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CASE STUDY

Fiona's FVII footprint

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Factor VII deficiency is a rare inheritable bleeding disorder that can be challenging to manage. Blood activity levels do not correlate with bleeding risk, and prophylaxis is a more difficult treatment option than for people with haemophilia due to the short half-life of factor VII. Acute bleeding manifestations and long-term complications are similar to those associated with haemophilia. This case study illustrates the psychological and physical impact of severe factor VII deficiency on a woman with impaired mobility due to haemarthropathy who must retain her independence to provide care for her elderly parents. She self-manages her joint pain and bleeding risk, but her life is limited by the need to avoid injury and her reluctance to engage fully with health services.

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Figure 1: Fiona's orthopaedic shoes
These specially designed shoes play an essential part in enabling Fiona, who has severe Factor VII deficiency, to manage physical disability caused by her disorder and maintain her independence.

Factor VII (FVII) deficiency is a rare inheritable bleeding disorder affecting 1 in 500,000 individuals; men and women are affected equally. Clinical manifestations are categorised as non-severe or severe. Non-severe manifestations mimic those of a platelet disorder and usually do not require treatment. They include epistaxis (60%), gum bleeding (34%), easy bruising (36%), and other minor bleeding (haematomas, haematuria). Sixty-nine per cent of affected females have menorrhagia. Severe manifestations include extensive bruising and hemarthrosis (19% each) and gastrointestinal (GI) bleeding (15%); central nervous system (CNS) bleeding is infrequent (2.5%) but serious and potentially life-threatening [1]. As with other bleeding disorders, arthropathy is a long-term complication of haemarthrosis.

The lower limit of the reference range for FVII activity is usually considered to be 70%, but clinical manifestations do not correlate well with FVII plasma levels and are not useful in defining bleeding severity. Laboratory testing for FVII activity is the method of choice for diagnosis and is also helpful for guiding management. Genetic abnormalities on the FVII gene are heterogeneous, causing quantitative or

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qualitative defects that result in a wide range of clinical phenotypes [1]. Predicting bleeding risk and formulating a strategy for replacement therapy for surgery or acute bleeding events are therefore important challenges.

FVII coagulant activity (FVII:C) of ≤2% correlates with an increased risk of severe bleeding; however, some patients with FVII:C <1% may not have spontaneous or provoked bleeds whereas others with FVII:C >5% may have a history of severe bleeds [1]. This lack of a relationship between clinical and laboratory phenotypes is not clearly understood but may be due to the variable involvement of platelets or other factors, such as tissue factor and von Willebrand factor.

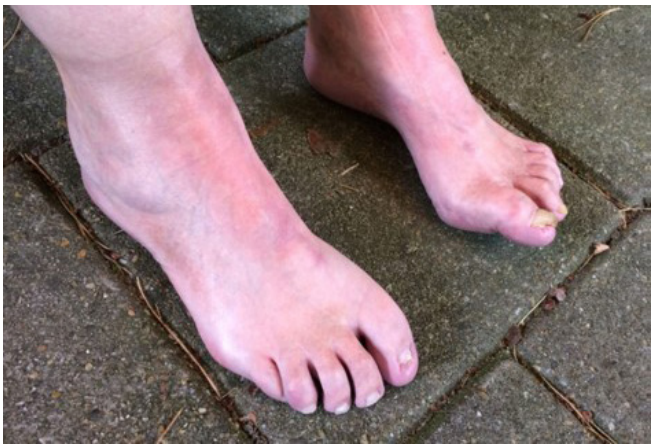

Figure 2. Fiona's ankles and forefeet are severely affected by haemarthrosis

Management in the Netherlands

Patients with FVII deficiency are treated in one of the seven Dutch multidisciplinary specialist centres, each of which is connected to a university hospital [2]. The main goal of treatment is to prevent bleeding and correct the deficiency in clotting factor [2]. Exercise is important: movement promotes neuromuscular and musculoskeletal function, strength and coordination, and helps to prevent bleeding [1]. Activities with a high risk of injury should be avoided and protective measures taken against the consequences of falls (for example, wearing a helmet when cycling). Acute haemarthrosis is treated by replacement FVII and physical measures (RICE: rest, ice, compression, elevation), followed by a week's immobilisation. Physiotherapy is initiated to restore range of motion and muscle strength when swelling is reduced [3]. The Haemophilia Joint Health Score (HJHS) is used to assess the knee, elbow and ankle at clinic visits.

Management of bleeds

The Netherlands national guideline states that the decision to offer replacement FVII therapy depends on the site and severity of bleeding and the baseline factor VII activity [2]. Mild bleeding associated with bruising and skin lacerations may not require factor treatment and can be controlled by applying local pressure at the bleeding site. Minimal mucosal bleeding episodes, such as epistaxis and during dental procedures, can be managed with antifibrinolytic agents such as tranexamic acid.

For spontaneous haemorrhage or mild trauma, therapeutic factor VII levels of 5-10% are sufficient to stop bleeding. For children and previously untreated adults with moderate–severe FVII deficiency, recombinant factor VIIa is usually the treatment of choice [2]. FVII replacement therapy is indicated for severe bleeds (e.g. recurrent haemarthrosis, GI and CNS haemorrhage) or as prophylaxis during major surgery unless FVII:C activity is >20%.

Patients with severe or recurrent bleeding are eligible for prophylaxis with FVII; however, this is less often a feasible treatment option than in the management of haemophilia because FVII and FVIIa have very short half-lives (<3 hours). Prophylaxis is generally initiated soon after the first severe bleeding episode [1].

This case study illustrates the physical and psychological challenges presented by FVII deficiency and its long-term complications for an individual who is determined to retain her independence so that she can fulfil her role as carer for her elderly parents.

CASE SUMMARY

Fiona (pseudonym) is 50 years old. She has severe factor VII deficiency (FVII <1%) which was diagnosed at an early age. She self-injects 30 IU/kg factor VII twice a week; additional doses are administered by the general practitioner as required.

Fiona was able to work as an accountant for two years after leaving secondary school, but increasing disability as a result of FVII deficiency resulted in her becoming unemployed and she now relies on a disability allowance. She has felt lonely and suffered from depression, but found that mindfulness helped her gain the strength and confidence she needed to accept and cope with her physical limitations. She recently began voluntary work in a library for two hours a week so that she had the company of other people.

Fiona lives alone, one hour's drive from her treatment centre. Her house is fully adapted to her physical limitations: it has no thresholds, a low countertop in the kitchen, and brackets to hold on to in the bathroom and toilet. She receives help to clean her house and

Figure 3. Fiona's swimming shoes

groceries are delivered to her home. She provides care for both her parents: her father has dementia and every day she drives her mother to a receive post-mastectomy treatment with hyperbaric oxygen.

Fiona's daily routine is tightly organised, alternating periods of activity and rest so that she can cope with the physical demands of her tasks. Her knees, ankles, forefeet and elbows are severely affected by haemarthrosis. Foot and ankle arthropathy have caused a rigid pointed position of the upper hock of about 30 degrees, one rigid depth of the entire forefoot and claw position of the toes (Figure 2). She is unable to walk without specially designed orthopaedic shoes (Figure 1). She treats joint pain with paracetamol.

With a proactive attitude to living and a need to be independent, Fiona knows the importance of maintaining reasonable fitness and joint mobility. She exercises by swimming twice a week in warm water. She uses swimming shoes (designed like her orthopaedic shoes) to walk to the water, helping to both maintain independence and minimise pain (Figure 3).

Fiona has a consultation with an orthopaedic surgeon every two years. On each occasion, she wants to be 'done' and leave as quickly as possible. She does not want any surgery on her ankle, despite the technical possibilities of a single arthrodesis or prosthesis [4-8]. Her commitment to caring for her parents means that she feels unable to afford the time off required for surgery and recovery, and she has a marked fear of bleeds. Fiona never visits a chiropodist because she is worried about a knife being used to provide foot care. She also buys pre-cut meat and vegetables so that she has no need to use a knife in the kitchen.

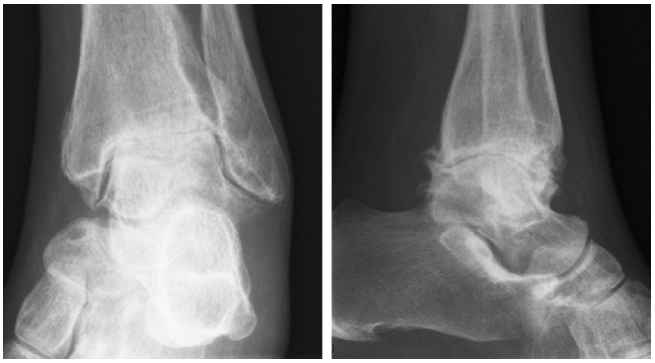

Figure 4. X-rays showing anteroposterior (left) and lateral (right) images of Fiona's 'no-load' ankle.

Orthopaedic care

Radiology of Fiona's ankle in an unloaded image shows cartilage loss from the upper sponge joint (USJ), osteophytes on the ventral and dorsal side of the USJ, and sclerosis (Figure 4). Ankle arthropathy influences movement and load of the forefoot and requires strength and endurance of the stabilising muscles around the ankle, knee and hip, which makes walking exhausting [9]. Although objective evidence of better outcomes is missing, most patients with bleeding disorders are prepared to wear wearing orthopedic shoes and/or insoles. The purpose of custom-made insoles is multiple: comfort, possible correction of a rearfoot deformity, and increasing ankle stability [10]. Based on expert opinion, correction of rearfoot abnormalities is not effective if there has already been bone-on-bone contact.

CONCLUSION

FVII deficiency presents a challenge for healthcare providers due to a lack of specific guidance on diagnosis, presentation and management. Medical management is complicated by the absence of a clear relationship between FVII:C activity and symptoms and risk of bleeds. In the case presented here, Fiona has found a way to live with FVII deficiency. With a positive outlook and using a range of adaptations, she has been able to manage her physical disability, maintain her independence and provide care for her parents.

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Informed consent has been obtained from the individual reported in this case study.

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