Takayasu Disease in Hospitalized Patients of Teaching Hospitals of Shiraz University of Medical Science: A Retrospective Study
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ABSTRACT
Takayasu arteritis is an inflammatory and obstructive disease of large size arteries, that is more prevalent in Asian and orient countries, although is not limited to especial race or geographic area. Etiology of this disease that is seen more, in young females is unknown yet, although some theories about role of infectious agents or autoimmune processes are present. The goal of this study was determination of epidemiologic character of Takayasu disease in our country (IRAN) that is an Asian country and has young population. In this retrospective research 20 patient with definite diagnosis of Takayasu arteritis that had been admitted in teaching hospitals of SHIRAZ University of medical science during 1985-2000 was studied and their medical records reviewed carefully. Results: Mean age of patients was 27.3 years old, that 70 % of them were between 10 to 30 years old. Weakness, headache and upper extremity claudication were the most prevalent symptoms. Hypertension and decreased brachial pulse were the most prevalent signs in physical examination. Among the clinical findings high prevalence of severe and very severe hypertension (40%) was remarkable. Microcytic anemia (70%) was the most prevalent laboratory finding in our patients. Regarding to vascular involvement, the most prevalent involved artery was left subclavian artery and involvement of renal arteries, with poorer prognosis, was in next degree of prevalence. Conclusion: Regarding to sex ratio, age of onset, symptoms and signs of presentation and vascular involvement, results of this study was relatively similar to medical text books statistics. High prevalence of severe and very severe hypertension in our patients may be due to high prevalence of involvement of renal arteries and abdominal aorta (8 patients of 17 patients with available angiography results). In course of hospitalization two patients was expired that in both of them severe involvement of renal arteries had been discovered angiographically. This finding can shows bad prognosis of Takayasu patients with renal artery involvement.

Keywords: takayasu disease, arteritis, vasculitis, hypertention.
1. Review Articles

1.1 Introduction

Takayasu disease that for the first time was reported by a Japanese ophthalmologist (Mikito Takayasu) in 1905 is a vasculitis of large arteries and is seen more in Asian countries. It is the third most common vasculitis of pediatrics, in the world (after Henoch shonlin purpura and Kawasaki disease) and involves young females more. (Miller, 2000). We have studied this disease in Iran country that is an Asian country with a young population and so it can be regarded of greats of importance.

Takayasu in his report in 1905 showed a unique involvement of retinal arteries of a 21 years old female. In 1940 Ohta, another Japanese scientist improved that this unique feature of retinal artery involvement has been produced due to ischemia after obstruction of cervical vessels. Shimizo and Sano in 1951 summarized clinical features of this disease in 6 of their own patients and 25 other patients and edited it in English language under name of pulseless disease and for this, it has been known as pulseless disease in western countries (Numano, 1999)

Takayasu disease is an obstructive and inflammatory disease of medium and large arteries with more involvement of aortic arc and it’s large branches that due to this, it referred to as Aortic arc syndrome (Fauci, 2001).

1.2 Epidemiology

Although Takayasu disease is more prevalent in eastern countries(Lindsay, 2001) and is seen more in Asian countries such as India, Srilanka, China, Korea, Thailand and Singapore (Jain S,1996), but is not limited to one special race or geographic area (Fauci, 2001).

Annually about 100_200 new patients of Takayasu are been diagnosed in Japan. The most cases have diagnosed at ages of 10 to 30 (Sergent, 2001)

In about 1/3 of cases, disease is initiated before 20 years of age and symptoms usually appear after age of 10 years, although it has involved children with age of 8 months. Takayasu is more common in girls of around puberty and young females (Fauci, 2001). The proportion of female to male is different from 2.5/1 to 4/1 and in some reports 8-9/1 (Sergent, 2001; Lindsay, 2001).

1.3 Etiology

There are some reports about relation of disease with some spirockettal, bacterial, mycobacterial and viral infections, but there isn’t any convincing document about role of these infectious diseases in promoting Takayasu disease (Sergent, 2001) Also, association of Takayasu disease with autoimmune diseases in several patients (Sergent, 2001) and foundation of anti endothelial cell antibodies in some patients and some other findings support from an autoimmune process role (Lindsay, 2001) In some studies in Asia, Takayasu disease has been reported in association with TB (Tuberculosis) (Miller, 2000).
1.4 Pathology

Pathologic findings of involved vessels show involvement of all three layers including intima, media and adventitia of vessels, that ultimately leads to occlusion and narrowing of vessels (Park, 1996).

1.5 Clinical presentation

Symptoms of disease often are nonspecific, including: malaise, headache, weakness, anorexia, fever, weight loss, night sweet, dyspnea, blurred vision, palpitation, claudication and vertigo (Sharma, 1996) In one research in Japan that has done on about 130 patients between 1974 to 1976, the most common symptoms were: numbness (72.3%), general weakness (66.8%), syncope (64.5%), palpitation (55.2%), neck pain (38.1%) and blurred vision (23.9%). In other research in India that has been done on 106 documented cases of Takayasu at a period of 16 years, the most common symptoms were: headache (44.3%), dyspnea (26.4%), syncope (26.4%), palpitation(18.9%), visual problems (12.3%), nausea & vomiting and weight loss(9.4%). In this research also hypertension with prevalence of 77.4% has been the most common findings in physical examination of patients(Jain,1996)

Overall in physical examination, high blood pressure, bruit on subclavian, carotid and abdominal aorta, decreased pulse of brachial artery, blood pressure difference between right and left extremities, retinopathy and arthritis may be seen (Fauci, 2001; Sergent, 2001). These presentations mainly depend on involvement of different arteries in this disease and so that the prevalence of presenting symptoms and signs varies in different reports. For example in Indian patients, due to high prevalence involvement of abdominal aorta and renal arteries, hypertension has been the most prevalent clinical findings and in Japanese patients, due to high prevalence involvement of aortic arc and carotid arteries, visual symptoms such as blurred vision and blindness, claudication and general symptoms such as weakness and malaise has been more common ( Numano, 1999).

This disease is the most common cause of renovascular hypertension in Asian south east countries such as: India, China, Korea and Japan (Jain, 1996). Overall, hypertension is seen in about ⅓ of patients.

1.6 Laboratory findings

Usually hypo chromic microcytic anemia associated with mild leukocytosis is seen in complete blood counts of patients. Polyclonal immunoglobulin has been increased in about ⅓ of Takayasu disease patients (Miller, 2000) Erythrocyte sedimentation rate in these patients increases and is usually equal to or more than 60 mm/hr .ANA, RF, and ANCA maybe rarely and occasionally be positive (Lindsley C B, 2001) In angiography of 90% of patients with Takayasu disease stenosis of left subclavian artery has been seen, (Round, 1998) and stenosis of right subclavian artery and left carotid and brachiocephalic arteries are in second degree of prevalence .Pulmonary arteritis and involvement of abdominal aorta also develop in half of patients
Involvement of vessels differs in different areas and countries, for example in Europe, United States and Japan the involvement of arteries is more obstructive than in patients in India, Thailand and Africa arterial aneurisms are more common forms of arterial involvement (Lindsley, 2001).

1.7 Diagnosis

Due to nonspecific clinical presentations, Takayasu disease often been diagnosed very late. There were no specific diagnostic criteria for this disease till 1988, when Ishikawa interpreted the first diagnostic criteria. This criterion included of 1 obligate criterion (age of under 40 years) 2 major criteria (1-stenosis and occlusion of right subclavian artery and 2-stenosis and occlusion of left subclavian artery) and 9 minor criteria (elevated ESR, carotid artery tenderness, hypertension and involvement of different arteries such as: aorta and main aortic branches) (Sharma, 1996).

In 1990 American Rheumatology College suggested a collection of 6 criteria for diagnosis of disease, and demonstrated that existence of 3 or more of these criteria documents this disease with high sensitivity (90.5%) and specificity (97.8%). These 6 diagnostic criteria are:
1- Age of onset of disease below 40.
2- Claudication of extremities.
3- Decreased pulse of one or both brachial arteries.
4- More than 10mmHg difference between systolic blood pressures of arms.
5- Bruit on subclavian artery or abdominal aorta.
6- Stenosis or occlusion of aorta or main its branches that is seen in angiography.

1.8 Prognosis

Course of disease is variable and spontaneous improvement also may occur. Mortality rate reports have been variable from less than 10% to 75%. 25% of patients never go to remission period. 5 years survival of patients with Takayasu disease has been reported till 35% (Miller, 2000).

1.9 Treatment

Prednisolone and mthotrexate have been applied for treatment of disease and for controlling of severe inflammations cyclophosphamide is used (Miller, 2000). Although therapy with glucocorticoids with doses of 40-60 mg, improves symptoms of disease, but no study has proven that this therapy alone increases the patient’s life-long.

Drug therapy with steroid for improvement of acute symptoms, plus surgery or angioplastic intervention for removal of arterial stenosis have increased the patient’s life-long and decreases mortality rate, (by decreasing risk of stroke, correcting HTN due to renal arterial stenosis and improving perfusion of different body organs).
With these treatments, mortality rate has reached to 10%. In patients who don’t response to steroid therapy, methotrexate with doses to 25 mg weekly have had good results, but prolong studies for proving this, is required (Fauci, 2001).

In cases of severe stenosis that the patient’s work has been disrupted or there is mortality risk for patients, surgery like bypass of involved artery is done (Round, 1998).

2. Our study

2.1 Methodology

In this retrospective research files of patients with impression of Takayasu disease that had been admitted in teaching hospitals of Shiraz city in Iran (3 great hospitals) from 1985 to 2000, have been studied. Data’s related to patients including age, sex, clinical presentations, laboratory findings, angiographies and type of treatment were extracted from files and this information were analyzed carefully. From total 28 files that reviewed, at last 20 patients had enough criteria for diagnosis of Takayasu disease. Our criteria for diagnosis of this disease have been the American College of Rheumatology criteria that suggested in 1990 and mentioned before.

2.2 Results

Regarding to age of patients, the range of our patients’ age was from 13 to 75 years old. (Mean age of patients was 27.3 years old). 70% of patients had an age of between 10 to 30 years. Also 90% of patients (18 pts) were below 40 years. In respect to sex, the proportion of female to male in our study was 4/1 (16 female and 4 male).

2.2.1 Clinical features

The most common symptoms of patients were weakness and headache with prevalence of 65%. Claudication of upper extremities was seen in 50% of patients. Prevalence of lower extremity claudication in patients was 25%. About 1/3 of patients had been presented with general nonspecific symptoms such as: fever and general weakness. (35% of patients) Ophthalmic symptoms had prevalence of 30%, and blurred vision was the most common. (25%) all presenting symptoms of our patients with their prevalence of them have been listed in Table 1.

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Number of patients (prevalence)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weakness</td>
<td>13(65%)</td>
</tr>
<tr>
<td>Headache</td>
<td>13(65%)</td>
</tr>
<tr>
<td>Upper extremity claudication</td>
<td>10(50%)</td>
</tr>
<tr>
<td>Fever</td>
<td>7(35%)</td>
</tr>
<tr>
<td>Numbness</td>
<td>7(35%)</td>
</tr>
<tr>
<td>Signs</td>
<td>Number of patient (prevalence)</td>
</tr>
<tr>
<td>--------------------------------------</td>
<td>--------------------------------</td>
</tr>
<tr>
<td>Hypertension (HTN)</td>
<td>15 (75%)</td>
</tr>
<tr>
<td>Decreased brachial pulse</td>
<td>15 (75%)</td>
</tr>
<tr>
<td>Systolic murmur in heart sound</td>
<td>11 (55%)</td>
</tr>
<tr>
<td>Bruit on abdomen</td>
<td>6 (30%)</td>
</tr>
<tr>
<td>Carotid artery bruit</td>
<td>4 (20%)</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>4 (20%)</td>
</tr>
<tr>
<td>Bruit on subclavian artery</td>
<td>1 (5%)</td>
</tr>
</tbody>
</table>

40% of patients (8 from 20 pts.) had systolic blood pressure of above 180 mmHg. Table 3 shows blood pressure range of our patients and their prevalence’s.

<table>
<thead>
<tr>
<th>Degree of blood pressure</th>
<th>Range of blood pressure (mmHg)</th>
<th>Number of patients (prevalence)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal blood pressure</td>
<td>&lt;140/90</td>
<td>5 (25%)</td>
</tr>
<tr>
<td>Mild HTN</td>
<td>140-159/90-99</td>
<td>3 (15%)</td>
</tr>
<tr>
<td>Moderate HTN</td>
<td>160-179/100-109</td>
<td>4 (20%)</td>
</tr>
</tbody>
</table>
2.2.2 Laboratory findings

Anemia was the most common laboratory findings in our patients (70%), that 50% of patients had microcytic anemia (MCV<80 fl). Hemoglobin level of below 12gr/ dl in females and below 14gr/dl in males has been accounted as anemia.

From total of 18 patients that their WBC counts were present, 8 patients had WBC count of above 10000/ µl. (44.4% of pts.) Erythrocyte sedimentation rate test had been done for 13 patients that from those 5 patients had elevated ESR (ESR ≥ 60mm/ hr).

Some immunologic laboratory test results of patients have been listed in Table 4.

Table 4: Results of some immunological tests of our Takayasu patients (20 pts)

<table>
<thead>
<tr>
<th>Laboratory test</th>
<th>Number of patients who test had been done for them</th>
<th>Number of patients with positive or high test result</th>
<th>Number of patients with negative or normal results</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP</td>
<td>12</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>ANA</td>
<td>10</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>RF</td>
<td>6</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>ANCA</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>C3</td>
<td>7</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>C4</td>
<td>6</td>
<td>2</td>
<td>4</td>
</tr>
</tbody>
</table>

2.2.3 Angiography

Angiographic results of 17 patients were present in their files. These results showed that the most common involved artery in our patients was subclavian artery (13 pts from 17 pts). Renal artery stenosis was present in 5 patients (from 17 pts.). Table 5 shows the different arterial involvement of patients with their prevalence with details.

From 17 patients that angiography has been done for them, 10 patients had involvement of more than 1 artery. In all of 17 patients involvement of arteries was obstructive or stenotic type and no arterial aneurysm had been seen in our patients.

All of 5 patients with renal artery involvement had HTN and 4 of them had severe and very severe HTN (BP>180/110 mmHg). Also very severe HTN had been seen in all 2 patients with aortic arc stenosis (BP > 210/120 mmHg).

Table 5: Involved arteries with type of involvement in angiographic findings our Takayasu patients (total: 17 patients with angiographic results)

<table>
<thead>
<tr>
<th>Involved artery</th>
<th>Number of pts. With involved</th>
<th>Number of patients with unilateral left</th>
<th>Number of patients with bilateral arterial</th>
<th>Number of patients with occluded</th>
<th>Number of patients with aneurysm</th>
</tr>
</thead>
</table>
2.2.4 Drug treatment

Treatment protocol for Fifteen patients included prednisolone 40 mg to 60 mg/day, some patients treated by antihypertensive drugs and cyclophosphamide.

2.2.5 Surgical treatment

Three out from 5 patients were treated by renal surgery:
1- Nephrectomy of right kidney for decreasing very severe HTN.
2- Replacement of stenotic part of renal artery by saphenous vein graft.
3- Auto transplantation of right kidney.
Also diagnostic and therapeutic surgery had been done for 3 patients that had been done for diagnosis and release of pressure on arteries.

2.2.6 Prognosis

In period of admission in hospital 2 patients had been dead that each of them had severe bilateral renal artery stenosis in their angiographies.

3. Conclusion

Results of this research confirm that Takayasu disease involves young women more. (Female/ male rate of 4/1 and mean age of patients were 27.3 years). Although there isn’t any specific diagnostic signs and symptoms for Takayasu disease, claudication, HTN and decreased brachial artery pulse are the most common findings in history and physical examination of patients.

It showed high prevalence of HTN in our patients, (75%) maybe due to relatively high prevalence of renal artery and abdominal aortic involvement in patients. High prevalence of decreased brachial pulse in our patients is due to high prevalence of stenosis and obstruction of subclavian artery.
Although anemia had a high prevalence in our Takayasu patients, (70%) but there isn’t any specific diagnostic laboratory test for Takayasu disease.

History and physical examination play an important role in diagnosis of Takayasu disease. (5 of from 6 diagnostic criteria can be diagnosed by true history and physical examination.)

This disease must be present in differential diagnosis of any young female patient with presentation of extremity claudication or signs of HTN and decreased brachial pulse.

It seems that involvement of renal arteries in Takayasu disease is associated with poor prognosis because 3 patients of our study with involvement of renal arteries had been needed to surgical operation and 2 patients with this involvement had been dead during hospitalization.

References


