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ORIGINAL STUDY

Adult Onset Still's Disease in Oman

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الْتِهابُ المَفاصِلِ الرُّوماتويديّ اليَفَعِيّ عند الكبار

الملخص: الهدف: إلقاء الضوء على الخصائص الديموغرافية والسريرية والمتغيرات المختبرية وحصيلة الإصابة بالمرض (إن أمكن ذلك) لمرض روماتزمي نادر الحدوث نسبيا وهو الْتِهابُ المَفاصِلِ الرُّوماتويديّ اليَفَعِيّ عند الكبار. ومقارنة النتائج التي نحصل عليها مع ما هو مسجل سابقا. **الطريقة:** تمت دراسة الحالة السريرية، التحاليل المختبرية والاشعاعية لستة من المرضى المصابين بالْتِهابُ المَفاصِلِ الرُّوماتويديّ اليَفَعِيّ عند الكبار عن طريق مراجعة ملخص يحتوي تفاصيل عن الحالة السريرية، ونتائج الفحوصات ذات العلاقة. تم تشخيص المرض اعتمادا على العلامات والأعراض السريرية مدعوما بنتائج الفحوصات المختبرية والاشعاعية لإثبات التشخيص أو استبعاد التشخيصات التفاضلية الأخرى. **النتائج:** بلغ معدل عمر المرضى (٢١,٦) سنة، ارتفاع الحرارة (٨٠,٢٪)، وجود الطفح الجلدي (٨٠,٢٪)، ألم المفاصل (١٠٠٪)، التهاب المفاصل (٦٦,٦٥٪) ومدة التصلب الصباحي لدى المرضى قيد الدراسة مطابقة لما هو مسجل سابقا. كانت غالبية المرضى من النساء (٨٠,٢٪)، وهي عالية نسبيا بالمقارنة مع الدراسات السابقة. أما نسبة عدد المصابين وشدة الإصابة بتضخم الطحال (٣٣,٣٪)، والكبد (١٦,٦٪)، والغدد اللمفاوية (١٦,٦٪) فقد كانت قليلة إذا ما قورنت مع الدراسات الأخرى. سجل حدوث حالة تجلط رئوي مميتة (١٦,٦٪) عند أحد المرضى - ولو أن المتعارف عليه هو بساطة الإصابات الرئوية. لم تسجل أية تأثيرات على الجهاز العصبي، وكذلك السمع والبصر. دراسة نتائج الفحوص المختبرية والإشعاعية بينت بأنها مطابقة لما سجله الباحثون الآخرون. **الخلاصة:** بينت الدراسة بأن الأعراض السريرية ونتائج الفحوصات المختبرية والاشعاعية مطابقة لدرجة ما لما هو مسجل سابقا. ومن المهم ذكر أن الْتِهابُ المَفاصِلِ الرُّوماتويديّ اليَفَعِيّ عند الكبار نادر الحدوث ولكن تعدد أعراض وعلامات المرض تجعله يشابه الكثير من الأمراض الأخرى. لوحظ سابقا وجود اختلافات في سمات الْتِهابُ المَفاصِلِ الرُّوماتويديّ اليَفَعِيّ عند الكبار تبعا لاختلاف المواقع الجغرافية . وقد يكون المرض مسؤولا عن مضاعفات تؤدي إلى تهديد حياة المصاب أحيانا.

ABSTRACT ***Objective:*** To 1. Highlight the demographic characteristics, clinical features, laboratory investigations and outcome if possible of a relatively rare disease (Adult Onset Still's Disease {AOSD}) and 2. To compare our results with those reported earlier by others. ***Method:*** A retrospective review of the clinical, laboratory and radiological manifestations in 6 patients admitted with AOSD. Data were collected from clinical summary of each case highlighting the demographic, clinical features and relevant investigation. The diagnosis was made on clinical base and supported by the laboratory and radiological examinations to confirm the diagnosis and/or exclude other differential diagnoses. ***Results:*** Mean age of patients (21.6), presence of fever (80.2%) and its pattern, skin rash (80.2%), arthralgia(100%), arthritis(66.65%), and the duration of morning stiffness, all these findings were compatible with earlier results. However young adult females constitute (80.2%) of our small group, which is quite high in comparison with others. Splenomegaly (33.3%), hepatomegaly(16.6%), and lymphadenopathy(16.6%) were less than that reported by others who have more serious intra-abdominal visceral involvement. One patient (16.65%) had a fatal pulmonary embolism, although usually pulmonary involvement is a mild one. None of our patients had neurological, ophthalmological or hearing involvement. The results of the investigations and radiological findings are more or less similar to those in other series. ***Conclusion:*** The clinical and laboratory characteristics of our small number of patients are more or less consistent with findings of others. It is important to keep in mind that AOSD is an uncommon syndrome with a range of signs and symptoms which are non-specific and may simulate a variety of connective tissue and general medical problems. Differences in the expression of AOSD were found between patients from different locations and the disease can be responsible for life-threatening complications.

George Frederic Still described a form of chronic joint disease in childhood in 1897.[1] This syndrome originally consisted of fever, arthritis, lymphadenopathy and splenomegally which may be associated with skin rash.[2] The rash is characterized by red evanescent macules with distinct borders and may be associated with isomorphic (koebner) phenomena.[3] The adult form was recognized for the first time in 1967.[4] It is primarily a disease of young adults, rarely diagnosed after the age of thirty five,[5] although it has been reported affecting patients in their seventh decade of life.[6,7] Arthralgias are present

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in virtually all patients with the fever spikes. Chronic arthritis with disability may be a sequel in up to 20% of cases.[8-10] Myocardial[11] and endocardial[12] involvement are rarely seen. Pulmonary involvement is usually transient and mild but severe restrictive lung disease has been observed.[13-15] Neurological,[16,17] hepatic,[9,18] ophthalmological involvement[19-21] and hearing loss[22] have been reported too. In rare cases renal disease may occur.[23]

Several sets of diagnostic criteria have been proposed[24-26] for the diagnosis; however, Cush *et al*[24] criteria are a practical guide. Here we present a personal experience of the clinical characteristics for 6 patients with Adult Onset Still's Disease (AOSD).

The objective was to study the natural history of our patients inflicted with this relatively rare disease, which may mimic many other diseases, and to compare our results with those reported by others.

METHOD

This is a review of the clinical, laboratory and radiological manifestations in 6 patients admitted under care of one of the authors (Faisal Al-Temimi) over 10 years time (1992-2002) with AOSD. Data were collected from the clinical summary of each case highlighting the demographic, clinical features and relevant investigation. The diagnosis was made on a clinical basis and supported by the laboratory and radiological examinations to confirm the diagnosis and/or exclude other differential diagnoses.

Table 1. ***Demographic characteristics of 6 patients with Adult Onset Still's Disease***

S. No	Age (Years)	Sex	Marital State	Occupation	Pregnancy
1	19	F	Married	House Wife	No
2	20	F	Single	Student	\
3	22	F	Single	House Wife	\
4	22	F	Single	Teacher	\
5	23	F	Married	House Wife	No
6	24	M	Single	P G Student	\

RESULTS

Five patients were females and one was a male. Demographic characteristics were as shown in Table 1. Duration of the disease was from 3 months to 7 years, Symptoms and/or signs of patients were as shown in Table 2.

DISCUSSION

AOSD is a cause of fever of unknown origin, and frequently diagnosis may have missed in its early stage. The diagnosis depends predominantly on clinical features. The combination of hectic temperature and the salmon pink colored skin rash should always raise the possibility. Our small group which consists of 6 patients illustrates many of the features of AOSD (5 females (80.2%)and 1 male (16.65%)), while 51% were females in Ohta A *et al* reviewed groups.[27] The mean age of our patients was 21.6% (19-24), which is compatible with what had been reported.[5] However, an

Table 2. ***Symptoms and signs***

Presenting Symptons/Signs		No. of patients	%
Fever > 39°C		3	50.0
Fever < 39°C		2	33.3
No Fever		1	16.65
	Continous	2	33.3
	Night Fever	2	33.3
	Hectic	1	16.65
	Fever & Chills	1	16.65
Skin Rash		5	80.2
	Pruritc	1	16.65
	Non Pruritc	4	66.6
	Trunk	4	66.6
	Trunk & Legs	1	16.65
Arthralgia		6	100.0
Arthritis		4	66.6
Morning Stiffness (30 mins - 2Hours)		4	66.6
Shortness of Breath, Cough		2	33.3
Sore Throat		3	50.0
Tachycardia (> 100/min)		4	66.6
Splenomegally		2	33.3
Hepatomegally		1	16.65
Pericardial effusion		2	33.3
Lymphadenopathy		1	16.65
Mouth ulcers		1	16.65
Menstrual disturbance		1	20.00
Hair loss		1	16.65
Upper Gastrointestinal bleeding		1	16.65

Table 3. ***Joints involved and their frequency in 6 patients Adult Onset Still's Disease***

Joints	No. of patients	%
Both Knees	4	66.6
Ankles	3	50.0
Wrists	3	50.0
Elbows	2	33.3
Hips	2	33.3
Cervical spine	2	33.3
Metacarpophalangeal joints	1	16.65
Metatarsophalangeal joints	1	16.65
Shoulders	1	16.65
Acromioclavicular joints	1	16.65
Sternoclavicular joints	1	16.65
polyarthritis	4	66.6
Arthralgia	6	100.0

onset up to the 7th decade of life has been described also.[6,7]

Of 6 patients 5 (80.2%) patients febrile at presentation and 2 (33.3%) patients had temperatures of more than 39°C, while one patient had a hectic temperature, this is compatible with that of Pouchot *et al,*[10] but slightly less than that of Ohta *et al.*[27]

Salmon pink, macular, or maculopapular skin rash was perceived in 5 (80.2%) patients. Only one (16.65%) patient suffered from pruritis. Rashes were present on the trunk in all the 5 patients, and involved the legs in one. This is in agreement with what has been reported earlier.[28.29]

In AOSD, the systemic complaints may overshadow the joints manifestations, actually joints involvement may develop 2 years after the initial onset of the disease.[6] In our group arthralgia was present in all patients especially during febrile episodes. Arthritis was seen in 4 (66.6%) patients only. One (16.65%) of the patients had persistent chronic arthritis; this is consistent with findings in patients reviewed by Ohta *et al*[27] and others.[8-10] The main joints affected [Table 3]

Table 4. ***Laboratory and radiological findings***

Test		No. of Patients	%
CBC			
Haemoglobin	< 11gms	4	66.3
	> 11gms	2	33.3
	Hypo Microcytic RBC's	3	50.0
	Hypo Normocytic RBC's	3	50.0
WCC	> 11000/dl	4	66.6
	< 11000/dl	2	33.3
	Neutrophil Leucocytosis > 80%	4	66.6
Platelets Count > 400, 000/mm^3		2	33.3
Elevated Erythrocyte Sedimentation Rate(ESR)		5	80.2
Elevated liver enzymes		2	33.3
Raised C-reactive protein		4/4	100.0
Negative Rheumatoid factor		6	100.0
Negative Antinuclear antibody(ANA)		5	80.2
Abnormal urine routine examintion (pyuria,albuminuria)		2	33.3
Negative VDRL		6	100.0
Chest X ray			
	Cardiomegally	1	13.65
Joints X-ray			
	Osteopenia	2	33.3
	Decreased J. space	2	33.3
	Sclerosis and, subchondral & cyst formation	1	16.65
Echocardiography study (ECHO)			
	RV enlargement	1	16.65
	Pericardial effusion	2	33.3

were those of the lower limbs, the knees in 4 (66.6%) patients, followed by ankles in 3 (50%) patients, wrists in 3 (50%) patients, then elbows. The axial joints and joints of the upper limbs are affected to lesser extent as shown in Table 3. A polyarticular pattern was seen in all 4 patients with arthritis. Significant (30 minutes-2 hours) morning stiffness was present in 4 (66.6%) patients. Two (33.3%) patients had cough and shortness of breath, one was an acute episode consistent with a pulmonary embolism which unfortunately led to death. It has been showned that mild transient pulmonary involvement not unusual the and severe restrictive lung disease has been observed.[13,14]

Fifty percent of our patients had sore throats. This figure is lower than that in Ohta *et al*[27] series (92%). The prevalence of pericarditis, was similar to that seen in children with Still's disease and may occur in adults too, early in the course of the disease and in association with systemic exacerbations.[30,31] In our patients, 4 (66.6%) patients had significant tachycardia, and 2 patients proved to have pericardial effusion by echocardiography, one of whom had right ventricular enlargement too (this patient had pulmonary embolism). However, echocardiography study was not performed for others who had asymptomatic cardiac involvement. Electrographic examination showed nonspecific asinus tachycardia.

Splenomegaly was seen in 2 (33.3%) patients, one (16.65%) patient had hepatomegaly and lymphadenopathy. These are lower than the figures of Ohta *et al,*[27] which were 52%, 42% and 63% respectively. Raised liver enzymes were present in 2 (33.3%) patients and serum albumin was normal in all our patients in comparison to raised enzymes in 73% and a serum albumin below 3.5 gm/dl in 81% of Ohta *et al's* reviewed patients.[27]

Menstrual disturbance was seen in 20% of females. Diffuse hair loss and mouth ulceration were each seen in one (16.65%) patient only. Alopecia was seen in 24% of Pouchot *et al* group.[10] Upper gastrointestinal bleeding was a presenting problem in one case (16.65%), after aspirin ingestion for high fever. No neurological, ophthalmological or hearing problems were present in our patients. Raised ESR was present in 5 (80.2%) patients in comparison to 99% of cases reviewed by Ohta *et al*.[27] The explanation for this is that one of our patients was in remission from the disease. Four (66.6%) patients had their haemoglobin levels below 11 gm and WBC more than 11000/dl while the platelets count was more than 400,000/dl in 2 (33.3). The RBCs were hypochromic normocytic in 3 (50%) patients and hypochromic microcytic in the other 3 (50%) patients. More than 80% had leucocytes, which were predominantly neutrophils in 4 (66.6%) of patients. The C-reactive protein was measured in 4 patients only and was found raised in all. The rheumatoid factor was negative in all patients, and the ANA was positive in one patient. In the patient with positive ANA there were no other supportive criteria to diagnose SLE and the anti ds-DNA was not present. This autoantibody profile is consistent with findings of others.[27]

The chest X-ray was normal in all except one which showed cardiomegaly, while articular x-rays showed osteopenia and decreased joint space in 2 (33.3%) patients, one of these two has long standing disease with joint sclerosis also.

CONCLUSION

The clinical and laboratory characteristics of our small number of patients are more or less consistent with the findings of others. It is important to keep in mind that AOSD is an uncommon syndrome with a range of signs and symptoms which are non specific and may simulate a variety of connective tissue and general medical problems. However, a physician should keep a high index of suspicion and the combination of hectic temperature and salmon coloured skin rash should suggest the diagnosis. It is important to reemphasize the fact raised by Bujack *et al*[19] that not all manifestations of the syndrome may be present with each febrile episode and careful collection of long term historical data can be of great assistance in making the diagnosis.

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