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Case Report

A current concept review of 9 year old boy with hemophilic arthropathy

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ABSTRACT

The knee is frequently affected by severe orthopedic changes known as hemophilic arthropathy (HA) in patients with deficiency of coagulation factor VIII or IX and thus this manuscript seeks to present a current perspective of the role of the orthopedist, physiotherapist and pathologist in the management of these problems. Lifelong factor replacement therapy (FRT) is optimal to prevent HA, however adherence to this rigorous treatment is challenging leading to breakthrough bleeding. In patients with chronic hemophilic synovitis, the prelude to HA, Synoviorthesis is the optimal to ameliorate bleeding, judicious physiotherapy to prevent chronic joint disease.

Keywords: Hemophilic arthropathy, Factor replacement therapy, Chronic hemophilic synovitis, Synoviorthesis

INTRODUCTION

Hemophilias are the commonest hereditary clotting deficiency disorder. They are X-linked recessive disorders. Hemophilia A is due to factor VIII deficiency. Hemophilia A is a severe and often fatal hemorrhagic diathesis that affects male children of certain families. This is evident from the writings of Rabbi Simon ben Gamaliel (second century AD) in the Talmud, and those of Maimonides, the Hebrew physician and philosopher, and Albucasis, the Arab (twelfth century).[1] Complete monographs have reviewed the early literature.[2] The hemostatic abnormality in hemophilia A (factor VIII deficiency/classic hemophilia) is a deficiency or abnormality of a plasma protein. This substance (the antihemophilic factor, AHF, AHG, factor VIII) was elusive and difficult to purify. The genetics of this disorder have been studied intensively.[3-5] In such a disorder, the defective gene is located on the X chromosome.[6] In males who lack a normal allele, defect is manifested by clinical hemophilia. Affected male will not transmit the disorder to his sons (generation II, numbers 4 and 5), because his Y chromosome is normal. However, all of his daughters will be carriers of the trait because of the presence of a normal allele from the mother. The female carrier will transmit the disorder to half of her sons (generation III, numbers 6 and 7) and the carrier state to half of her daughters (generation III, numbers 8 and 9).

Hemarthrosis is the most common, the most painful, and the most physically, economically, and psychologically debilitating manifestation of the inherited coagulation disorders. Patho physiologically bleeding presumably originates from the synovial vessels and develops spontaneously or as the result of imperceptible or trivial trauma. Hemorrhage occurs into the joint cavity or into the diaphysis or epiphysis of the bone. In the acute stage, the synovial space is distended with blood. Muscular spasm further increases the intra-synovial pressure. Hemorrhage into the periarticular structures is a common complicating feature that occurs most often around small joints.

The joint may regain normal function after the first episodes of hemarthrosis. More often, however, the absorption of intra-articular blood is incomplete, the retained blood produces chronic inflammation of the synovial membrane, and the joint remains swollen, tender, and painful for months or years, often in the absence of bleeding. Acute hemarthrosis almost invariably recur from

time to time. With each recurrence, the synovium becomes progressively more thickened and vascular; folds and villi, which predispose to synovial injury during even minimal activity, may form. Proliferating synovium often fills and distends the joint, which remains swollen and enlarged in the absence of bleeding or pain (chronic proliferative synovitis).[7] Together with the weakening of the periarticular supporting structures, this process predisposes the joint to recurrent episodes of bleeding. Repeated bouts of hemarthrosis, with the associated subchondral and synovial ischemia, result in progressive loss of hyaline cartilage, particularly at the margins of the joint. Large punched areas of destruction are sometimes produced by subchondral hemorrhages and, in the cancellous structure of the bone, cavitation may be caused by intraosseous hemorrhage. Through disuse, diffuse demineralization of the involved bones also may occur. Subperiosteal hemorrhages are not common.

The terminal stage of hemarthrosis is called chronic HA.[8] It is manifested by fibrous or bony ankylosis of the larger joints; complete destruction may take place in the smaller articulations because of the weaker joint structure and the thinner cortices of the smaller bones. Other permanent sequelae of hemarthrosis include atrophy and proliferation of bone, roughening of the articular surfaces with lipping and osteophyte formation, bone necrosis and cyst formation, stunted growth as the result of interferences with nutrition of the bone, and accelerated development and overgrowth of the epiphysis caused by excessive blood flow. Chronic HA is less common now because of widespread use of prophylactic replacement therapy.

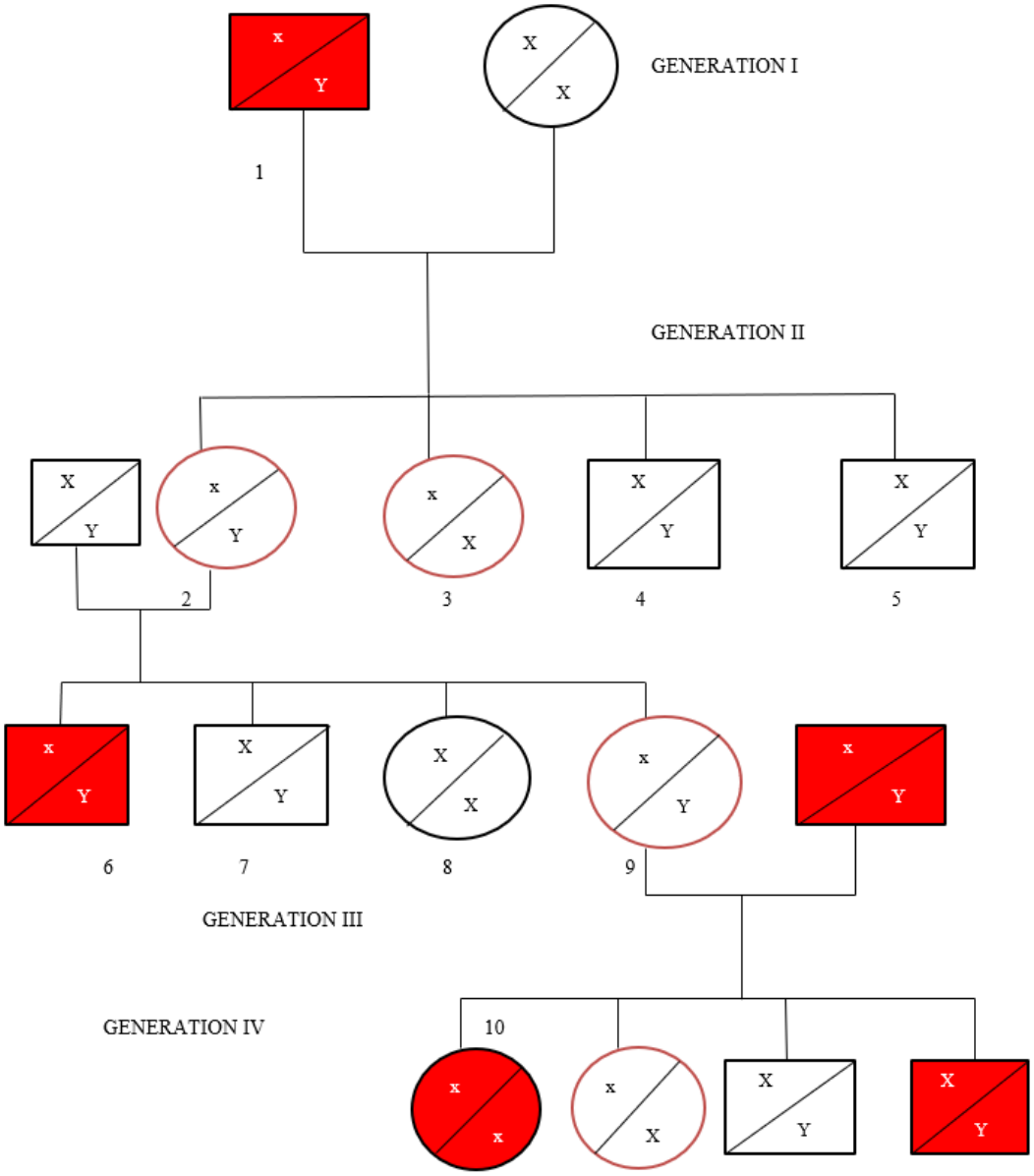


Figure 1: The inheritance of hemophilia A and B. The pedigree is hypothetical.

X=normal X chromosome, x=abnormal X chromosome, squares indicate male, circles indicate female, fully shaded squares/ circles indicate affected members, brown-shaded circles indicate carriers.

CASE REPORT

A 9 year old male presents DR. Virdi hospital orthopedic OPD with the following chief complaints exacerbating pain, inability to stand. Physical examination revealed muscle spasm and limited motion of the affected right knee joint. The joint was warm, inflamed, grossly distended and discolored, external evidence of the joint bleeding was absent.

Past medical history of illness

Patient was diagnosed with hemophilia A at the age of one and a half year when his parents saw some unidentified changes around his joints (ankles, elbows, hips, shoulders, small joints of the hands). Laboratory investigations revealed factor VIII functional inactivity. They visited AIIMS Delhi to seek medical attention due to unavailability of antihemophilic factor injection at Amritsar, as GNDH started importing injection now the patient is regularly being infused with the Antihemophilic Factor Injection at Guru Nanak Dev hospital Amritsar.

Clinical manifestations

The most dramatic manifestation of hemophilia A is exsanguinating hemorrhage from a tivial traumatic injury.[9] However, the most characterstic bleeding manifestations, such as hemarthrosis, often develop without significant trauma. Their frequency and severity generally relates to the blood level factor VIIIc. Three categories of severity may be distinguished arbitrarily. Severe deficiency (factor VIIIc level less than 1 U/dl) is manifested clinically by repeated and severe hemarthroses that almost invariably result in crippling arthropathy in the absence of replacement therapy; such severe cases often are cakked classic hemophilia. Moderate deficiency (factor VIII level of 1 to 5 U/dL) is associated with less frequemt and less severe hemarthroses and seldom results in serious orthopedic disability.

Replacement therapy for hemophilia A

Replacement therapy for children with hemophilia with concentrates of factor VIII or IX is recommended. As FFP is frozen, it retains all factors at their hemostatic levels including labile factors V and VII. Each unit of factor VIII/kg increases the level by 1%. To achieve a target of 30% factor VIII, required for management of most hemarthroses, a dose of 15 U/kg every 12-24 hours for 1-2 days is required. In a major, e.g. intracranial hemorrhage, the target factor level is 80-100% correction; the dose needed to achieve this is 40-50 U/kg every 8-12 hours for 7-14 days. Primary prophylaxis is a better mode of management. Patients with severe hemophilia (<1% measurable level), are given factor replacement 2-3 times a week to reduce the risk of bleeds, enable more activity and less deformities.

Orthopedic management of knee hemarthrosis

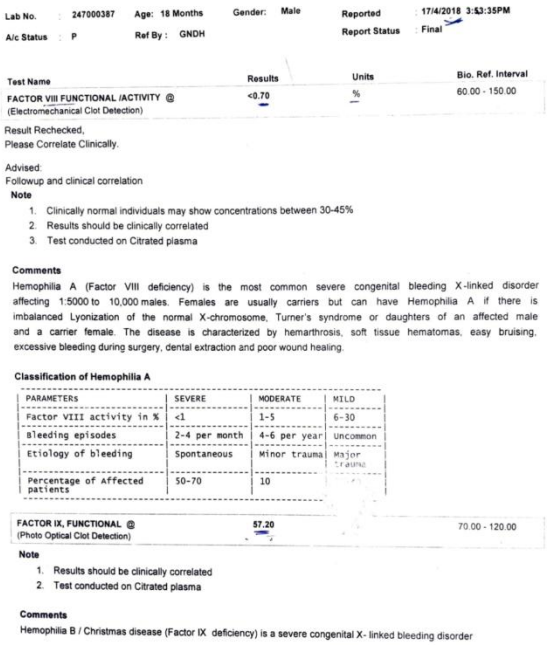
Synoviorthesis a medical synovectomy, may be achieved with the intra-articular injection of chemicals such as osmic acid, rifampicin, and rifamycin or radioactive colloids such as yttrium-90 (^{90}Y), erbium-169 (^{169}Er), dysprosium-165 (^{165}Dy), and gold-198 (^{198}Au), among others. The procedure may be used in patients with chronic effusive conditions, as well as in those with hemophilia to terminate recurrent hemarthrosis. Chemical agents are believed to be less efficacious than radioactive colloids, and among these, beta-emitting radioisotopes such as ^{90}Y, ^{169}Er, and ^{165}Dy are preferred over gamma-emitting radioisotopes such as ^{198}Au, which cause total body irradiation.

Figure 2: HA shows the sequelae of recurrent joint bleeding, severe pain and signs of inflammation.

Physical therapeutic interventions for knee hemarthrosis

The isometric technique of alternation contraction and relaxation is beneficial. When the patient quadriceps was in the fair range, the patient was encouraged to achieve full knee extension in the sitting or supine position. Active resistive exercises were started when the patient had 90 degree of ROM in the knee and had less than 15 degree flexion contracture. The active resistive exercise was initiated with 1-lb weight twice daily with 10 repetitions for 1 week, which was then advanced to a 2-lb, weight and then after another week to 3-lb. Uncertainly hemarthrosis developed the patient returned to isometrics, and again go through the process of advancing from active antigravity to active resistive exercise starting with 1-lb weight. Once the ROM and strength improve, patient used stationary bicycles, or other isokinetic exercise machines to strengthen muscles. Physiotherapy is continued during the

next six months at frequency of twice weekly and patients were also encouraged to do PT at home and to have some recreational activities whenever possible. Follow-up was continued for 15 months focusing on number of bleeding episodes in the target joint, range of motion (ROM), and strength of quadriceps muscle.



Lab No. : 247000387 Age: 18 Months Gender: Male Reported : 17/4/2018 3:53:35PM
A/c Status : P Ref By : GNDH Report Status : Final

Test Name	Results	Units	Bio. Ref. Interval
FACTOR VIII FUNCTIONAL /ACTIVITY @ (Electromechanical Clot Detection)	<0.70	%	60.00 - 150.00

Result Rechecked,
Please Correlate Clinically.

Advised:
Followup and clinical correlation

Note
1. Clinically normal individuals may show concentrations between 30-45%
2. Results should be clinically correlated
3. Test conducted on Citrated plasma

Comments
Hemophilia A (Factor VIII deficiency) is the most common severe congenital bleeding X-linked disorder affecting 1:5000 to 10,000 males. Females are usually carriers but can have Hemophilia A if there is imbalanced Lyonization of the normal X-chromosome. Turner's syndrome or daughters of an affected male and a carrier female. The disease is characterized by hemarthrosis, soft tissue hematomas, easy bruising, excessive bleeding during surgery, dental extraction and poor wound healing.

Classification of Hemophilia A

PARAMETERS	SEVERE	MODERATE	MILD
Factor VIII activity in %	<1	1-5	6-30
Bleeding episodes	2-4 per month	4-6 per year	Uncommon
Etiology of bleeding	Spontaneous	Minor trauma	Major trauma
Percentage of Affected patients	50-70	10	

FACTOR IX, FUNCTIONAL @ (Photo Optical Clot Detection)	57.20	70.00 - 120.00

Note
1. Results should be clinically correlated
2. Test conducted on Citrated plasma

Comments
Hemophilia B / Christmas disease (Factor IX deficiency) is a severe congenital X- linked bleeding disorder

Figure 3: Laboratory investigations depicted significant decreased units of factor VIII.

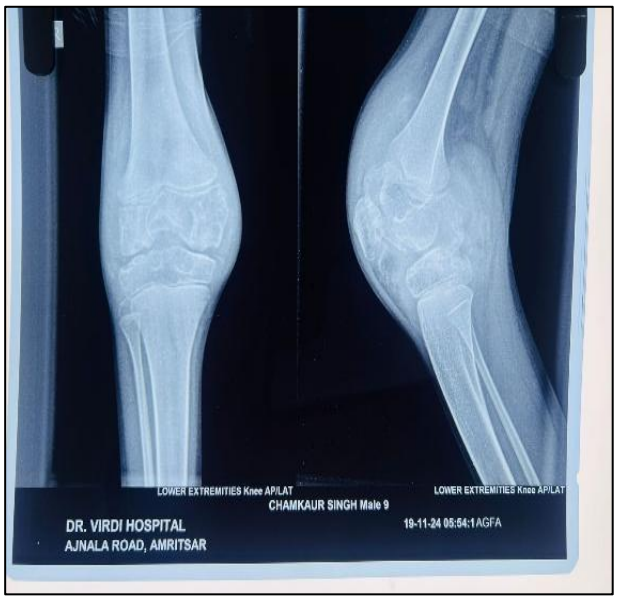


Figure 4: Radiographic images of 9 year old boy with hemophilia A shows decreased interarticular space, significant soft tissue changes.

DISCUSSION

The literature reviewed show that professionals have a high range of therapeutic tools at their disposal for the treatment of the main musculoskeletal disorders reported in patient with hemophilia. Patient with hemarthrosis should receive adequate replacement therapy, because only in this manner can the permanent disability resulting from repeated bleeding into the joints be minimized. Pain usually is relieved promptly and is a reliable index of the therapeutic response. Early but careful physiotherapy aimed at restoring the full ROM of the affected joint should be instituted as soon as the acute stage of hemarthrosis has resolved. More energetic physiotherapeutic technique should be carried out only in conjunction with an adequate course of replacement therapy. Various orthotic devices such as braces have proved useful in reducing the frequency of recurrent hemarthrosis, particularly in knee and ankle joints.[8]

Chronic degenerative joint disease in hemophiliacs is difficult to treat effectively. Non-steroidal anti-inflammatory agents may be helpful. In particular, salsalate or choline magnesium trisalicylate may be useful in patient with bleeding disorders because these drugs have anti-inflammatory activity, but do not impair platelet function. Daily or alternate-day prophylactic therapy with factor concentrates may prevent or significantly delay progression of HA. Synoviorthesis is considered when synovitis and recurrent bleeding are not controlled with factor replacement, anti-inflammatory medications. It is especially recommended in patient with inhibitors to the clotting factor.[9,10] Recently, Rodriguez-Merchan et al published their results of radionuclide synoviorthesis using either yttrium-90 or rhenium-186 in a large cohort of 500 subjects over a 38-year period. There was a reduction in pain severity and in the number of episodes of hemarthrosis. In this emerging case report marked significant improvement was noted in patient when both physiotherapeutic measures and synoviorthesis amalgamated together.

CONCLUSION

Hemophilic patient suffers from a series of musculoskeletal disorders, which are associated with important functional disability. The outcome of this case report suggests an alternative treatment program to improve ROM as well as decrease the bleeding frequency in the hemophilic knee. In this way, not only is bleeding into the joints is prevented but also the development of synovitis and articular degeneration (HA).

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