: subcutaneous

Table 2. Follow up of renal function

	1 month	3 month	4 month
Blood pressure (mm Hg)	110/70	140/80	130/80
Renal function test :			Not evaluated
Serum creatinine	2.15	1.42	
Blood urea nitrogen	37	20	
Albumin	2.89	3.5	
Urinalysis :			Not evaluated
Blood	5+	2+	
Protein	2+	1+	
Erythrocyte (microscopic)	25-50	-	
USG kidney			Normal

USG: ultrasonography

DISCUSSION

Henoch-Schonlein Purpura is a leukocytoclastic small vessel vasculitis driven by an IgA-immune complex that mostly affects children. The traditional HSP triad includes purpura, arthritis, and abdominal discomfort. The buttocks and lower limbs are often affected by this rash, which starts as symmetrical erythematous macules and progresses to purpuric papules. HSP affects six to 24 children in every 100,000 children under the age of 17, depending on the ethnicity of the child. An estimated 70 occurrences per 100,000 youngsters are reported each year in Asia. HSP in adults is estimated to occur in 3.4 - 14.3 cases per million, a 20-fold fewer cases than in children. Typically, the disorder is more common in males.[8] Relapses are common in HSP. Previous studies have shown that relapses occur at a rate of 2.7% to 51.7%. Relapses are usually characterized by a fresh outbreak of a skin condition that is often accompanied by gastrointestinal and renal symptoms.[9] An estimated third of individuals have relapses, usually 4 months after the first onset and with reduced symptoms.[10]

About 20% to 80% of individuals with HSP have kidney involvement, commonly known as Henoch-Schonlein Purpura Nephritis (HSPN), which is characterized by microscopic or macro-hematuria and proteinuria, as well as nephrotic syndrome and

decreased kidney function. Most patients with renal involvement in HSP have a fair prognosis, and HSP is considered self-limiting. In contrast, one to seven percent of patients are diagnosed with end-stage renal disease (ESRD). Recurrence, angioedema, and beginning in the winter were all linked to an increased likelihood of renal involvement, as was the length of time between the onset of the symptoms and their diagnosis, rural residence, and recurrence. Renal involvement is classified to mild, moderate, and severe forms. A mild form is characterized with hematuria, proteinuria < 0.5 gram/day, and normal glomerulus filtration rate (GFR). A moderate form is characterized by hematuria, proteinuria > 0.5 gram/day, and normal GFR. Severe form show acute or rapidly progressive renal failure with crescentic lesions.[11]

The patient in this report was a 45-year-old male who had red rashes on both of his arms, thighs, legs, and waist as a symptom. He also complained of a burning sensation on the rash, nausea and vomiting one day before admission. This is the first time the rashes have appeared. From physical examination there were multiple palpable purpuras of varying sizes, from 0.5 cm to 1 cm. The diascopy test was negative. The symptoms of the patient are compatible with the symptoms of HSP.

Henoch-Schonlein Purpura's etiology is unknown, but an upper respiratory tract infection may be a possible cause. Other infectious agents, immunizations, medicines, and insect bites have been linked to the disease. An exclusion diagnosis, HSP, has no particular diagnostic tests. Thrombocytopenic purpura and secondary immune complex vasculitis must be ruled out. The EULAR/PRINO/PRES classification criteria and the ACR in 1990 are often used to diagnose HSP. In addition to palpable purpura, the clinical presentation includes familiar symptoms such as stomach discomfort, arthritis, and nephritis, as well as other organ involvement and concomitant problems. Inflammatory markers (ESR, CrP, and/or C3 and/or C4) are generally somewhat raised in the blood, as are high-titer autoantibodies (such as ANCA and ANA) and IgM, although the results of the tests are not always specific. Diagnosis calls on the use of feces and urine as sources of occult blood.[12] To aid in the diagnosis, IgA immunofluorescence staining has been shown to be effective. To monitor for glomerulonephritis, it is suggested that patients undergo frequent urine testing for the first six months following the beginning of their illness.[13]

The diagnosis of HSP in this case was based on anamnesis, physical examination, laboratory examination, and histopathological examination. In this patient we have already performed a complete blood count, urinalysis, and renal function test. The result showed anemia (9 g/dL), hyperglycemia 299 mg/dL, and increase in BUN (37 mg/dL) and creatine serum (2.15 mg/dL). Urinalysis showed protein +2, bilirubin +1, blood 5+, leucocyte 1+, and microscopic leukocyte 0-2, erythrocyte 25-50. Urinalysis and renal function tests showed there was renal involvement. Hematuria, proteinuria, nephritic/nephrotic syndrome, and renal failure are all signs of renal involvement. Mao et al. reported a prior meta-analysis in which they concluded that renal damage in HSP patients was associated with older age, higher blood pressure, C3, hemoglobin, and urea nitrogen, as well as reduced albumin.[14] The conclusion of the histopathology examination was leukocytoclastic vasculitis concordant with HSP.

The diagnosis of type 2 diabetes mellitus was based on laboratory findings of 172 mg/dL fasting blood glucose and 216 mg/dL postprandial plasma glucose at 2 hours. Metformin consumption is suspected as a predisposing factor in this case. He has been taking metformin since November 2018 and last consumed it in the middle of December 2018. According to a study from 2006, a 33 year-old woman who self-medicated with metformin was thought to have developed vasculitis as a result.[15] Although immunofluorescence is an important diagnostic marker, the limitation of facilities prevents us from using it in this situation.

The diagnosis of HSP is made clinically, although confirmation by histological analysis, from skin or renal biopsy, is sometimes helpful.[11] The American College of Rheumatology (ACR) established diagnostic criteria for HSP in 1990. Two of the four traits have to be present for the requirement to be met. Patients had to be 20 years or younger at the time of beginning, have palpable purpura (no thrombocytopenia), have bowel angina (diffuse stomach discomfort or a diagnosis of intestinal ischemia), and have histologic alterations demonstrating granulocytes in tiny arterioles and venules (leukocytoclastic vasculitis).[16] According to the 2006 International Consensus Conference, the criteria were widespread abdominal discomfort and any biopsy demonstrating predominant immunoglobulin (Ig) deposition, arthritis (acute, any joint) or arthralgia, and renal involvement (any hematuria or proteinuria).[12,13]

The ACR and ICC both agreed that HSP was a valid diagnosis. The patient met the criteria of the ACC since they exhibited palpable purpura without thrombocytopenia, generalized abdominal discomfort, and a biopsy that revealed leucocytoclastic vasculitis. Also, based on the presence of palpable purpura,

abdominal pain, kidney involvement, and histopathology findings, this patient was diagnosed with HSP according to the ICC.

Patients should be educated to rest, elevate afflicted extremities during the active phase of the illness, and reduced their activity level in order to prevent the purpura.[6] In most situations, therapy is aimed at alleviating symptoms and preventing the progression of the illness. Treatment of pain with acetaminophen is part of supportive therapy, which also involves appropriate hydration, nutrition, and electrolyte balance.[2] There are non-steroidal anti-inflammatory medications (NSAIDs) and acetaminophen/paracetamol for analgesia in arthritis or arthralgia situations.[12] Patients with renal involvement should not use NSAIDs.[6]

Though contentious, it is recommended that corticosteroids be administered only in certain clinical situations when symptoms of a moderate HSP-related illness appear. When treating severe bullous lesions, corticosteroid medication is often essential, although skin disease is seldom severe enough to merit treatment. NSAIDs are the first-line treatment for arthritis and arthralgias, with corticosteroids reserved for the most severe cases of pain or swelling. In a randomized control experiment compared to placebo-treated subjects, corticosteroids have been shown to lessen the intensity and duration of gastrointestinal discomfort. On the first or second day of hospitalization, patients who were treated with corticosteroids had a lower incidence of abdominal surgery, endoscopy, abdominal imaging, and the need for analgesics than those who were not. Renal HSP symptoms can't be prevented by corticosteroid treatment, although it may hasten the cure of modest renal problems that are already present. When administered early in the hospitalization process for HSP patients with significant articular or gastrointestinal pain, these studies show that corticosteroids should only be given to those who have failed to respond to other supportive therapies.[2]

Abdominal and joint discomfort might be lessened by the administration of prednisone (1 mg/kg/day for four weeks).[17] Renal symptoms were not prevented, although they were well treated with prednisone. Last but not least, Jauhola et al. reported 223 newly diagnosed pediatric IgA cases in their publication. Both prednisone and non-prednisone-treated individuals saw no significant differences in their clinical course (abdominal or joint pain, and renal involvement) at six months.[2] It may be necessary to provide pulse methylprednisolone (30 mg/kg to 1 g) in conjunction with immunosuppressive treatment in patients with severe or life-threatening HSP disease symptoms. When HSP complications are severe or life-threatening, additional immunomodulatory therapies such as plasmapheresis, azathioprine, cyclosporine, cellcept, methotrexate, intravenous immunoglobulins, rituximab, and cyclophosphamide have been used, but there are no clear indications of efficacy for these treatments.[2]

Due to the patient's mild gastrointestinal and moderate renal involvement, dexamethasone was administered without the need of adjunctive immunosuppressive therapy. Dexamethasone 0.5mg 3x2 tablets, cetirizine 2x10 mg, ranitidine injection 2x50 mg and ceftriaxone 2x1 gram were given to the patient. Lisinopril 1x5 mg was given to lower the blood pressure. The internal department administered novorapid 6 units and levemir 12 units to manage blood sugar. In this patient, mild proteinuria 1+ persisted after 3 months of follow up. The corticosteroid was withdrawn because the proteinuria was less than 1 gram per day, but he maintained taking lisinopril 1x5 mg and insulin to keep his diabetes under control.

HSP was recognized as a valid diagnosis by both the ICC and the ACR. The patient met the ACR criteria for palpable purpura without thrombocytopenia, widespread abdominal discomfort, and a biopsy that revealed leucocytoclastic vasculitis. Also, based on the presence of palpable purpura, abdominal pain, kidney involvement, and histopathology findings, this patient was diagnosed with HSP according to the ICC. Urinalysis and renal function tests showed there was renal involvement. Significant renal involvement is more common in adults. All patients with HSP should be closely monitored for the development of renal symptoms, which is why we advise them to do so. For the first month, weekly blood pressure and urinalysis tests are advised, followed by biweekly examinations for months 2-6. Those patients whose blood pressure and urinalysis remain normal after six months will have their monitoring come to an end since long-term renal impairment is rare in this patient group.

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